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13. ABSTRACT *(Maximum 200 words)*
This study was designed to determine if the intravenous use of meperidine intraoperatively decreased the incidence of post-operative shivering in patients who were anesthetized using the Ohmeda UPAC drawover vaporizer. It determined if the incidence of postoperative shivering was greater in patients who were anesthetized using the UPAC than those who were anesthetized using conventional anesthesia machines. This was a quais-experimental, prospective, double-blinded, 2x2 randomized study design. Subjects in the treatment group received 25 mg meperidine intravenously approximately 20 minutes prior to the end of surgery. Control group subjects received a placebo. All subjects received general anesthesia using the Ohmeda UPAC drawover vaporizer. Shivering was assessed postoperatively by the nursing staff in the PACU using four criteria adopted by the investigators to evaluate postoperative shivering. If 2 of the 4 criteria were present, the definition of shivering was met. Chi square was used to determine the association of meperidine administration to shivering. Chi square was also used to compare the proportion of shivering in the control group to the proportion of shivering in the control group using a conventional anesthesia machine (Horn et al., 1998). Data analysis revealed that 47.6% of the subjects in the control group shivered while 31% of the subjects in the treatment group shivered ($p=.22$). When the incidence of shivering in the control group (47.6%) was compared to the incidence of shivering in the control group by Horn (40%), no statistical significance was found ($p=.623$). When the overall incidence of shivering was examined in two age groups (<30 years of age vs. >30 years of age), statistically less shivering was found in subjects greater than 30 years old ($p=.033$). The investigators concluded that 25 mg meperidine intravenous did not significantly reduce the incidence of shivering with use of the UPAC drawover anesthesia system. The incidence of shivering in our control group was not statistically different from the Horn study. Subjects older than 30 years old shivered significantly less than subjects younger than 30 years old, though this could not be attributed to whether the subject received meperidine or not.

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THE EFFECT OF INTRAOPERATIVE ADMINISTRATION OF MEPERIDINE ON POSTOPERATIVE SHIVERING USING THE OHMEDA UNIVERSAL PORTABLE ANESTHESIA COMPLETE (UPAC) DRAWOVER VAPORIZER

By

CPT Ryan J. Wilcox, B.S.N.

CPT Thomas G. Baughan, B.S.N.

A Cluster Research Study

submitted in partial fulfillment

of the requirements for the degree of

Master of Science in Nursing

The University of Texas Health Science Center at Houston

School of Nursing

November, 2000

THE UNIVERSITY OF TEXAS
HEALTH SCIENCE CENTER AT HOUSTON
SCHOOL OF NURSING

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ABSTRACT

This study was designed to determine if the intravenous administration of meperidine intraoperatively decreased the incidence of post-operative shivering in patients who were anesthetized using the Ohmeda UPAC drawover vaporizer. Also it determined if the incidence of postoperative shivering was greater in patients who were anesthetized using the UPAC than those who were anesthetized using conventional anesthesia machines.

This was a quasi-experimental, prospective, double-blinded, 2x2 randomized study design. Subjects in the treatment group received 25 mg meperidine intravenously approximately 20 minutes prior to the end of surgery. Control group subjects received a placebo. All subjects received general anesthesia using the Ohmeda UPAC drawover vaporizer. Shivering was assessed postoperatively by the nursing staff in the PACU using four criteria adopted by the investigators to evaluate postoperative shivering. If two of the four criteria were present, the operational definition of shivering was met.

Chi square was used to determine the association of meperidine administration to shivering. Chi square was also used to compare the proportion of shivering in the control group to the proportion of shivering in the control group using a conventional anesthesia machine (Horn et al., 1998).

Data analysis revealed that 47.6% of the subjects in the control group shivered while 31% of the subjects in the treatment group shivered ($p = .22$). When the incidence of shivering in the control group (47.6%) was compared to the incidence of shivering in the control group by Horn (40%), no statistical significance was found ($p = .623$). However, when the overall incidence of shivering was examined in two age groups (≤ 30

years of age vs. >30 years of age), statistically less shivering was found in subjects greater than thirty years old ($p = .033$).

The investigators concluded that 25 mg meperidine intravenous did not significantly reduce the incidence of shivering with use of the UPAC drawover anesthesia system. Also, the incidence of shivering in our control group was not statistically different from the Horn study. However, subjects greater than thirty years old shivered significantly less than subjects younger than thirty years old, though this could not be attributed to whether the subject received meperidine or not.

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THE EFFECT OF INTRAOPERATIVE ADMINISTRATION OF MEPERIDINE ON POSTOPERATIVE SHIVERING USING THE OHMEDA UNIVERSAL PORTABLE ANESTHESIA COMPLETE (UPAC) DRAWOVER VAPORIZER

By

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APPROVED:

THE UNIVERSITY OF TEXAS
HOUSTON
HEALTH SCIENCE CENTER

The Committee for the
Protection of Human Subjects

NOTICE OF APPROVAL TO BEGIN RESEARCH October 15, 1999

HSC-SN-99-044 - "Does the IV Administration of 25 mg of Meperidine Intraoperatively Decrease the Incidence of Postoperative Shivering with Use of the Universal Portable Anesthesia complete Drawover Anesthesia System"
PI: Ryan J. Wilcox, CPT, MSN Student; et al

PROVISIONS: Unless otherwise noted, this approval relates to the research to be conducted under the above referenced title and/or to any associated materials considered at this meeting, e.g. study documents, informed consents, etc.

APPROVED: At a Convened Meeting

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CHAIRPERSON: Anne Dougherty, MD 11/11/2

Subject to any provisions noted above, you may now begin this research.

CHANGES - The P.I. must receive approval from the CPHS before initiating any changes, including those required by the sponsor, which would affect human subjects, e.g. changes in methods or procedures, numbers or kinds of human subjects, or revisions to the informed consent document or procedures. The addition of co-investigators must also receive approval from the CPHS. ALL PROTOCOL REVISIONS MUST BE SUBMITTED TO THE SPONSOR OF THE RESEARCH.

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CHAPTER I

Introduction

The human body is a beautifully designed control system. Homeostatic balance is maintained by a variety of intertwined physiological functions. Among these is the regulation of body temperature. Humans need to maintain an internal temperature at a nearly constant point for normal physiological and metabolic functions to occur (Bissonnette & Nebbia, 1994). If the internal temperature deviates significantly from this constant point, usually about 37° C, metabolic functions deteriorate, and the end result could be death. The deep tissue, or core temperature is usually tightly maintained to within ± 0.4 to 0.5° C of this set point (Bissonnette & Nebbia, 1994; Chinyanga, 1984).

Thermoregulation, according to Bissonnette and Nebbia (1994), is controlled by essentially two mechanisms: behavioral and physiological responses (see Figure 1). Behavioral mechanisms involve conscious, voluntary actions while physiological actions are unconscious, involuntary responses, involving fine motor control via the central nervous system (Bissonnette & Nebbia, 1994). Physiological warm responses include vasodilation and sweating while behavioral responses are actions such as turning down the thermostat or opening a window. Physiological cold responses are vasoconstriction, nonshivering thermogenesis, and shivering, whereas behavioral cold responses involve actions like putting on a coat or turning up the thermostat. As the body deviates from the internal "set-point" (≈ 37° C) these responses are activated. When the hypothalamus receives input from hot or cold receptors, indicating that body temperature has deviated beyond its interthreshold range of ± ≈ 0.5° C, it sends nerve impulses to other parts of the body, triggering warm or cold responses.

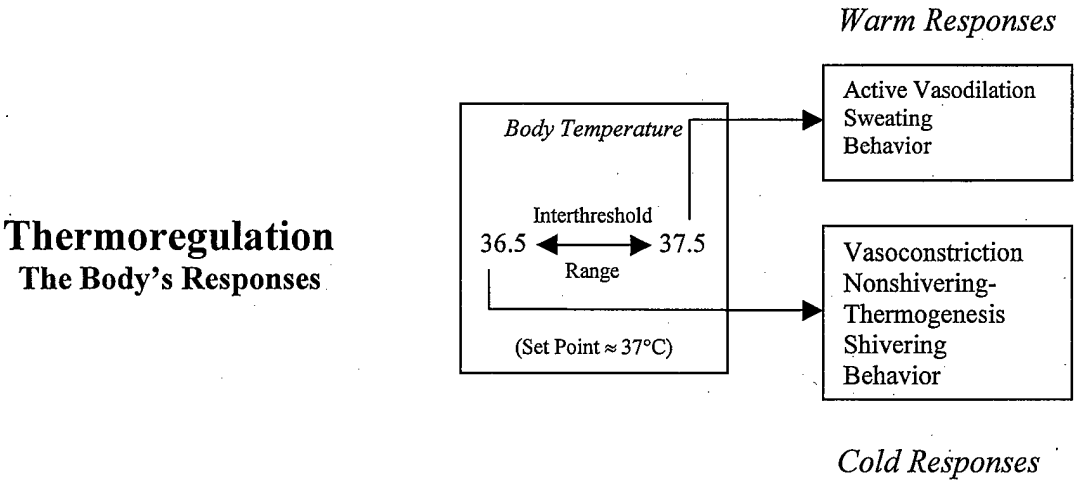


Figure 1. The thermoregulatory model. From Sessler, D. (1994). Temperature monitoring. In Miller (Ed.), Anesthesia (p. 1365). New York: Churchill Livingstone. Copyright 1994 by Churchill Livingstone. Adapted with permission.

Hypothermia, which is a common occurrence seen in the perioperative and postoperative periods, may elicit this thermoregulatory cold response. Hypothermia is defined as a reduction in the body temperature below the body's interthreshold range, the point where the cold responses would normally be initiated. There are four reasons that predispose the surgical patient to peri and postoperative hypothermia. General anesthesia induced impairment of the thermoregulatory center is the primary cause. When exposed to conditions that predispose the surgical patient to hypothermia, the body's behavioral and physiological regulatory functions are impaired, allowing its temperature to vary. During surgery, the interthreshold range can vary by as much as 6° C (Sessler, 1997b). Studies have shown that 40-60% of patients transported to the postanesthesia care unit after surgery are significantly hypothermic (Sessler, 1997a; Stotman, Jed & Burchard, 1985; Vaughan, Vaughan & Cork, 1981). Prolonged hypothermia can have substantial detrimental effects on the body as seen in severe cold injuries. As hypothermia worsens, the body decreases circulation to extremities to try and conserve heat and preserve vital organ functions. However, even hypothermia of 34.5° can pose adverse effects on the cardiovascular, central nervous, and other organ systems as well as significantly increasing oxygen consumption and metabolism (Lilly, 1990).

In addition, peripheral vasodilation, a cold operating room and a decreased metabolic rate also contribute to this hypothermia. First, anesthesia induced vasodilation allows for a redistribution of heat from the core to the periphery. Normally the core temperature is maintained by controlling warm blood distribution between the core and peripheral tissues. As core temperature increases, more blood is diverted to peripheral tissues to allow heat to dissipate. As core temperature decreases, peripheral vasoconstriction is

triggered to keep warm blood in the body's core. As general anesthesia is introduced, this regulation is impaired and unopposed peripheral vasodilation occurs. More warm blood is shunted to peripheral tissues, allowing an increase in the core cooling effect. This accounts for an initial rapid decrease in core temperature (Sessler, 1997b). Secondly, exposure to a cold operating room environment allows for heat transfer to the environment by radiation, convection, evaporation, and conduction. Even in a controlled surgical environment, the requirements of surgery may leave large portions of the body uncovered. Surgically preparing the operative site requires liquid cleansing and antiseptic solutions be applied to the skin, which further increases evaporative heat loss. Surgical exposure of internal organs compounds the evaporative heat losses. Thirdly, general anesthetic agents produce a decrease in metabolic rate and, therefore, metabolic heat production. This decrease in heat production coupled with the increased heat losses compounds the risk of becoming hypothermic. All three of these reasons predispose the surgical patient to perioperative and postoperative hypothermia, but as seen previously, anesthesia induced impairment of the thermoregulatory center is the predominant cause (Sessler, 1997a).

Shivering, the body's reaction to hypothermia, is a common post-operative occurrence seen after both general and regional anesthesia. Shivering is defined as a muscular spastic tremor, or shaking that occurs as a normal physiological response to an actual or perceived heat loss. As the body attempts to produce heat to compensate for the sensed heat loss, muscular shaking is triggered by specific heat loss receptors located in the brain, spinal cord, and skin. Impulses generated in these receptors travel to the hypothalamus, which is considered the body's thermoregulatory control center. Here the

signals are processed (the pathways and neurotransmitters are still poorly understood) then impulses are sent to skeletal muscles and shivering occurs (Horn, Sessler, Standl, Schroeder, Bartz, Beyer & Esch, 1998b). Postoperative shivering may also be a nonthermoregulatory response. This form of shivering is proposed to be a muscle spasticity in direct response to volatile anesthetic agents, or may be caused by exaggerated spinal reflexes unopposed by the brain which is still partly anesthetized (Lilly, 1990). Therefore, not all postoperative shivering may be related to thermoregulation.

Reports differ as to the prevalence of postoperative shivering. Some form of postanesthetic shaking, a spontaneous and uncontrolled muscular activity, has been reported in up to 67% of patients (Vogelsang, 1991). In a recent study by Horn, Standl, Sessler, von Knobelsdorff, Buchs & Esch (1998a), (N = 120) 40% of the patients in the control group shivered postoperatively. Sessler (1998b) states that this number may be decreasing because of recent trends in anesthesia of using higher doses of opioids perioperatively and actively warming patients during surgery. The end result is a decreased incidence of postoperative shivering (Sessler, 1998). However, not all operative environments allow for large amounts of opioids and active warming devices may not always be readily accessible or cost effective, particularly in military field environments.

Shivering is the body's most aggressive attempt to conserve heat and prevent hypothermia, however, it creates problems postoperatively because of the emotional and physical demand it places on an already stressed body. Shivering is generally described as a very uncomfortable feeling. Some patients described it as a feeling of "loss of

control" (Holdzclaw, 1990) or "freezing to death" (Lilly, 1990). Some also stated that their shivering was the most memorable and painful aspect of their surgical experience. Muscle metabolism can be dramatically increased leading to a subsequent need to increase one's minute ventilation and cardiac output. Oxygen consumption can increase by as much as 500 to 700% (Lilly, 1990). Patients with impaired cardiorespiratory systems may be unable to meet or tolerate this increase in oxygen requirement and develop metabolic and respiratory disturbances (Holtzclaw, 1990). Respiratory acidosis followed by metabolic acidosis and venous desaturation can occur which, coupled with ventilatory problems, will result in hypoxia (Lilly, 1990). In addition, postoperative shivering can cause a disruption of delicate surgical repairs from uncontrolled muscle spasticity at the surgical site, an increase in intraocular pressure, and the risk of dental damage from violent teeth chattering (Lilly, 1990).

There have been many studies which use pharmacological agents to treat postoperative shivering. Physostigmine, clonidine, and meperidine have all been shown to inhibit shivering (Alfonsi, Hongnat, Lebrault, & Chauvin, 1995; Horn et al., 1997, 1998). Meperidine is reportedly more effective in treating postoperative shivering than similar drugs because of its actions at both mu (μ) and kappa (κ) opioid receptors (Alfonsi et al., 1998; Kurz et al., 1993). Intravenous injections of meperidine at various points of time during and after surgery have been investigated with positive results in controlling shivering. In a computer-controlled infusion study by Alfonsi et al. (1998), meperidine was shown to inhibit shivering better than would be expected based on its potency. These researchers also reported that meperidine, given at an equianalgesic dose, inhibited shivering better than sufentanil. Meperidine acts by keeping the body's natural

shivering responses interrupted after the volatile anesthetic agents' effects have dissipated. Its mechanism of action is accomplished by lowering the shivering threshold, thus lowering the limit at which shivering would normally occur. This allows the anesthetized patient, stressed from surgery, sufficient time to fully emerge and rewarm without placing any additional burden on his physiological recovery systems.

As previously discussed, general anesthesia induced impairment of the thermoregulatory center is the primary cause of perioperative and postoperative shivering. These volatile anesthetic agents are delivered to the patient by using a vaporizer; a device designed to control the amount of volatile agent a patient inhales. Vaporizers can be designed for specialized use with one particular agent, or can be a more versatile, multi-agent design.

Modern operating rooms are equipped with anesthesia machines using single agent vaporizers with supplemental oxygen, air and nitrous oxide. The basic function of an anesthesia machine is to receive compressed gases from a source and deliver a known, controllable mixture of gases and anesthesia agents at a titratable flow rate to the common gas outlet, through an anesthesia circuit and ultimately to the patient. Flow control assemblies incorporated in to the vaporizers allow for precise control of fresh gas flow mixtures. Semi-closed or closed breathing circuits are used with uni-directional valves, carbon dioxide absorbents, and waste gas scavenger systems allowing for partial rebreathing of expired gases. The machines are equipped with safety devices designed to help prevent hypoxic gas mixtures from being delivered to patients. Electricity and pressurized gases are necessary for these machines to operate.

Military anesthesia performed in the field predisposes the surgical patient to an increased risk of developing hypothermia and its negative sequela. Many times surgery and anesthesia must be accomplished in austere conditions where keeping the patient warm is difficult at best. On the battlefield or in humanitarian relief missions, active warming devices and conventional anesthesia machines are not always available. Even when they are, pressurized gases and the electrical power needed to operate them may not be available. Bulky, heavy, hard-to-manage anesthesia devices are impractical in these environments. As a result, the military has adopted for field use the Ohmeda Universal Portable Anesthesia Complete (UPAC).

The UPAC is a small, lightweight, easy-to-use, portable anesthesia system. This device is a temperature compensated, variable bypass, multi-agent, drawover vaporizer. The UPAC is primarily designed for spontaneous or assisted ventilation with a self-inflating ambu bag. It uses ambient air as the carrier gas, which can be enriched with supplemental oxygen. The system does not require an external power source or an external pressurized gas source to operate it. Rebreathing of expired gas does not occur with this system, therefore a fresh gas flow equal to tidal volume is necessary to support ventilation. High fresh gas flows with the lack of rewarming and rebreathing of expired gases may cause cooling of the patient's respiratory tract. This has the potential, secondary to humidity and moisture loss, for cooling the core temperature more than the conventional anesthesia machine, which can have up to a 40-60% shivering rate (Horn et al., 1998b; Horn et al., 1997; Sessler, 1997b; Vogelsang, 1991). Although much research has been done with the UPAC, no studies have looked at the incidence of postoperative shivering with its use, or its effect on body temperature. As stated, there have been many

studies which use pharmacological agents to treat postoperative shivering, however, no studies have looked at these agents specifically using the UPAC drawover vaporizer.

Our study had a twofold purpose. First, our study determined whether postoperative shivering could be prevented in patients who are anesthetized using the Ohmeda UPAC drawover vaporizer by perioperative administration of 25mg meperidine intravenously as compared to patients who received an intravenous placebo. If successful in preventing postoperative shivering, this simple prophylactic treatment would be a useful adjunct for many military nurse anesthetists who provide anesthesia in austere environments. Second, our study will compared the incidence of postoperative shivering in the UPAC control group with the control groups of recent studies using conventional anesthesia machines.

Statement of the Problem

Did the intravenous injection of 25mg of meperidine iv 20 minutes prior to the end of surgery decrease the incidence of shivering in the postoperative period in patients who received general anesthesia via the Ohmeda UPAC drawover vaporizer? Second, was the incidence of postoperative shivering in patients who received anesthesia via the Ohmeda UPAC drawover vaporizer different than that seen after using conventional anesthesia machines?

Theoretical Framework

The conceptual framework for this study was derived from the science of physiology and pharmacology. According to Berne and Levy (1996), physiology is a branch of science primarily concerned with the regulatory mechanisms of individual organ systems and cells. Pharmacology is defined by Benet (1996) as an extensive science of drugs

based on physical and chemical properties, biochemical and physiologic effects, mechanisms of action, absorption, distribution, biotransformation, excretion, and therapeutic uses in a living organism. The physiologic model explains the mechanism of shivering while the pharmacologic model explains the mechanism by which the independent variable in this study, meperidine, is postulated to prevent shivering (Figure 2).

General anesthesia was administered using the Ohmeda UPAC system. Shivering is postulated to occur via 2 mechanisms: volatile general anesthesia agents (halogenated hydrocarbons and their isomers) interfere with the temperature regulating ability of the body, allowing the body to cool below its normal interthreshold range and through the direct effects of volatile anesthetics on the brain and spinal cord. As the core temperature cools, the anesthetic agents block the normal rewarming processes mediated by the hypothalamus from occurring. These effects quickly disappear as the agents are removed after surgery when anesthesia is complete. Once the suppressing effect of the agent is gone, shivering is triggered as the body attempts to raise its reduced core temperature. Volatile anesthetics may also directly trigger shivering, perhaps as a result of the body's sequence of emergence from anesthesia, with the spinal cord awaking prior to the brain's full recovery. This allows spinal reflexes uninhibited by the brain to be manifest, and cause a shivering-like response.

Demographic characteristics such as age and gender play a part in the body's ability to maintain thermoregulation and have also been shown to impact on the volatile agents' intensity of effect (Chinyaga, 1984; Lopez, Sessler, Walter, Emerick, and Ozaki, 1994). The surgical environment, including ambient temperature, humidity, body surface

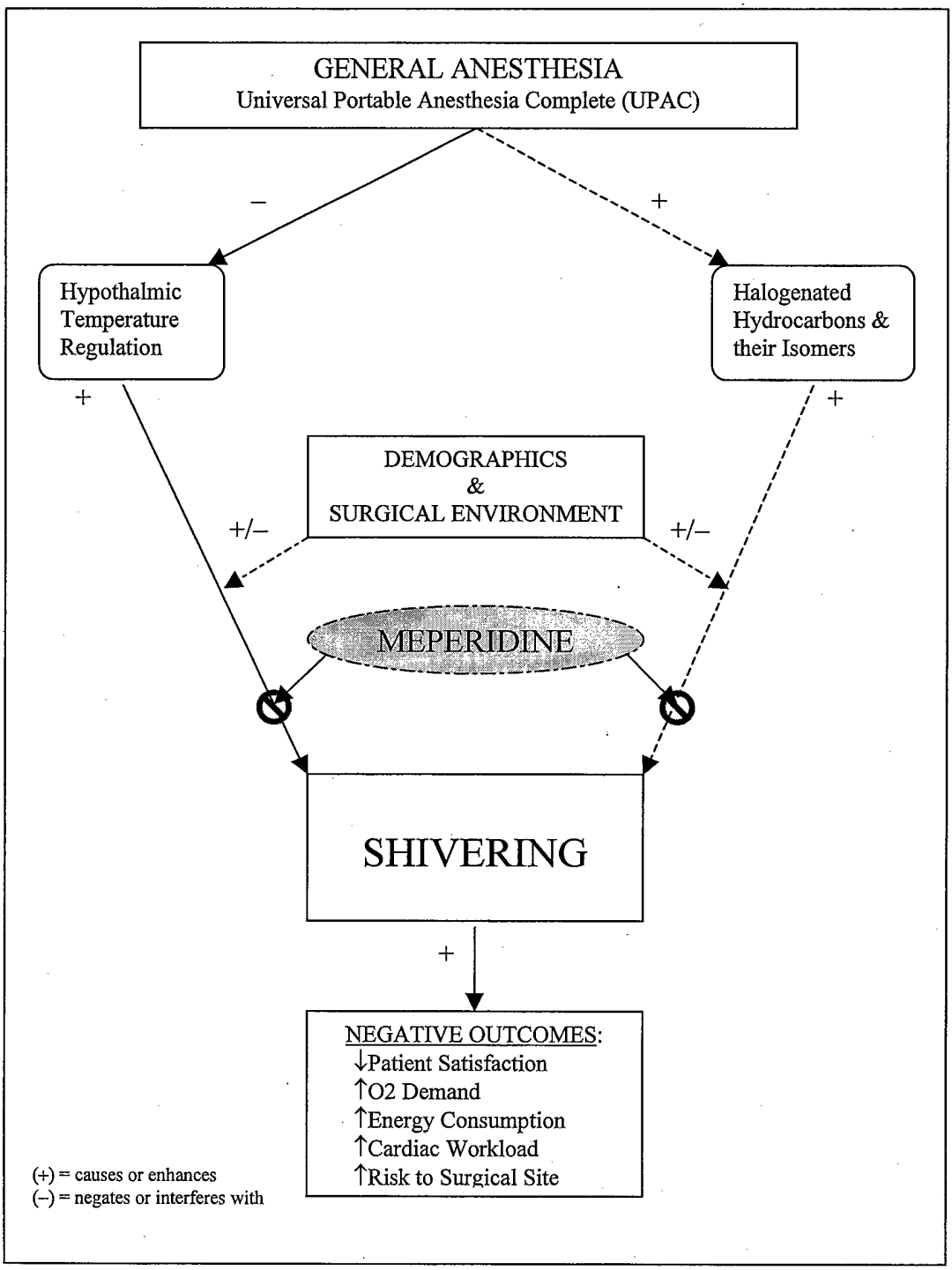


Figure 2. Theoretical framework: meperidine's effect on postanesthetic shivering

exposed, and the total anesthesia time, have also been associated with shivering postoperatively. Several research studies have shown the importance of decreasing shivering because of its effect on patient satisfaction (Holdzclaw, 1990; Lilly, 1990), oxygen demand of muscle tissues, energy consumption, the workload of the heart, and disruption of delicate surgical repairs.

Pharmacological agents have been shown to stop shivering in the postoperative patient. Meperidine, with its actions at both mu (μ) and kappa (κ) opioid receptors, is more effective than other opioids in treating postoperative shivering. Meperidine acts by lowering the shivering threshold and interrupting the body's natural physiological responses after the volatile anesthetic agents' effects have diminished. By lowering the shivering threshold, the temperature at which shivering would normally occur is lowered (Sessler, 1994). Preemptive treatment with meperidine allows the anesthetized patient who is stressed from surgery to have sufficient time to emerge fully and rewarm without placing additional burden on his recovery systems. Administering meperidine intraoperatively interrupts the body's normal shivering pathway and thus decreases the incidence of postoperative shivering.

Purpose

The purpose of this study was to determine the incidence of postoperative shivering in patients who received 25mg meperidine iv 20 minutes prior to the end of surgery compared to patients who received a placebo when both groups received general anesthesia using the Ohmeda UPAC. Additionally, this study determined the incidence of shivering in the control group compared to the control group of a recent study using a conventional anesthesia machine (Horn et al., 1997).

Definition of Terms

Shivering

Conceptual Definition. Shivering is a protracted generalized course of involuntary skeletal muscle contractions that is usually under voluntary control (Hemingway, 1963).

Operational Definition. Shivering was operationally defined in this study by four criteria: (1) Presence of electrocardiograph (ecg) artifact presence, (2) palpable mandibular vibration, (3) visible fasciculations of the head, neck, or trunk, and (4) generalized shaking of the body with or without teeth chattering. When two of the four criteria were met, shivering had occurred.

Hypothermia

Conceptual Definition. Hypothermia is a subnormal body temperature produced by exposure to cold, sometimes artificially induced in the operating room to slow metabolic processes and facilitate surgery (Cayne, 1992).

Operational Definition. Hypothermia was defined as the decrease of body core temperature to a point below the normal lower temperature threshold set point (≈37° C) where shivering would normally occur (Chinyanga, 1984).

Opioids

Conceptual Definition. Opioids are compounds including natural and synthetic drugs and biological peptides that interact with opioid receptors.

Operational Definition. The opioid for this study was defined as meperidine 25 mg (1 cc) iv.

Postoperative period

Conceptual Definition. The postoperative period is the recovery period following an operation.

Operational Definition. For this study, the postoperative period was the recovery period extending from the time of emergence from general anesthesia to discharge from Post Anesthesia Care Unit, approximately 60 minutes.

Drawover vaporizer

Conceptual Definition. A drawover vaporizer is a volatile agent anesthetic delivery device which is designed such that the carrier gas passes through a chamber drawn by the negative pressure generated during spontaneous respiration or by a self-inflating ventilation device (*e.g.*, the ambu bag or Oxford inflating bellows). The carrier gas may be ambient air or may be supplemented with oxygen from another source.

Operational Definition. The drawover vaporizer for this study was the Ohmeda UPAC (See appendix A).

Placebo

Conceptual Definition. A placebo is "Either an active or inactive substance given to satisfy a patient's demand for medicine. Also used in controlled studies of drugs. The placebo is given to a group of patients and the drug being tested is given to a similar group; then the results obtained in the two groups are compared." (Thomas, 1993, p. 1516-1517).

Operational Definition. For this study a placebo was defined as a syringe of 0.9% normal saline for intravenous injection, identical in appearance and amount (1cc) to the meperidine syringe.

Hypotheses

Patients who are given a 25 mg (1 cc) meperidine intravenous injection intraoperatively will have a lower incidence of postoperative shivering than similar patients in the control group who are given the placebo solution (0.9% normal saline, 1 cc intravenously). Secondly, patients in the UPAC control group will have a higher incidence of shivering than patients in control groups of studies that used conventional anesthesia machines (Horn et al., 1997).

Significance

Given the large incidence of postoperative shivering (Horn et al., 1997) and the detrimental impact that it has on the surgical or traumatically stressed patient (Sessler, 1997a), obtaining information on preemptive treatment to reduce its occurrence would be valuable. Along with the physiological well being of the patient, their satisfaction is also a concern to anesthesia providers. Preventing an event described by many as the most uncomfortable aspect of their surgical experience would go far in avoiding a dissatisfied post-surgical patient.

With the current state of affairs in the world, the United States military is continuously involved around the world in military, peacekeeping, or other relief missions. Since the UPAC is an anesthesia delivery system used in the field by the military, its use in situations where active warming of patients is not possible is highly likely. This fact and the lack of research into shivering associated with the use of theUPAC warrant investigation into preventative shivering measures. It would be beneficial to anesthesia care providers to find an easy, readily accessible intervention to

prevent postoperative shivering when using the Ohmeda UPAC or any other anesthesia system for general anesthesia in austere environments.

Assumptions

1. Extraneous variables were minimized by the researchers' action described in the protocol.
2. Meperidine 25 mg iv was an adequate dose to lower the shivering threshold sufficiently.
3. Exclusion criteria screened out patients with temperature regulation abnormalities.
4. Shivering was adequately defined using the study's criteria for recognition of shivering.
5. General anesthesia causes thermoregulatory impairment and can lead to postoperative shivering.
6. Error was minimized by providing training for data collectors on recognition of postoperative shivering and the use of standardized assessment criteria.

Limitations

1. The use of a convenience sample and limiting the sample to ASA I and ASA II patients limited the generalizability of this study. Demographic data were gathered and the sample was described.
2. The use of spontaneously breathing or hand ventilated patients limited the generalizability of this study to similar populations.
3. Differences between subjects could not be controlled, such as type and length of surgery and response to general anesthesia. To control for some extraneous variables

room temperature and humidity were monitored, patients were limited to ASA I or II classification, and lower age limit was set at 18 years.

Summary

It has been shown in previous studies that postoperative shivering is a common occurrence in the PACU. The use of inhalation agents appeared to increase the incidence of shivering through their effect on the thermoregulatory center and through their direct effect on the brain and spinal cord. Little research, however, had been done specifically with drawover vaporizers that use volatile inhalation agents and their effect on shivering or with the prevention of shivering when using these devices. With the military's extensive deployments to third world countries and reliance on the UPAC for surgical anesthesia, an inexpensive, readily available shivering prevention intervention would prove very valuable. Meperidine has proven itself in numerous studies to be an equianalgesic superior anti-shivering pharmacological intervention which terminates shivering when compared to other agents (Alfonsi et al., 1998). By using meperidine perioperatively, the current study investigated its effectiveness in preventing post operative shivering in patients who underwent surgery with general anesthesia administered using the Ohmeda UPAC drawover vaporizer. The overall objective was to prevent shivering rather than treating it after it had begun. This may help avoid untoward patient risk and increase comfort and satisfaction with surgical experiences.

CHAPTER II

Review of the Related Literature

The use of meperidine to decrease the incidence of postoperative shivering has been well studied (Alfonsi et al., 1998; Burks, Aisner, Fortner & Wiernik, 1980; Pauga, Savage, Simpson & Roy, 1984). Because of meperidine's "special" property to decrease shivering with relatively few side effects (Macintyre, Pavlin & Dwersteg, 1987), makes this drug useful in evaluating its effectiveness when used at different time periods in relation to the end of a surgical procedure. In particular, the use of meperidine intraoperatively to decrease postoperative shivering has gained renewed interest to stop shivering before it begins (Grundmann, Berg, Stamminger, Juckenhoel & Wilhelm, 1997; Horn et al., 1998a).

The purpose of this literature review was to explore the question "does the administration of meperidine intraoperatively decrease the incidence of postoperative shivering with use of the UPAC drawover anesthesia system?" Also, the incidence of shivering in the control group was compared to the incidence of shivering in recent research studies. This chapter will discuss thermoregulation, shivering, heat loss, general anesthesia, anesthesia adjuncts, isoflurane, opioids, and the UPAC.

Thermoregulation and Shivering

Thermoregulation maintains internal body temperature. Central core body temperature for humans is maintained within 0.4° C of the internal set point of approximately 37° C (Bissonnette & Nebbia, 1994). The hypothalamus is considered the thermoregulatory control center, and compares thermal input from the skin, tissues and deep organs. Themoregulatory information is derived from three components: 1) afferent

thermal sensing, 2) central regulation, and 3) efferent responses. Sensed deviations from the thermostatic "set point" initiate compensatory output effector responses that warm or cool the body to restore normal conditions. If core temperature deviates from this set point, metabolic functions may deteriorate (Sessler, 1997b, 1994).

Afferent thermal sensing begins with stimulation of functionally specific cold-sensitive thermoreceptors in the skin, brain, and spinal cord that induces shivering. Hypothalamic receptors sense blood temperature and receive afferent impulses from peripheral receptors (Hardy, 1980). Cutaneous impulses travel small myelinated alpha (α) fibers and non-myelinated C fibers and enter the dorsal root of the spinal cord, cross to the opposite side, traversing the lateral spinothalamic tract to the thalamus, to the rostral reticular system and terminating in the hypothalamus (Hensel, 1970). Central regulation occurs at the preoptic area of the hypothalamus where incoming signals from the periphery, reticular formation and CNS sensors are integrated. Input information is compared to the "set point". If this information is different than the set point, efferent responses are developed which induce shivering (Hardy, 1980).

Afferent signals activate the hypothalamus, which send impulses to the primary shivering center and autonomic nervous system. The autonomic nervous system plays an indirect role only. The primary shivering center in the posterior hypothalamus mediates shivering impulses via the extrapyamidal system (Hemingway, 1963). Extrapyamidal impulses stimulate shivering directly. Descending pathways traverse the midbrain, pons, and medulla oblongata through the lateral funiculus of the spinal cord (Ingram, 1960). Pathways traverse the spinal cord via the anterior motorneurons and give rise to nerve fibers leaving the spinal cord by anterior roots. Anterior root fibers innervate the muscle:

type α-fibers, which activate muscle motor units and type α-gamma (γ) fibers, which activate the muscle spindle fusimotor system (Sato, 1981). Tension of the muscle spindle during shivering sets up feedback oscillations so that each efferent impulse results in multiple rebound contractions.

The thermoregulatory response is described in the literature by threshold, gain, maximal response, and interthreshold range (Bissonnette & Nebbis, 1994; Lopez et al., 1994; Sessler, 1997a, 1997b). The gain is the slope of the response intensity compared to the difference between the temperature input and the temperature threshold. Interthreshold range is the sensitivity of the thermoregulation system in which no regulatory responses occur. This is the range of temperatures between the warmth and cold response thresholds. Temperature falling above or below this range will trigger thermoregulatory responses. Maximal response is the highest temperature output. An internal temperature threshold is set for both heat and cold responses. When input from all sources exceeds the upper threshold (hyperthermia) or falls below the lower threshold (hypothermia), the body initiate defenses or responses in an attempt to maintain the initial set point.

The determination of threshold temperature is unknown, but many variables influence individual thresholds. Painful stimulation will slightly increase the vasoconstriction threshold (Sessler, 1997a). Other research also has shown that circadian rhythm, gender, exercise, and anesthetics, influence thermoregulatory thresholds.

Lopez et al. (1994) determined that women thermoregulate at a significantly higher temperature than men do. A sample size of eight men and eight women, all non-anesthetized healthy adults, took part in the study. Hyperthermia was induced by forced

air warming followed by central venous infusion of cold lactated Ringer's solution to induce hypothermia. Both sweating and vasoconstriction thresholds were significantly greater in women than men ($p = 0.01$ and $p = 0.02$). Vasoconstriction occurred after a small amount of cooling (0.2° C), shivering occurred after a difference of about 1.4° C. Shivering response thresholds were about 0.3° C greater in women. The interthreshold range remains unchanged at 0.2° C. Although the sample size was small, the baseline established is consistent with other studies showing that women will begin to shiver at a higher temperature then men.

Heat Loss

Operating room temperature is the most critical factor influencing heat loss because it determines the rate at which metabolic heat is lost by radiation, convection and conduction from the skin and by evaporation from within surgical incisions. In austere environments where room temperature control may not be available, understanding the way heat is lost and alternative methods to suppress the body's response a decrease in temperature becomes important.

In a naked adult surrounded by air at normal room temperature, about 60% of total body heat loss results from radiation. Radiation refers to the infrared rays emanating from all objects above absolute temperature. Conduction, due to direct transfer of heat between objects that are in contact with the skin and which are at different temperatures, normally accounts for a small fraction (3%) of the heat loss and is self-limiting. A naked adult seated in a room at a comfortable temperature and without gross air movement loses about 12% of his body heat by conduction to air and then convection, which is the transfer of heat from air passing by, objects. Increasing air movement will increase heat

loss by convection within limits. Body water is lost 'insensibly' from skin and lungs at a rate of 600 ml per day by evaporation. Controlling the rate of sweating therefore controls heat loss by insensible evaporation from the skin. Humidifying the environment reduces loss by evaporation (Chinyaga, 1984). Controlling the humidity will conserve heat and reduce the negative effects of increasing room temperature by decreasing the drying of sweat and secretions.

The operating room temperature should be maintained between 24° C and 28° C (Chinyaga, 1984). Consequently, increasing room temperature is one way to minimize patient heat loss. The difficulty with this strategy is that room temperature exceeding 23° C generally are required to maintain normothermia in patients undergoing all but the smallest procedures (Sessler, 1994). Because surgeons generally do not tolerate this high of a temperature and regulation of temperature in austere environments may not be possible, alternate methods of controlling the results of a decrease in body temperature need to be found.

Intravenous infusions of cold blood or other fluids may cause hypothermia during operations. A unit of refrigerated blood or 1 liter of crystalloid solution administered at room temperature decreases mean body temperature $\approx 0.25°$ C (Sessler, 1994). Heat loss due to cold intravenous fluids thus becomes significant when large amounts of crystalloid or blood are administered.

Another important source of heat loss is the surgical site, particularly the open abdomen or chest. Heat is lost from these sites by radiation from the warm surface of the viscera and by evaporation of water from the moist serous surfaces. In animal experiments, exposure of the small and large bowel caused a fall in body temperature

during operations which were more than double that of animals which had no operations and almost double that of animals whose intestines were eviscerated but not exposed to the air. It was deduced that the heat loss was a combination of radiation and evaporation from the moist peritoneum (Chinyaga, 1984).

Simple thermodynamic calculations indicate that less than 10% of metabolic heat production is lost via the respiratory tract (Sessler, 1994). The loss results because of the body heating and humidifying inspired gases. Because little heat is lost via respiration, even active airway heating and humidification minimally influence core temperature (Hynson & Sessler, 1992). Respiratory heat loss is a function of metabolic rate and therefore usually remains constant during anesthesia. Consequently, the fraction of total heat lost via the respiratory tract decreases dramatically during large operations in which substantial heat is lost from evaporation within surgical incisions (Sessler, 1994). Airway heating and humidification thus becomes progressively less effective. McEvoy and Carey (1995), compared ventilator circuits with humidifier and heated wires to Heat Moisture Exchangers (HME) in coronary artery bypass graft patients. They reported a significant difference in the incidence of shivering between the two groups ($p \approx 0.02$); 50% of the HME group shivered whereas only 32.9% of the other group shivered. One problem of this study was in the use of a heating blanket concurrently in both groups during surgery, which is a confounding variable.

General Anesthesia & Shivering

Hypothermia during anesthesia is a common perioperative temperature disturbance. Responses to hypothermia include: internal redistribution of heat, thermal imbalance, and thermoregulation. Metabolic heat production is increased by non-shivering

thermoregulation. Environmental heat loss is decreased by cutaneous vasoconstriction and behavior maneuvers. Successful behavioral responses include increasing the ambient temperature and external warming devices (Bissonnette & Nebbia, 1994; Sessler 1997b). Studies have shown that cutaneous skin warming is effective in maintaining normothermia and preventing shivering. Shivering occurs after maximum vasoconstriction, nonshivering thermogenesis, and behavioral interventions are unsuccessful in maintaining the temperature above the threshold. Shivering increases the metabolic rate more than 2-3 times the normal rate, which may lead to adverse effects.

General anesthesia decreases vasoconstriction and shivering thresholds. Initially, there is a redistribution of body heat from the core to the periphery. This results in a rapid decrease (1-1.5° C) in the core temperature during the first hour of anesthesia (Sessler, 1997b). A decrease in heat production and an increase in heat loss, results in a thermal imbalance. During anesthesia, heat production is reduced because of decreased muscle activity, decreased metabolic rate, and decreased work of breathing. This phase lasts about 2-3 hours, which reflects a linear decrease (≈ 0.5-1.0° C) in mean body temperature (Bissonnette & Nebbia, 1994). The final phase is achieved when heat production equals heat loss, or thermal steady state. Cutaneous vasoconstriction has a minimal impact on preventing heat loss at this point.

Matsukawa et al. (1995) studied body heat content and the extent of hypothermia after induction of anesthesia. Six healthy, non-surgical male volunteers were studied to determine the difference between cutaneous heat losses and metabolic heat production. Data was collected before and after induction of general anesthesia. Redistribution was found to be the major cause of core hypothermia for the first hour and even after three

hours of anesthesia. The authors also determined that proximal extremity heat content decreased after induction of anesthesia, but distal heat content increased. Redistribution hypothermia accounted for 81% of the core temperature decrease in the first hour, but only 43% of the temperature decrease during the next two hours.

General anesthesia decreases the thermoregulatory threshold, which triggers the body's response to hypothermia by about 2.5° C. Vasoconstriction and non-shivering thermogenesis are the only responses available to patients that are hypothermic, anesthetized, and paralyzed (Bissonnette & Nebbia, 1994). The temperature threshold for these responses depends on the anesthetic agent and dose administered (Sessler, 1997a). Many studies have been done on the relationship of volatile anesthetics on the hypothermia threshold for both surgical and non-surgical volunteers.

Brain anesthetic concentrations usually decrease rapidly during the initial postoperative period, allowing re-emergence of the thermoregulatory responses, including vasoconstriction and shivering. These responses combine to decrease heat loss, constrain metabolic heat to the thermal core, and increase metabolic heat production.

Postoperative recovery of thermal equilibrium is delayed because thermoregulatory responses are impaired. Full implementation of protective thermoregulatory responses may be limited by: (1) residual volatile anesthetic, (2) opioids administered to treat surgical pain or (3) a delayed effect of intraoperative hypothermia.

Anesthesia Adjuncts

Midazolam is a commonly administered premedicaton for sedation and anesthesia. Kurz et al. (1997) tested the hypothesis that midazolam increases the sweating threshold while decreasing vasoconstriction and shivering threshold. Eight volunteers were studied

on two days, once without the drug and once at a target total plasma concentration of 0.3 ug/ml midazolam. Each day, skin and core temperatures were increased sufficiently to provoke sweating and then reduced to elicit peripheral vasoconstriction and shivering. From these calculated thresholds, thermoregulatory effects of midazolam were determined.

Midazolam decreased the core temperature that triggered vasoconstriction to 37.1 $\pm$ 0.2° C ($p = 0.0002$). Similarly, midazolam decreased the shivering threshold to 35.9 $\pm$ 0.3° C ($p = 0.03$). Although this is significant, this relatively small increase contrasts markedly with the 3-5°C interthreshold ranges produced by clinical doses of volatile anesthetics, propofol, and opioids. Midazolam is unlikely to prove an effective treatment for postoperative shivering and would not facilitate induction of deliberate hypothermia by inhibiting thermoregulatory vasoconstriction.

Propofol was similarly tested by the same research group. Five volunteers were studied on four days: 1) control; 2) a target propofol blood concentration of 2 ug/ml; 3) a target concentration of 4 ug/ml; and 4) a target concentration of 8 ug/ml. From the calculated core temperature thresholds, the propofol concentration curves for the vasoconstriction, and shivering thresholds were analyzed using linear regression. Propofol significantly decreased the core temperature triggering vasoconstriction ($r^2 = 0.98 \pm 0.02$) and shivering ($r^2 = 0.95 \pm 0.05$). Reductions in the shivering and vasoconstriction thresholds are similar; that is, the vasoconstriction to shivering range increases only slightly during anesthesia.

Benefits and Adverse Effects of Perioperative Hypothermia

Benefits of mild perioperative hypothermia include protection against cerebral ischemia and hypoxia, and the impairment of acute malignant hyperthermia (Sessler, 1994). Hypothermia may be induced for neurosurgical patients. Unfortunately, serious complications have been associated with hypothermia. These adverse effects usually relate to shivering, increased oxygen consumption, and cardiovascular changes (Lilly, 1990).

The incidence of postoperative shivering has been reported from 40-65% (Crossley, 1992; Horn et al. 1998a). Shivering increases muscle metabolism, oxygen consumption, cardiac output demand, and ventilation. It is a potentially serious complication, increasing oxygen consumption ($V0_2$) and carbon dioxide production (Vco_2) to 380% above normal basal values and minute ventilation to 400% above basal values (Macintye, Pavlin & Dwerstag, 1987). Increase in cardiac output demand may precipitate congestive heart failure, myocardial ischemia, or metabolic acidosis (Lilly, 1994; Sessler, 1997a, 1994). In addition, postoperative shivering may increase intraocular and intracranial pressures and aggravate wound pain by stretching incisions (Sessler, 1994).

Even mild hypothermia reduces resistance to surgical wound infection by directly impairing immune function, decreasing the cutaneous blood flow, and reducing the delivery of oxygen to tissue. Together, these factors can increase hospital stays by approximately 20% (Kurz, Sessler, and Lenhardt, 1996). Mild hypothermia reduces platelet function and decreases the activation of the coagulation cascade (Michelson et al., 1994). It may also decrease the metabolism of most drugs, including propofol and the

muscle relaxants vecuronium and atracurium, prolonging the post-anesthetic period (Sessler, 1997a).

Isoflurane

The minimal alveolar concentration of volatile anesthetics decrease about 5%/ 1° C reduction in core body temperature. Hypothermic tissue increases the solubility of volatile anesthetics (Sessler, 1994). During general anesthesia, the threshold for vasoconstriction is reduced significantly (Sessler, 1997a). Shivering is rare during surgery because the thermoregulatory defenses are impaired by general anesthesia. When anesthetic concentrations decrease, thermoregulatory responses re-emerge.

Vasoconstriction and shivering occur in an attempt to decrease cutaneous heat loss, reserve core metabolic heat, and increase metabolic heat production. Core temperatures return to normal values following discontinuation of anesthesia. Normothermia is delayed in part because of the heat debt acquired during surgery (Sessler, 1994). Postoperative temperatures rise slowly, sometimes requiring up to five hours to return to a normal range. This delay may be due to residual volatile anesthetic on board.

Ciofolo, Clergue, Devilliers, Ammar and Viare (1989) studied the effects of isoflurane on changes in ventilation, oxygen uptake, and carbon dioxide output during the first hour of anesthesia. After discontinuing isoflurane, postoperative tremors were observed in all ten surgical patients within 7.1 ± 1.2 minutes. An increase in oxygen uptake and a decrease in the alveolar-arterial carbon dioxide gradient were associated to this shivering type episode.

Sessler, McGuire, Moayeri, and Hynson (1991) determined that the central hypothermia following induction of isoflurane anesthesia does not result from increased

cutaneous heat loss. Five healthy, non-surgical volunteers had anesthesia induced with isoflurane, with subsequent monitoring of temperature, blood flows, and end-tidal isoflurane concentrations. They found that vasodilatation induced by isoflurane increased heat loss only 7% during the first 30 minutes of anesthesia. They concluded that heat loss to the environment did not contribute significantly to the 1.2 $\pm$ 0.2° C central hypothermia, that this was mainly the result of redistribution of heat within the body.

Following this study, Sessler, McGuire, Hynson, Moayeri, and Heier (1992) tested the extent that vasoconstriction decreased cutaneous heat loss during isoflurane anesthesia. Five healthy, non-surgical volunteers had anesthesia induced with isoflurane. The thermoregulatory threshold for vasoconstriction was 34.6 $\pm$ 0.4° C. End tidal isoflurane concentration was 0.96 $\pm$ 0.07%. Mean skin-surface temperature during vasoconstriction was 31.2 $\pm$ 1.1° C. These thresholds were similar to previous research with non-anesthetized volunteers by the same authors. Vasoconstriction decreased total cutaneous heat loss 26% during anesthesia without surgery.

Research determining isoflurane thermoregulatory thresholds are conflicting. Stoen and Sessler (1990) found that isoflurane produced a dose dependent lowering of the thermoregulatory vasoconstriction threshold. The thermoregulatory threshold is inversely proportional with end-tidal isoflurane concentrations and decreases approximately 3° C/ 1% end-tidal concentration. The time interval between induction of anesthesia and significant vasoconstriction was longer in subjects with higher end-tidal isoflurane concentrations.

Xiong et al. (1996) also found isoflurane produced a dose dependent reduction in the vasoconstriction and shivering thresholds. There was a decrease of approximately 4.6° C

at an end-tidal concentration of 1% isoflurane. Isoflurane produced a nonlinear reduction in the vasoconstriction threshold. The investigators postulated that this difference from previous research is due to the variations of methods used in the studies. From this data, Kurz et al. (1997) developed a model evaluating thermoregulatory effects. Thermoregulatory impairment from various anesthetic drugs was outlined. Volatile anesthetics produce a nonlinear reduction in the cold response thresholds.

Isoflurane produces a type of clonic muscular movement that is not common to shivering (Ikeda et al., 1998). Ikeda et al. studied ten healthy non-surgical volunteers during isoflurane anesthesia. Isoflurane was shown to significantly reduce shivering from $36.4 \pm 0.3°$ C to $34.2 \pm 0.8°$ C. A saw tooth-shivering pattern was observed during isoflurane anesthesia. Shivering was characterized by episodes of intense shivering followed by quiescent periods. Isoflurane anesthesia increased the gain of shivering significantly. They postulated that the clonic activity combines with shivering to increase the gain of shivering. Isoflurane reduced the maximum shivering intensity by about 30%; this might be due to the decrease in systemic oxygen consumption during anesthesia. During this study, only 0.7% end-tidal isoflurane concentrations were used.

Cohen (1967) noted this phenomenon in patients receiving the halogenated hydrocarbon, halothane. Observations of muscle spasticity have been seen with other halogenated hydrocarbons and their isomers.

To follow up this study, Horn et al. (1998b) tested the hypothesis (N = 120 surgical patients) that the postoperative tremor seen with isoflurane may be non-thermoregulatory. They defined tremors in patients that were normothermic and vasodilated as non-thermoregulatory. From this study they concluded that the incidence of postoperative

shivering was inversely related to core temperature. Of the unwarmed group that received isoflurane, 69% shivered. In the warm group that received isoflurane, 34% shivered ($p < 0.05$). The incidence of shivering also was similar with desflurane. Normal thermoregulatory defenses are the most likely reason for shivering. These defenses are activated because of cold exposure and anesthetic thermoregulatory impairment. This data reflects that postoperative shivering is common in normothermic patients.

To evaluate physiologic responses to mild perianesthetic hypothermia, Sessler, Rubinstein and Moayeri (1991), measured postanesthetic activity in nine volunteers. Each subject received normothermic isoflurane anesthesia, hypothermic isoflurane anesthesia and hypothermia alone on one of three days. Three patterns of postanesthetic muscular activity were identified.

The first was a tonic stiffening that occurred in some normothermic and hypothermic subjects when end tidal isoflurane concentrations were $\approx$ 0.4-0.2%. This activity appeared to be largely a direct, non-temperature dependent effect of isoflurane anesthesia. In conjunction with lower residual anesthesia concentrations, stiffening was followed by a synchronous, tonic waxing and waning pattern and spontaneous electromyographic clonus, both of which were thermoregulatory. EMG intensity from the pectoralis, trapezius, and quadriceps muscle were well correlated when tremor was most intense ($r = 0.6$). Tonic waxing and waning was by far the most common pattern and resembled that produced by cold induced shivering triggered by hypothermia. Spontaneous clonus resembled flexion induced clonus and pathologic clonus and did not occur during hypothermia alone; it may represent abnormal shivering or an anesthetic induced modification of normal shivering. The authors concluded that among the three patterns of

muscular activity, only the synchronous, tonic waxing and waning pattern could be attributed to normal thermoregulatory shivering.

Opioids

The effects of opioid analgesics on body temperature are complex and dependent upon dose, species, presence of tolerance and dependence, ambient temperature and time of administration. It now appears that there are multiple opioid receptors involved in temperature regulation (Martin, 1984).

Adler, Geller, Rosow and Cochin (1988), studied the effects on body temperature of mice treated with several narcotic analgesics and observed at different temperatures (20° C, 25° C, and 30° C). Morphine produced both hypo- and hyperthermia. The hypothermic response predominated at 20° C and hyperthermia at 30° C. Hydromorphine, levorphanol, oxymorphone, methadone, etonitazene, fentanyl and etorphine generally shared this pattern. Hypothermia was seen at 20° C following administration of meperidine and codeine; however, significant hyperthermia was not seen at 30° C.

Meperidine, an opioid receptor agonist, predominately effects the mu (μ) receptor, but has some affinity for kappa (κ) and theta (θ) receptors (Reisine & Pasternak, 1996). Meperidine is reportedly considerably more effective in treating shivering than are equianalgesic doses of relatively pure μ-receptor agonists, such as morphine and fentanyl (Pauga et al., 1984). Kurz et al. (1993) speculated meperidine's special antishivering activity may be mediated by its κ-activity. They tested the hypothesis that the antishivering activity of meperidine will be minimally impaired by low-dose naloxone (blocking most μ-receptors), but largely prevented by high-dose naloxone (blocking all μ

and most κ receptors). Twelve volunteers participated in the study in which shivering was induced by a cold infusion of lactated ringers solution. Six were given a placebo infusion or a 0.5 ug/kg/min naloxone (low dose) infusion on one of two days. The second group received a saline infusion or a 5 ug/kg/min naloxone (high dose) infusion on one of two days. Fifteen minutes later all twelve subjects received an intravenous bolus of 1 mg/kg meperidine. Pupillary diameter and light reflex amplitude were used to quantify opioid-receptor agonist activity; shivering intensity was evaluated using oxygen consumption.

Results of the study found that administration of naloxone alone did not alter oxygen consumption, pupil size, or the pupillary reflex. No pupillary constriction was detected in either group when naloxone and meperidine were combined; in contrast, meperidine alone decreased pupil size and amplitude of the light reflex ($p < 0.05$). Combined administration of meperidine and low-dose naloxone also significantly reduced oxygen consumption ($p < 0.05$), but the reduction and duration of the reduction was less than during saline. When the subjects were given a high-dose naxolone, meperidine only slightly reduced oxygen consumption.

They concluded that the antishivering property of meperidine is not fully mediated by the μ-receptor. Although meperidine has well known nonopioid actions, stimulation of the κ-receptors seems a likely alternative explanation.

Earlier it was discussed how thermoregulatory shivering could be characterized by its threshold, gain and maximum intensity (see Figure 4). Ikeda et al. (1998b) conducted a study to determine if meperidine reduces the gain and maximum intensity of shivering

more than alfentanil. Hypothermia was induced in ten volunteers. A control group received no drug; a target meperidine concentration of 1.2 ug/ml was given in the second group and a target alfentanil concentration of 0.2 ug/ml in the last group. Shivering was evaluated using oxygen consumption and electromyography. A sustained increase in oxygen consumption identified the shivering threshold. The gain of shivering was calculated versus core temperature regression, and as the slope of electromyographic intensity versus core temperature regression.

Both drugs significantly reduced the shivering threshold, but neither reduced the gain or maximum intensity of shivering. These results suggest that meperidine's special antishivering effect is primarily mediated by disproportionate reduction in the shivering threshold.

Meperidine has been tested as a shivering suppressant for shaking chills induced by pyrogenic drugs (Burks et al., 1980). Nine patients were randomly assigned to treatment and ten to placebo groups. Treatment was intravenous meperidine, 25-60 mg (mean = 45 mg), or isotonic saline. Comparisons between groups showed significantly shorter duration of shivering among those receiving meperidine ($p < 0.025$).

Pauga et al. (1984) studied one hundred consecutive subjects whom shivered following general or regional anesthesia and a surgical procedure. Subjects were randomly assigned 25 mg meperidine, 2.5 mg morphine, 25 ug fentanyl or sodium chloride 0.9%, given in equal intravenous volumes over 15 a minute period. The effects

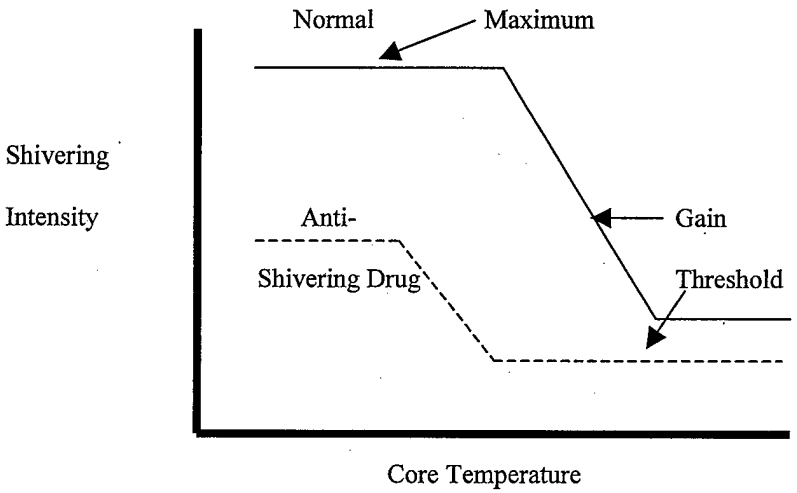


Figure 3. Three major components of shivering. From " Meperidine and Alfentenil do not reduce the Gain or Maximum Intensity of Shivering," by Ikeda, T., Sessler, D.I., Tayefeh, F., Negishi, C., Turakhia, M., Marder, D., Bjorksten, A.B., & Larson, M.D., 1998, Anesthesiology, 88(4), p. 859. Reprinted with Permission

were evaluated every 5 minutes after the first injection. Results showed there was a spontaneous, time-related disappearance of shivering in the sodium chloride treated group. In the meperidine treated group, shivering disappeared more than twice as fast as in the control group. The difference was highly significant at 15 and 20 minutes ($p < 0.001$) and was unrelated to weight, body temperature or duration of anesthesia. Women responded sooner than men, reaching significance at 10 minutes ($p < 0.05$), while men did so only at 20 minutes. Morphine and fentanyl had little or no significant effect. Nausea and vomiting were minimal and of equal incidence in narcotic and placebo treated patients.

Horn et al. (1998a) administered physostigmine, meperidine and clonidine intraoperatively, to compare the incidence of postoperative shivering. Sixty patients, American Society of Anesthesiologists (ASA) I or II, scheduled for elective ear, nose, or pharyngeal surgery, were premedicated with 0.1 mg/kg of midazolm 45 minutes before surgery. General anesthesia was induced with propofol (2 mg/kg), fentanyl (1.5 ug/kg) and paralyzed with vecuronium (0.1 mg/kg) to facilitate tracheal intubation. Isoflurane with nitrous oxide was administered for maintenance. Physostigmine 0.04 mg/kg, saline (control), meperidine 0.5 mg/kg, or clonidine 1.5 ug/kg was administered 5 minutes prior to extubation. All patients awoke within 20 minutes of extubation. Core temperatures were similar in each group ($35.8 \pm 0.8°$ C). Oxygen saturation exceeded 94% in all patients and was similar in each group. There were no clinical important differences in heart rate among the groups. Mean arterial blood pressure increased 10 minutes after administration of saline, physostigmine, and meperidine and subsequently remained

elevated for 20 minutes. Results showed that no postoperative shivering occurred in the meperidine and clonidine group while physostigmine significantly reduced shivering compared to the control group.

Macintyre et al. (1987) measured the efficacy of meperidine in reducing the metabolic responses to postanesthesia shivering and compared pulmonary gas exchange during shivering and after visible shivering had been suppressed by treatment with meperidine. Fourteen ASA I patients were studied. All patients had received a volatile anesthetic and nine were given narcotics (eight fentanyl, one morphine) during their anesthesia.

Results showed that meperidine, 25 mg intravenously, successfully suppressed visible shivering within 5 minutes of injection in eleven of the fourteen patients. The remaining three required an additional 25 mg to stop shivering. In shivering patients, minute ventilation (Vo_2) and carbon dioxide production (Vco_2) were 380% above the calculated basal value. The injection of meperidine was followed by significant ($p < 0.00001$) reductions in both Vo_2 and Vco_2. Minute ventilation increased markedly during shivering, the mean being more than 400% above basal values. Meperidine decreased the minute ventilation significantly ($p < 0.00001$), affected by reductions in both tidal volume and respiratory rate. Metabolic acidosis seen in all patients improved after visible shivering had been attenuated by meperidine as indicated by significant increases in pH ($p < 0.001$) and serum bicarbonate ($p < 0.005$). No patient suffered any side effects from meperidine; and particular, there was no respiratory depression, nausea or vomiting. In conclusion, meperidine is an effective method of reducing the elevated metabolic demand of shivering.

Universal Portable Anesthesia Complete

Until now, all studies discussed have utilized the circle breathing system, which differs significantly from the UPAC draw-over system. The UPAC draw-over is different from conventional circle systems in the following ways:

1. During spontaneous ventilation, the bag does not inflate/deflate as the patient breathes.
2. During pre-induction oxygenation, oxygen flow is required equal to the minute volume, and assisted ventilation is recommended.
3. Anesthetic vapor or supplemental oxygen may not be delivered to the patient in absence of small negative pressure breath are generated by the patient or small positive pressure ventilations generated by squeezing the bag rapidly enough to close the rebreathing value. Therefore assisted ventilation maybe required.
4. The inspired oxygen concentration will be affected by the patient's tidal volume, the patient's inspiratory flow rate, the flow of supplemental oxygen and the size of the reservoir.
5. The amount of dead space in this breathing circuit is essentially the same as in a conventional circle system.
6. Inspiratory and expiratory resistance is slightly greater with the UPAC than with a circle system. Patients may require assisted ventilation to ensure adequate breathing volumes.

Surprisingly, no studies have been done documenting the incidence of shivering with the UPAC system. It was very interesting that no post-operative shivering was noted in any of the clinical trials read by the researchers of this study. Whether there was shivering and it was not observed or it was not documented, or if there really was no postoperative shivering, remains unknown. Given these differences and the lack of studies, research into this question seems prudent.

The UPAC is a temperature and flow compensated draw-over system designed specifically for use in the mobile battlefield environment. The UPAC weighs about 5 pounds and measures 7-1/2 in. x 5-1/8 in. x 3-3/4 in, and the vaporizer holds 85 ml of liquid anesthetic. It can be used with halothane, enflurane, isoflurane or diethylether anesthetic agents. The apparatus comprises a vaporizer of sturdy construction incorporating temperature-compensation by means of a bimetallic strip-operated outlet valve, a non-specific filling port, 22mm taper input and output ports, and a non-return valve in the downstream outlet. The apparatus is supplied in a sturdy transport case and comes with antistatic hoses, a self-inflating bag, and a non-rebreathing patient valve with a scavenging shroud. A one-way valve at the facemask, combined with the nonreturn valve at the vaporizer outlet, ensures the one-way movement of air from the air inlet to the facemask. Air is drawn through the UPAC by the recoil negative pressure created by filling of the deflated self-inflating bag or by the negative inspiratory effort of the patient. Airflow within the vaporizer is governed by a rotary valve, which is controlled by adjusting the concentration setting dial.

Two calibrated concentration dial disks are available; isoflurane/halothane and diethyl ether/enflurane. The reversible disk, graduated from 0.5% to 5%, is provided as a

convenient concentration dial for isoflurane/halothane. The main dial, which is attached to the vaporizer, is graduated alphabetically from A to F. As air enters the vaporizer, the vertical rotary valve divides the stream; some enters the vaporizer chamber and some bypasses the vaporizer. As the bypass gap is reduced, greater proportions of air enters the vaporizing chamber. A wick in the vaporizing chamber increases the surface area for evaporation. Heat is required for evaporation of the liquid anesthetic. A temperature compensation valve controls the orifice where the mixture of air and anesthetic exits the vaporizing chamber to mix with the air bypassing the vaporizing chamber (Clayton, 1995).

Output from the vaporizer is dependent on flow rate (tidal volume and respiratory rate), inspiratory /expiratory rate, and temperature. High flow rates do not allow enough time for temperature compensation, so the liquid cools rapidly and output falls. Temperature compensation is accomplished by a bimetallic strip that controls the vaporizing chamber outlet opening, allowing the same concentration in the circuit at reduced temperatures. If the flow rate is kept constant and the temperature of the liquid anesthetic is raised or lowered during ambient temperature changes, the output of the agent will become temperature dependent (Clayton, 1995).

A nipple is provided at the vaporizer inlet for connecting supplemental oxygen. Oxygen improves the safety margin for the patient and should be added whenever available. A ventilator and scavenger apparatus also can be used with the UPAC (Clayton 1995).

Lunn and Young (1995) conducted vapor output studies with isoflurane and enflurane. The output of vapor was measured at different gas flows between 4 and 12

L/min. A Cape TC50 ventilator simulated spontaneous breathing and a Siemans test-lung was connected to the non-rebreathing valve stimulating the patient. The rate was set at 16 breath/min for all studies. Output studies at room temperature showed, with tidal volumes greater than 250 ml, that there is a consistent difference between 0.1% to 0.6% excess in the measured against dialed concentration at a minute volume of 4 L/min. As the minute volume increased, this difference became less for higher dialed concentrations until the output failed to reach that dialed when a minute volume of 9 L/min was exceeded. For isoflurane, the output was most accurate when the dial was set at 3%, where as with enflurane, output was most accurate at 2.4%. The performance of the device was most consistent when the minute volume was between 6 and 9 L/min.

Lunn and Young (1995) and Borland et al. (1983) found similar results on how temperature affects vapor output. At temperatures less than 20° C, the output was less than that dialed, while at temperatures greater than 20° C, the output was greater than dialed (Lunn & Young, 1995). Changes in ambient temperature showed that the output of the halothane and diethyl ether was near to the vaporizer setting in the ambient temperature range of 22.5-30.0° C and throughout a concentration setting of 0-15% (Borland et al., 1983). Contrary to the results of these studies, Ali and Brock-Utne (1992), found that isoflurane output at 39° C ambient temperature was within 0.5% of the set dial concentrations, except at the 5% setting. No discussion of the finding was given or obvious.

These studies show that there is some variability in the output characteristics of the UPAC. Given these results and that isoflurane can induce its own type of shivering,

might lead to the perceived subjective increase in the incidence of shivering with use of the UPAC system.

Lunn and Young (1995) found that a supplemental flow of 4 L/min ensured oxygen concentration of 45-80% at the patient valve, the concentration being inversely proportional to the minute volume in an almost linear manner. With a supplemental flow of 1L/min, the inspired oxygen concentration varied between 25% and 50%. They also found that additional oxygen was required to maintain arterial saturations in spontaneously breathing patients as opposed to controlled ventilation.

Borland et al. (1983) found that thirty-two patients breathing spontaneously during halothane anesthesia were given varying degrees of oxygen enrichment (1-4 L/min) to the inspired air. Only four patients showed evidence of alveolar hypoventilation (end-tidal Pco2 > 5.3 kPa). Twenty-two patients with moderate hyperventilation had oxygen saturations below 95% despite added fresh gas flows of oxygen up to 4 L/min.

Restall, Thompson, Johnston & Fenton (1990) found no electroencephalogram changes, fairly stable blood pressures and apparently acceptable oxygen saturations at 1 L/min and also found only a small incidence of vomiting post-operatively in the study with sixty patients. Lunn & Young (1995) found adequate anesthesia was easily maintained during controlled ventilation with dialed isoflurane concentrations of 1.5-2%. There were no reports of awareness. In a study of two hundred and seven patients, no difficulties related to diethyl ether were experienced (Borland et al., 1983).

The manufacturer suggests flow rates between 4 and 6 L/min for halothane, isoflurane and enflurane deliver concentrations close to the dial setting. If the flow rate is kept constant and the temperature of the liquid anesthetic is raised or lowered during

ambient temperature changes, the output of the agent will become temperature dependent. At about 22° C, the output concentration is approximately equal to the dial settings. This is fairly consistent with the current research except for the Ali and Brock-Utne (1992) study, which is in contrast to all the other studies.

Casinelli & Reynolds (1994) developed six standards for use of the UPAC in the modern hospital to meet regulatory standards. These standards allow training of military anesthesia providers. 1. Two qualified anesthesia care providers be present in the operating room throughout the procedure. 2. Each patient will have continuous monitoring. 3. Adequate ventilation will be assessed with quantitative and qualitative methods. 4. Adequacy of the patient's vital signs will be assessed with the appropriate methods. 5. Continuous airway pressure monitoring, intraoperative records maintained, and a number of additional measures to include an active scavenging device.

The UPAC is small, durable, convenient anesthesia delivery system with use intended for the military battlefield, or similar type situation. Battlefield casualties will most likely be drawn from a population of young, healthy patients, which is what the UPAC was intended for and what the research supports for use with.

Summary

Hypothermia and the shivering response continue to be a common perioperative problem. This chapter has discussed thermoregulation, shivering, heat loss, general anesthesia, hypothermia and its effect on the body, isoflurane, opioids and the UPAC system.

Thermoregulation information is derived from three components; 1) afferent information, which carries the sensed temperature changes to the 2) regulation center, the

hypothalamus, where the information is processed and transmitted via 3) efferent impulses to induce the shivering response if the sensed temperature is below the set point. Numerous anesthesia variables that influence the thermoregulatory cold thresholds include: gender, circadian rhythm, exercise, pain, and anesthetics. Many of these factors are not controllable in the anesthesia setting, but some can be to a limited extent.

The operating room temperature is one of the most important factors influencing body temperature. Because of the difficulty in regulating the ambient temperature in austere environments, alternate ways to alleviate the body's response to decreased temperature needs to be found.

General anesthesia has been shown to inhibit the body's response to decreased temperature. Therefore, during surgery, the temperature will decrease unchecked. When the patient awakens from the general anesthetic, they will shiver in an attempt to induce the warming process. Postoperative shivering has been shown to increase oxygen consumption, carbon dioxide production and cardiac output. Increases in cardiac output may precipitate congestive heart failure, myocardial ischemia, or a metabolic acidosis. In addition, shivering can be uncomfortable to the patient and increase hospital stays.

Isoflurane has also been shown to induce a type of postoperative shivering. Ikeda et al. (1998a) concluded that isoflurane produces a type of clonic muscular movement that is not common to temperature induced shivering. Cohen (1967) suggested this might be due to halogenated hydrocarbons.

Much research has been done to determine the mechanism of heat loss during anesthesia in an attempt to avoid adverse effects. Many studies have shown the success of administering meperidine intraoperatively to prevent postoperative shivering using a

regular circle anesthesia delivery system (Grundmann et al., 1997; Horn et al., 1998a). Because of the complete lack of research on the incidence of postoperative shivering with the UPAC drawover system, our study determined the effectiveness of administering 25 mg meperidine intraoperatively when delivering isoflurane from the UPAC drawover anesthesia system. Also, we determined the incidence of shivering in our control group and in comparison to recent research studies.

CHAPTER III

Methodology

The purpose of this study was to determine the effect of 25 mg meperidine iv administered intraoperatively on postoperative shivering while using the UPAC draw-over anesthesia system. This study incorporated a second question which compared the incidence of shivering in the control group to control groups of recent research studies. The investigators used a prospective, randomized, quasi-experimental, blinded clinical trial design. The incidence of shivering in the postoperative period was recorded as yes or no, based on the criteria developed for determining shivering. This chapter discusses the population, sample and setting, instrumentation, procedures for data collection, protection of human subjects, study design and proposed data analysis.

Population, Sample, and Setting

The investigators used a convenience sampling technique to select the population for this study. Convenience sampling is defined as utilizing the most readily available individuals as study subjects (Polit & Hungler, 1995). The convenience sample included patients who were to undergo a surgical procedure requiring general anesthesia provided by the UPAC draw-over system, who had met all inclusion criteria, and consented to participate in the study. The sample included patients from a large southeast medical center with a regional referral pattern. They ranged in age from eighteen years of age and older, were legally competent to give consent, and scheduled to undergo a surgical procedure requiring a general anesthetic. Only patients classified as I or II on the American Society of Anesthesiologists (ASA) rating scale were asked to participate in the study. The ASA classification provides an overall impression of the complexity of the

patient's medical condition (Appendix B). Emergent or semi-emergent (ASA I & II) patients were also included.

Exclusion criteria for this study consisted of those patients who refused to participate in the study and patients with documented allergies to meperidine. In addition, patients were excluded if they had disease processes and/or states in which temperature regulation could be altered or were potentially abnormal. Therefore, patients with the following conditions were excluded from the study: thyroid disease, Raynaud's syndrome, Parkinson's disease, pregnancy, ASA category III, IV or V, and patients who took vasodilating, vasoconstricting and beta-adrenergic blocking drugs.

In order to select a sample number large enough to show significance during data analysis, a power analysis was performed using the computer program SamplePower version 1.2 (SPSS, Inc), in accordance with Cohen's *f,* a method of standardizing effect size (Cohen, 1992). This program was used to conduct a power analysis for the key outcome variable of the study, the incidence of postoperative shivering, which is a nominal level variable. The size of the treatment effect generated by the proposed study was estimated evaluating a study done by Horn et al. (1998a). A post hoc calculation of their achieved power was completed. In that study, the administration of 0.5 mg/kg of meperidine or a placebo (0.9% normal saline) was given intravenously, five minutes before the patient was extubated in the operation room. The incidence of postoperative shivering in the meperidine group was 0% compared to 40% in the control group. Power for the proposed statistical analysis was calculated using a parametric ANOVA model because no nonparametric model was available. The proposed effect size of a 40% difference between groups in the incidence of shivering translated to a Cohen's *f* value

0.40, a large effect size. Using a level of significance of 0.05 (alpha = 0.05), power was 80 (p = 0.80), with a sample size of 16 per group (total sample size for the study = 32).

Instrumentation

Informed consent was obtained on all subjects. When informed consent was obtained, a purple and white label was placed on the patient's chart identifying them as a study subject. Data collection was completed on the day of surgery. The instrumentation used in this study included the Data Collection Tool (Appendix C) and the Genius® tympanic thermometer.

Data Collection Tool

A 61 item Data Collection Tool was developed by the investigators to document relevant patient demographic data, pertinent preoperative, intraoperative and postoperative information (see appendix C). The postoperative information included the PACU nurse's evaluation of the presence or absence of postoperative shivering based on stated criteria. After reviewing the literature, the authors were not able to find any comparable survey or appropriate criteria to assess shivering. Therefore, criteria were developed by triangulating objective and subjective criteria, used by two previous research studies (Abbey et al., 1973; Holtclaw, 1986).

In the Abbey et al. (1973) original study, a clinical assessment scale for shivering severity based on the stages of muscle involvement was completed. Staged on an ordinal scale of 0 to 4, shivering was ranked as 0 = no evidence; 1 = palpable muscle tone in the masseters; 2 = palpable evidence of muscle tone in the pectorals; 3 = general continuous shivering without teeth chattering; and 4 = general continuous shivering with teeth chattering. Interrater reliability between data collectors was established and further

validated by EMG (electromyographic measurement). In a follow up study, Holtzclaw (1986) adapted the previously mentioned scale for use with postoperative cardiac patients by including the palpable mandibular hum, and modifying the teeth chattering criterion. She found this scale to be reliable for shivering detection in its initial stages of testing.

Based on the two studies by Abbey and Holtzclaw, the investigators adopted four criteria to evaluate postoperative shivering. If the patient displayed or exhibited two of the four criteria, then the operational definition of shivering was met. Criteria for assessment of shivering were: 1) ECG artifact; 2) palpable mandibular vibration; 3) visible fasciculation of the head, neck, trunk; and 4) generalized shaking of the entire body with or without teeth chattering.

Other related studies on shivering done by Ikeda et al. (1998b) concluded that meperidine does not reduce the gain or maximum intensity of shivering. This suggests that meperidine's special antishivering effect is primarily mediated by a disproportionate reduction in the shivering threshold. Simply stated, meperidine either stops shivering or it doesn't. In support of Ikeda, the most current research studying postoperative shivering doesn't make statistical use of the ordinal level data gathered (Horn et al., 1998a; Alfonsi et al., 1995). Horn and Alfonsi only cited the percentage of shivering found in each group. Postoperative shivering will be recorded on the Data Collection Tool as nominal level data (yes or no).

Genius Tympanic Thermometer

Temperature was measured in this study for two reasons. First, to monitor the amount of potential heat loss of study subjects who underwent general anesthesia provided with the UPAC anesthesia system. Secondly to examine whether or not there

was a difference in the core temperature of subjects assigned to the experimental and control groups.

For clinical purposes, temperature can be measured at a number of body sites. Anatomical sites are chosen for measurement because of their accessibility, comfort, accuracy and safety. The gold standard of temperature measurement comes from the use of the pulmonary artery catheter, which measures core temperature accurately. However, use of the pulmonary artery catheter requires insertion of a large bore catheter into a major vessel, such as the subclavian or internal jugular vein. Serious complications may occur while inserting the catheter. The placement of a pulmonary artery catheter is not appropriate for ASA I and II patients and, therefore, was not chosen for this study.

Rectal temperature, although convenient, is not particularly accurate as a measure of core temperature. "It is affected by heat-producing organisms in the bowel, cool blood returning from the legs and insulation of the feces" (Ehrenwerth & Eisenkraft-Anesthesia Equipment, 1993, p. 270). Rectal temperature changes too slowly to follow intraoperative changes in core temperature.

The esophagus is a safe and accurate site for assessment of core temperature during general anesthesia. It requires the placement of an esophageal stethoscope and temperature probe into the distal third of the esophagus to avoid cooling by respiratory gases in the trachea. Subjects in this study who did not require endotracheal intubation precluded the placement and use of an esophageal stethoscope.

"Although skin temperature contributes to total body heat, it reflects peripheral perfusion rather than core temperature" (Ehrenwerth & Eisenkraft-Anesthesia Equipment, 1993, p. 269). When an anesthesia care provider was unable to obtain an

esophageal temperature, continuous monitoring of the patient's skin temperature was recorded.

Tympanic temperature is easy to obtain, accurate, safe and comfortable for the patient. The temperature of the blood supplied to the tympanic membrane correlates well with core temperature because of its close proximity to the hypothalmus, which is the area of the brain responsible for controlling thermoregulation. For these reasons, a tympanic thermometer was utilized to access core temperature in all study subjects.

Studies have shown that the Genius® tympanic thermometer (model# 3000A) is both reliable and valid. Edge and Morgan (1993) compared the Genius infrared tympanic thermometer to a National Physical Laboratory (NPL) calibrated thermometer and a pulmonary artery catheter. Edge and Morgan (1993) stated "the bias of the Genius® compared to the NPL thermometer was 0.08^0C, while its precision was $\pm$ 0.06^0C. The correlation of the Genius® thermometer was excellent when compared with a pulmonary artery catheter ($r^2 = 0.997$, $p = 0.0001$) in intensive care patients" (p.605). Robinson et al. (1998) found good correlation between the Genius® thermometer and pulmonary artery catheter (-0.4 ± 0.50^0C) in 18 adult cardiac patients.

The Genius® thermometer has been found to be accurate, quick, noninvasive and convenient to use, with little patient discomfort. Equipment sterilization is not required because disposable probe covers are used and therefore, problems of cross infection are eliminated. Also, the Genius® thermometer has been used in the Post Anesthesia Care Unit (PACU) at the study site for several years and the nursing staff was familiar with its use.

Preoperative temperature was assessed when the patient was transferred from the litter to the operating room table. Secondly, an intraoperative measurement of temperature was taken after administration of the study solution. Thirdly, temperature was taken upon admission to the PACU. Intraoperatively, the investigators took the first three measurements with the Genius® tympanic thermometer. Postoperative assessment of the patient's temperature was recorded by the PACU nurse at four data collection points using the same temperature device used intraoperatively. Vital signs and temperature was monitored and documented at 15, 30, 45 and 60 minutes postoperatively.

The school faculty and PACU nurses completed a structured training session prior to the data collection period. Inservices included instructions on the requirements for completing the Data Collection Tool and definitions of the criteria used to identify postoperative shivering in the study.

In order to ensure interrater reliability, a videotape was designed demonstrating the different stages of shivering. The PACU nurses were shown a situation where an actor displayed a shivering response. The PACU nurses were then asked to determine if the criteria for shivering were met. A simple formula suggested by Polit and Hungler (1995), was used to compute reliability. The number of agreements was divided by the number of agreements plus the number disagreements by the PACU nurses. A reliability of 0.80 was considered the lowest acceptable coefficient for a well-developed tool. However, for a newly developed instrument, a reliability of 0.70 is considered acceptable (Burns and Grove, 1997). All PACU nurses obtained 100% agreement with the demonstrated

shivering criteria presented on video tape.

Procedure for Data collection

Potential study subjects were identified from the projected operating room schedule five days in advance. They were assigned to a student registered nurse anesthetist (SRNA) and/or school faculty member, a certified registered nurse anesthetist (CRNA). On the day of surgery, if the patient met inclusion criteria, they were asked to participate in the study. A thorough explanation of the study was given to the patient and informed consent was obtained (Appendix D). If the patient agreed to participate, a research packet was obtained from a locked cabinet in the anesthesia classroom. Each packet contained the Data Collection Tool, Protocol (instructions), Informed Consent, Subject Identification Number and a sealed envelope with random assignment to one of two groups. The sealed envelope was given to the pharmacy after informed consent was obtained. The contents of the envelope indicated to the pharmacist, which study solution was to be issued to the anesthesia care provider (ACP). The ACP was "blinded" to the subject's solution assignment. A master list of patient assignments was kept locked in inpatient pharmacy and in the office of the program director of the anesthesia school.

The study solution was transported back to the operating room by the assigned ACP and then placed in the top drawer of the anesthesia chart. The study solution remained locked in the anesthesia cart until it is administered. The ACP was responsible for completing all documentation such as the Data Collection Tool and all paper work relating to accountability of the narcotic administered. Once the patient was admitted to the PACU, the post anesthesia care unit (PACU) nurse completed the postoperative section of the Data Collection Tool. Once completed, all study packets were stored in a

designated box in the PACU, labeled "Study Packets and Anesthesia Buck Slips". At the end of the duty day, the completed packets were collected by the SRNA or school faculty CRNA and placed in a locked cabinet in the anesthesia classroom.

Protocol

A protocol was developed by the investigators to outline the procedure for data collection. This protocol was used to ensure a consistent approach to every subject in the study.

Only the anesthesia faculty and the investigators administered anesthesia to subjects in the study. The UPAC draw-over anesthesia system was utilized to administer isoflurane via mask, endotracheal tube (ETT), or laryngeal mask airway (LMA). Patients were kept spontaneously breathing or hand ventilated throughout the surgical procedure. The ACP determined whether the administration of a muscle relaxant was appropriate. A muscle relaxant may have been utilized to facilitate the placement of an endotracheal tube. The type of surgery or surgeon's preference for muscle relaxation may also have dictated the use of a nondepolarizing muscle relaxant. In these cases, mivacurium was used. Succinylcholine was used for a rapid sequence induction technique.

1. A machine check of the UPAC drawover anesthesia system was completed per FDA approved guidelines prior to surgery. A machine check was completed on the Ohmeda anesthesia machine as a backup system.
2. The operating room ambient temperature was maintained between 68^0 and 76^0 Fahrenheit, and relative humidity was maintained between 50% and 60% per Hospital Standing Operating Procedure #E-4.

3. One blanket and one sheet were placed on the patient in the preoperative holding area.
4. Peripheral intravenous access was established to infuse Lactated Ringer's solution and medications.
5. Lactated Ringers (IV fluids) were kept in the PACU at room temperature.
6. Anxiolysis and sedation was achieved with the intravenous administration of midazolam in 0.5-1.0 mg increments.
7. The patient was transported on a litter to the designated operating room.
8. Once the patient had been transferred to the OR table, two warm sheets were placed over him. The sheets were retrieved from a warmer located in the central core. The temperature of the warmer was maintained at 42^0C by the OR personnel.
9. Standard of care patient monitors were applied (Electrocardiogram (ECG), noninvasive blood pressure cuff, pulse oximeter, esophageal or skin temperature, oxygen analyzer and respiratory gas monitor (RGM) which monitors end tidal carbon dioxide levels ($ETCO_2$) and inhaled anesthetic concentrations). Baseline vital signs, to include temperature measurement by the Genius® tympanic thermometer (model# 3000A), were taken at this time.
10. The patient was denitrogenated and received a $FIO_2 > 0.85$ with oxygen flows of 4-6 l/min.
11. Fentanyl was given in 25-50 ug increments iv to provide analgesia.
12. Thirty mg Toradol iv push (30 seconds-5 minutes) was also used to provide analgesia.

13. Techniques of induction/intubations:

    A. If a rapid sequence induction was indicated, 2-2.5 mg/kg propofol and 1.0-1.5 mg/kg succinylcholine were used to facilitate intubation.

    B. If intravenous induction with endotracheal intubation was indicated, 2.0-2.5 mg/kg propofol and 0.15-0.25 mg/kg mivacurium in divided doses over 60 seconds, were used to facilitate intubation.

    C. If a mask or LMA case was indicated, 2.0-2.5 mg/kg propofol was used for induction and to facilitate placement of the LMA.

14. A balanced technique of isoflurane, oxygen and air was used as the maintenance anesthetic. Fresh gas flows were kept between 4-6 l/min. Fentanyl 2-6 ug/kg was titrated as needed.

15. If a muscle relaxant was used, a PNS (peripheral nerve stimulator) was utilized to monitor train of four.

16. Twenty minutes prior to the end of the case, the ACP administered the study solution (1cc). Subjects randomly received 25 mg meperidine (1cc) or normal saline (1cc) iv push. Vitals signs were taken immediately after the solution was administered and the temperature was taken with the Genius® tympanic thermometer (model# 3000A).

17. As the patient emerged from anesthesia and demonstrated appropriate extubation criteria, the subject was extubated.

18. Patients were transported to the PACU and baseline vitals signs were taken. Temperature was taken with the Genius® tympanic temperature device (model # 3000A).

19. Vital signs were recorded by the assigned PACU nurse every 15 minutes for a total of 60 minutes on the Data Collection Tool sheet.
20. The patient was evaluated for shivering criteria as listed on the Data Collection Tool. If 2 of the 4 criteria were checked "Yes" the operational definition for postoperative shivering was met.
21. If the subject shivered in the PACU, up to 50 mg meperidine iv push was given in divided doses, to alleviate shivering. If the subject weighed less than 70 kg, the dose of meperidine was decreased. Maximum total dose of meperidine did not exceed 1 mg/kg.
22. If the subject complained of pain in the PACU, 2-4 mg morphine iv push every 10-15 minutes was administered. Maximum total dose of morphine did not exceed 15-20 mg.
23. The PACU nurse documented the administration of any post-operative medications on the Data Collection Tool.
24. The PACU nurse placed completed study packets in the box labeled "Study Packets and Anesthesia Buckslips" in the PACU. All packets were picked up at the end of the duty day by the ACP and placed in a locked cabinet in the anesthesia classroom.

Protection of Human Subjects

Patient's participation in this study did not incur any additional risks above those that apply to the traditional risks associated with general anesthesia. Written informed consent was obtained from the study subject per the University of Texas-Houston Health Science Center (UT-HHSC) and the established guidelines practiced at the designated study site.

Potential subjects were identified from the proposed operating room schedule five days in advance. On the day of surgery, subjects were asked to participate in the study. Potential subjects were then made aware that their participation is voluntary. They were informed that they have the option to withdraw from the study at any time without consequence. All aspects of the study, to include benefits, risks and confidentiality were also discussed. If the subject agreed to participate in the study, a signature on the informed consent was obtained and then placed in the subject's medical records (Appendix D).

Patient confidentiality was maintained by limiting access to identifying information. Personnel with access to study information included the investigators and the school faculty CRNAs. To further insure confidentiality, the patient's name was coded by assigning an identification number. Only that number was recorded on the Data Collection Tool. A purple and white sticker was attached to the patient's chart identifying that patient as a study subject. A sticker with the impression of the patient's stamp-plate and the subject's research identification number was made and placed in a logbook to correspond to the identification number. The logbook was carried throughout the day by the student anesthetist or school faculty and secured in a locked cabinet in the anesthesia classroom at the end of the duty day. A communication book was also used to record pertinent study information and was kept in a locked cabinet in the anesthesia classroom. All completed forms and logbooks are currently maintained in a locked file cabinet in the anesthesia classroom, and will be destroyed five years following completion of the study. Subjects were informed that the results of this study would be disseminated in accordance with the University of Texas-Houston Health Science Center and the United States Army

requirements. Study subjects were informed that the results may be submitted for publication in professional journals, and that they would not be personally identified in any published report.

Study Design

This was a quasi-experimental, prospective, double-blinded, 2x2 randomized study design. In the study, subjects were not randomly selected, but were randomly assigned to the control or experimental group. Randomization was achieved by using SPSS (Base 8.0) for windows computer program. The control group consisted of subjects who received the placebo 0.9% normal saline (1cc). The experimental group received 25 mg meperidine iv (1cc).

Potential threats to internal validity included selection bias, threat of instrumentation, attrition and extraneous variables. Selection bias was controlled by randomization of subjects' assignment, as previously stated. Providing school faculty and PACU nursing staff with instruction on proper recording of information on the Data Collection Tool and performing interrater reliability testing minimized the threat of instrumentation. To account for normal attrition, an additional 20% of the calculated sample size was included in the total sample. An attempt to control extraneous variables was made by: (a) Maintaining the operating room temperature between 68^0 F-76^0 F and recording the operating room temperature before a subject entered the operating room, (b) maintaining all IV fluids at room temperature, and (c) dosages/concentrations of the anesthetics administered were in accordance with the guidelines outlined in the protocol. Establishing a standard protocol that was used for each patient and adhering to inclusion and exclusion criteria helped control for extraneous variables.

Potential threats to external validity included convenience sampling and experimental effects. Although it was necessary to use convenience sampling, subjects were randomly assigned to the experimental and control groups. Demographic data was collected to allow for a complete description of the study sample. The investigator's subconscious influence or communication of their expectations to the study subjects may have biased the results. This was controlled for, to some extent, by the double-blind nature of the study.

Proposed Data Analysis

The study subjects were randomly assigned to one of two groups, the control group or the experimental group. The hypothesis was evaluated by comparing the proportion of subjects that shivered in each group. The dependent variable, shivering (nominal level data), was evaluated as yes or no in each group. Chi square was used to determine the association of administration of meperidine to shivering. In addition, chi square was used to compare the proportion of shivering in the control group to the proportion of shivering in control groups of recent research studies. If the difference between groups was statistically significant, then it could be stated with confidence that the addition of 25 mg of meperidine IV intraoperatively decreased the incidence of postoperative shivering. If the difference between control groups was statistically significant, then it could be stated with confidence that there was a difference between the UPAC control group and a recent research study control group (Horn et al., 1998a), in the absence of postoperative shivering. Descriptive statistics were used to evaluate demographic data to include age, gender, ASA category, total anesthesia time, narcotic doses, inspiratory and expiratory isoflurane concentrations, type of surgery and patient temperature.

CHAPTER IV

Analysis of Data

In this chapter, the investigators discuss data and data analysis for this study in the following order: sample characteristics, primary findings and secondary findings. All data analysis was performed using SPSS version 10.0 for Windows.

Sample Characteristics

The convenience sample in this study was drawn from patients who received general anesthesia for surgery at a regional medical center in the southeastern United States. A total of 53 patients agreed to participate in this study. Of the 53 patients, 3 attrited from the study for the following reasons. One patient had ECG changes upon initial monitoring in the operating room suite that differed from the preoperative ECG and the surgery was subsequently cancelled. One patient had surgery completed before the study solution could be administered. One patient, because of difficulty in ventilation, was placed on a conventional anesthesia machine in order to maintain a higher inspired oxygen concentration. Three additional patients that met the criteria for inclusion in the study refused to participate. Of these, one was female and two were male. The reason for patients' refusal was that they simply did not want to be involved in a research study. All three patients stated that they did not want to be a "guinea pig."

Of the remaining 50 subjects, twenty-one subjects were randomly assigned to the control group and twenty-nine subjects were randomly assigned to the treatment group. Randomization was completed using Sample Power version 1.2 (SPSS, Inc.) for 120 potential subjects. Data collection was terminated at the deadline, resulting in the N=50 and unequal groups.

Patient sample characteristics for the 50 subjects enrolled in the study are presented in Table 1. Sample characteristics included age, gender, ASA classification, and procedure. The ages of the subjects ranged from 19 to 56 with a mean age of 33.8 years (SD 10.22). Subjects were young, with 70% of the sample between the ages of 19 and 39 and 44% between the ages of 19 and 30.There were more females (56%) in the study than males (44%). There were nine males (41%) in the control group and 13 (59%) in the treatment group. Twelve females (43%) were in the control group and 16 (57%) in the treatment group.

The anesthesia care provider determined the ASA (American Society of Anesthesiologists) physical classification for each patient. Subject representation was closely proportional between the control group (twelve ASA I and nine ASA II, n = 21) and treatment group (fifteen ASA I and fourteen ASA II, n = 29) for both physical classification categories.

The convenience sample consisted of the following surgical procedures from one of four surgical services: orthopedics, plastics, urology, or EENT (eye, ear, nose, throat). The largest category was orthopedics making up 50% (n = 25) of the sample followed by plastics at 42% (n = 21) with smaller numbers in EENT at 6% (n = 3) and urology at 2% (n = 1).There were a greater number of males (72%) having orthopedic surgery than females (28%). Conversely, there were more females (95%) having plastic surgery than males (5%).

Data Gathering

Initial data collection began prior to induction of anesthesia by the anesthesia care provider when the subject's age, gender, ASA classification, procedure, and baseline vital

Table 1

Sample Characteristics for the Control Group and Experimental Group

Characteristics	n(%)	Control(%) [n=21]	Treatment(%) [n=29]
Age			
19-30	22(44)	12(55)	10(45)
30-39	13(26)	3(23)	10(77)
40-56	15(30)	6(40)	9(60)
Gender			
Male	22(44)	9(41)	13(59)
Female	28(56)	12(43)	16(57)
ASA			
I	27(54)	12(44)	15(56)
II	23(46)	9(39)	14(61)
Procedure			
Orthopedics	25(50)	9(36)	16(64)
Plastics	21(42)	10(48)	11(52)
Urology	1(2)	1(100)	0(0)
EENT	3(6)	1(33)	2(67)

Note: % for n = percent of total subject population. Others are for percent of the n for that characteristic. Age = Age in years. ASA = American Society of Anesthesiologists physical classification. Procedure = category of surgical procedure performed on subject.

signs, as well as the ambient operating room temperature and humidity were recorded on the data collection tool (see Appendix C). The second data collection point occurred at the time of induction, when vital signs and induction medications were documented. The third data collection point occurred when the researcher was notified by the surgeon that there was approximately 20 minutes remaining until the end of surgery. At that time the study solution was administered, the time noted and vital signs recorded. The fourth data collection point occurred at the time of emergence and the subject was transported to the PACU. The remaining data collection points were in accordance with PACU recovery protocol. Baseline vital signs were recorded every 15 minutes for one hour and the subject was evaluated for the study's shivering criteria. If 2 of the 4 shivering criteria were identified, shivering was deemed present and recorded as such by the PACU nurse.

Primary Findings

This study was designed to determine if the intraoperative administration of 25 mg meperidine iv would reduce the incidence of postoperative shivering using the UPAC drawover vaporizer for general anesthesia.

Hypothesis 1: Subjects who are given a 25 mg (1cc) meperidine intravenous injection intraoperatively will have a lower incidence of postoperative shivering than similar subjects in the control group who are given the placebo solution (0.9% normal saline, 1 cc intravenously).

Power analysis was calculated for a large effect size using the computer program Sample Power version 1.2 (SPSS, Inc), in accordance with Cohen's *f*, to standardize effect size (Cohen, 1992). Power is the ability of the test to detect small but important findings such as differences of associations (Polit & Hungler, 1995). The likelihood of

detecting a difference (the power) is directly related to sample size. If the sample is too small, it is not possible to show that anything is statistically significant. If the sample size if too large, then everything may be shown to be significant (Norman & Streiner, 1994). The size of the treatment effect to be generated by this study was estimated evaluating the Horn et al. (1998a) study. A post hoc calculation of their achieved power was completed and power for this study was calculated using a parametric ANOVA model because no nonparametric model was available. Cohen (1992) identified 4 parameters of power: 1) significance level, 2) sample size, 3) effect size, and 4) power. The proposed effect size of a 40% difference between groups in the incidence of shivering translated to a Cohen's *f* value of 0.40, a large effect size. A power analysis was done for this study using a level of significance of 0.05 (alpha = 0.05), a power of 80 (p = 0.80), a sample size of 16 per group (total sample size = 32), and an effect size of 40%. Chi-square analysis was used to analyze the nominal data because chi-square analysis shows the association between two nominal variables.

Summary statistics for the Chi-square are presented in Table 2. The control group (n=21) had 10 subjects shiver and 11 subjects who did not shiver. The experimental group (n = 29) had 9 subjects shiver and 20 subjects who did not shiver. Forty-seven percent (10 of 21) of the control group shivered, while 31% (9 of 29) of the experimental group shivered. While the raw numbers showed less subjects in the treatment group shivered than those in the control group, there was no statistical difference between the control group and the experimental group when the incidence of postoperative shivering was analyzed (p= 0.233). Hypothesis one was therefore rejected.

Table 2

Chi-square Results for Shivering: Control vs Experimental Group

Shiver	Treatment: No	Treatment: Yes	Total
No	11	20	31
Yes	10	9	19
Total	21	29	50

Pearson Chi-square (1) = 1.422, $p = 0.233$

Note: $p < 0.05$ is significant

Hypothesis 2: Subjects in the UPAC control group will have a higher incidence of shivering than subjects in control groups of studies that used conventional anesthesia machines.

Comparison data was obtained from the Horn et al. (1998a) study, a recent study of shivering using a conventional anesthesia machine. The control group in this study had an occurrence of shivering comparable to rates of shivering reported in other recent literature (Grundmann et al., 1997 & Horn et al., 1997). The control group in the Horn et al study was compared with the control group of the current study. Summary statistics are represented in Table 3. The Horn et al. control group ($n = 15$) had 6 subjects who shivered and 9 subjects who did not shiver, while the current study control group had 10 subjects who shivered and 11 subjects who did not shiver. This data was then compared using a chi-square analysis. Results showed that 40% (9 of 15) of the Horn et al control group shivered while 47.6% (10 of 21) of the current study control group shivered, however, there was no statistical significance found when the incidence of postoperative shivering was compared between these two control groups ($p = 0.623$). Hypothesis two was rejected.

Secondary Findings

Additional data were collected on age of the subjects, their gender, body temperature change from baseline to post-induction, isoflurane as a percent of exhaled concentration, the time interval between meperidine administration and extubation, operating room temperature and humidity at the time of induction, and total anesthesia time from induction to extubation. Data are summarized in Table 4. Very little differences were found between the means and standard deviations of the control and treatment groups

Table 3

Chi-square Results for Shivering: Control Group vs Horn, et al. (1998a) Control Group

		Control		
		Horn, et al Study	Current Study	Total
Shiver	No	9	11	19
	Yes	6	10	17
	Total	15	21	36

Pearson Chi-square (1) = 0.241, p = 0.623

Note: $p < 0.05$ is significant

Table 4

Variables and Shivering Incidence in the Control and Treatment Groups

	Control	Treatment
Age (yr)	33.35 ± 11.38	34.41 ± 11.38
Body temperature change (F°)	0.975 ± 0.964	0.972 ± 0.960
Expired isoflurane conc. (%)	0.99 ± 0.26	1.10 ± 0.26
Gender (male/female)	9 / 12	13 / 19
Solution/extubation interval (min)	21.71 ± 8.56	30.34 ± 15.08
OR temperature (F°)	69.85 ± 1.71	70.38 ± 1.74
OR humidity (%)	44.95 ± 10.83	44.33 ± 10.47
Total anesthesia time (min)	118.95 ±46.80	116.07 ± 48.28
Mean blood pressure	70.26 ± 10.42	72.95 ± 9.96
Heart rate	68 ±16.2	73 ± 16.1
Shivering (%)	47.6	31

Data are mean ± SD
Body temperature change is between time induction and administration of study solution
Expired isoflurane concentration is an average % during surgery
OR temperature and humidity is at time of induction

in any area. Age, body temperature change, expired isoflurane concentration, minutes from study solution administration to extubation, operating room temperature and humidity, total anesthesia time, mean blood pressure and heart rate all had very similar means and standard deviations between the groups.

Subjects experiencing postoperative shivering were compared by age. Subjects were divided into groups of 30 years of age and under and 31 years of age and over. Summary statistics are presented in Table 5. Comparison of the results showed that 12 subjects in the 30 and under age group shivered and 10 did not, while 7 subjects in the over 30 age group shivered and 21 did not. Chi-square analysis on this data showed a statistically significant difference ($p = 0.033$) in the two age groups. Subjects 30 years of age or less had a significantly greater overall incidence of postoperative shivering than subjects over 30 years of age.

The data was also analyzed in regards to the incidence of shivering in the control group versus the treatment group in the 30 and under age group and the over 30 age group. Summary statistics are presented in Table 6. Results showed that 8 subjects in the control group under 30 years old shivered and 4 did not, while 2 subjects over 30 years old in the control group shivered and 7 did not. In the treatment group, 4 subjects out of 10 in the 30 and under age group shivered, while 5 subjects out of 19 in the over 30 age group shivered. These findings trend toward significance in the under 30 age group receiving treatment, however, chi-square analysis on the data shows no statistical difference ($p = 0.100$) between the control and treatment groups in the two age groups. Therefore, no statistical significance could be attributed to these findings.

Table 5

Age Comparison in Overall Occurrence of Shivering

Shiver	Age ≤30	Age ≥31	Total
No	10	21	31
Yes	12	7	19
Total	22	28	50

Pearson Chi-square (1) 4.565, $p = 0.033$

Note: $p < 0.05$ is significant

Table 6

Age Comparison in Control and Treatment Groups

		Control		Treatment		
		≤ 30	> 30	≤ 30	> 30	Total
Shiver	Yes	8	2	4	5	19
	No	4	7	6	14	31
	Total	12	9	10	19	50

Pearson Chi-square (3) 6.255, $p = 0.100$

Note: $p < 0.05$ is significant

Data were also collected on the change in body temperature of subjects from the initial preoperative tympanic temperature to their temperature at the time of administration of the study solution. This data was analyzed to see if any difference in shivering could be related to a percent change in body temperature of subjects from pre to post induction of anesthesia. An independent t-test was used to analyze the difference concerning the mean change in body temperature between the shivering and nonshivering groups. There was no statistically significant difference between the two groups ($p = 0.330$). The mean percent change in body temperature of the subjects who shivered was 1.268, and the mean percent change for the subjects who did not shiver was 0.842.

The isoflurane concentration in the expired gas volume was also analyzed. The range of isoflurane concentration was 0.6% to 1.6%. The group who shivered ($n = 19$) had a mean expired concentration of 1.053% while the non-shivering group ($n = 31$) had a mean expired concentration of 1.048%. Because the difference between the means of two groups were compared, an independent t-test was used to analyze the difference between the isoflurane expired concentration of the shivering and non-shivering groups. There was no statistical difference ($p = 0.315$) in the expired isoflurane concentrations between the two groups.

Data were collected on gender in both the control group and treatment group. In the control group, ($n = 21$), 9 subjects were male and 12 were female. Of the 9 male subjects, 6 shivered and 3 did not shiver. Four of the 12 female subjects in the control group shivered while 8 did not. The treatment group ($n = 29$), had 13 male subjects and 16 female subjects. Five of the treatment group male subjects shivered while 8 did not. Four of the female treatment group subjects shivered while 12 did not. Chi-square was used to

determine if any difference in postoperative shivering between the control group and the treatment group could be related to gender. Since the analysis was performed post hoc and experimental variables were used to separate subjects into groups, 3 of the 8 cells had fewer than the minimum n of 5. However, the results still clearly indicate no significant trends in subject outcomes. There was no statistical difference ($p = 0.221$) between males and females in the control verses the treatment groups and the incidence of postoperative shivering.

The time interval between the administration of meperidine to the time of extubation was also analyzed. Of the 29 subjects who received meperidine, 9 shivered and 20 did not shiver. The mean elapsed time between the administration of meperidine and time of extubation in subjects who shivered was 33.55 minutes (SD 18.93). The mean elapsed time between the administration of meperidine and time of extubation in subjects who did not shiver was 23.5 minutes (SD 12.82). Independent t-tests showed no statistical significance ($p = 0.283$) between the two means.

In summary, both hypotheses were not supported. The administration of 25 mg meperidine iv intraoperatively 20 minutes prior to the end of the surgery using the UPAC drawover vaporizer for general anesthesia did not provide statistically significant decreases in the incidence of postoperative shivering. Nor were there statistically significant differences between the incidence of postoperative shivering using the UPAC drawover vaporizer versus using conventional anesthesia machines. No statistically significant differences could be found when looking at factors of percent body temperature change, expired isoflurane concentration, gender, time interval between meperidine administration and extubation, operating room temperature and humidity,

length of surgery (total anesthesia time), mean blood pressure and heart rate. Statistical significance was found in overall postoperative shivering rates in subjects 30 years of age or less when compared to subjects over 30 years of age.

CHAPTER V

Discussion, Conclusions, Implications, and Recommendations

The use of meperidine to decrease postoperative shivering has been well documented (Alfonsi et al., 1995; Burks et al., 1980; Pauga et al., 1984). Recently, studies have shown the effectiveness of meperidine given intraoperatively to decrease shivering postoperatively with use of conventional anesthesia circle systems (Grundmann et al., 1997; Horn et al., 1998a). To date, no studies have looked at the effect of giving meperidine intraoperatively with use of the Ohmeda UPAC system.

The purpose of this study was to determine the incidence of postoperative shivering in subjects who received 25 mg meperidine iv 20 minutes prior to the end of surgery compared to patients who receive a placebo when both groups receive general anesthesia using the Ohmeda UPAC. Additionally, this study determined the incidence of shivering in the control group using the Ohmeda UPAC and compared it to the incidence of shivering in a control group of a recent study by Horn et al. (1998a), which used a conventional anesthesia machine. In this chapter, the investigators interpret findings as they relate to the research cited in the literature review. The hypotheses are explained in light of the theoretical framework. The investigators will explore strengths and weaknesses of the research, including limitations to the study. Finally, implications for nursing and recommendations for further research are discussed.

Discussion

Hypothesis 1: Subjects who are given a 25 mg (1cc) meperidine intravenous injection intraoperatively will have a lower incidence of postoperative shivering than

similar subjects in the control group who are given the placebo solution (0.9% normal saline, 1cc).

There was no significant difference in the incidence of postoperative shivering between the control and treatment groups. Data analysis revealed that 47.6% subjects in the control group shivered, while 31% of the subjects in the treatment group shivered ($p = 0.233$). No statistical differences were found in the demographics, total anesthesia time, body temperature change, expired isoflurane concentration, gender or ASA classification between the two groups. Therefore, no generalizations can be made regarding the effectiveness of meperidine to prevent postoperative shivering when using the Ohmeda UPAC.

The results of this study do not support the literature which suggested that there should be a difference in the incidence of postoperative shivering between the control and treatment groups, however the total dose and timing of administration may be mediating factors. In a study completed by Horn et al. (1998a), the investigators administered physostigmine, meperidine and clonidine iv intraoperatively, to compare the incidence of postoperative shivering. Sixty subjects were looked at of similar category (ASA I or II). They were scheduled for elective ear, nose, or pharyngeal surgery. However, the dosing of meperidine (5 mg/kg) and the timing of the administration (5 minutes prior to extubation) were different. The results showed that postoperative shivering occurred in neither the meperidine ($p < 0.05$ versus saline) nor clonidine groups. Grundmann et al. (1997) also studied 60 healthy subjects (ASA I or II) scheduled for elective microsurgical vertebral disc resection. Subjects were allocated to one of three groups; subjects received iv meperidine (0.3 mg/kg), clonidine or normal saline. Subjects in Grundmann's study

received an average dose of 24 mg meperidine which was similar to the 25 mg dose used in this study. Like the Horn study, meperidine was administered 5 minutes prior to extubation. Grundmann's data analysis revealed a 25% incidence of shivering in the meperidine group ($p < 0.05$) compared to a 55% incidence of shivering in the normal saline group. The incidence of postoperative shivering in this study differs from that reported by Horn and Grundmann, however, our treatment group did show a decreased number of subjects experiencing postoperative shivering when compared to the number of subjects in the control group using the Ohmeda UPAC. This study used 25 mg meperidine iv, 20 minutes prior to extubation, where as the studies discussed previously used a mg/kg dosage regimen and administered meperidine 5 minutes prior to extubation. Possible explanations for not finding significance in the incidence of postoperative shivering between the control and treatment group may be attributed to the dose of meperidine used and time of administration of meperidine.

There have been many studies that support the effectiveness of meperidine to terminate shivering once it was identified. Burks et al. (1980) examined the efficacy of administering iv meperidine to subjects who experienced shaking chills and fever, which is commonly associated with infusions of amphotericin B. Nine subjects received a mean dose of 45 mg meperidine iv as soon as the patient began to shake. Burks reported a 100% cessation of shaking in the treatment group within 30 minutes from administration of meperidine. In a study by Pauga et al. (1984), 25 mg meperidine iv was given to healthy subjects ($N = 100$) who shivered in the PACU after general or regional anesthesia. Twenty-seven subjects in the meperidine group received 6.25 mg increments every five minutes over a period of twenty minutes. Eighty-nine percent of the subjects in

the treatment group stopped shivering at the fifteen-minute interval period. Pauga et al. (1984) hypothesized that their lower success rate, 89% versus 100% in the Burks study, could be explained by their lower maximal dose, 25 mg vs. 60 mg. Alfonsi et al. (1995) gave even a larger dose of meperidine, 0.85 mg/kg (mean of 54 mg) to 52 healthy subjects who shivered in the PACU following general anesthesia. Only 8% of the subjects in the treatment group continued to shiver versus 100% of the subjects in the saline group. These results suggest that cessation of shivering may be related to the dose of meperidine given post operatively rather than the timing of administration. A review of data in our study revealed that five of the subjects in the treatment group (male) required an additional 12.5 mg meperidine iv and one subject (female) required an additional 25 mg meperidine iv to stop shivering in the PACU. It is possible that the dose of 25 mg meperidine used in this study was too small to prevent shivering in a portion of our population.

The time of meperidine administration may also have contributed to not finding a significance in the incidence of shivering between the treatment and control group. The administration interval chosen for this study was meperidine iv 20 minutes prior to extubation to ensure its maximal peak effect. The treatment groups received 25 mg meperidine iv at a mean time of 28.5 minutes prior to extubation. Omoigui (1995) states that the peak effect of meperidine is approximately 5-20 minutes and its duration of action is 2-4 hours. However, both Horn et al. (1998a) and Grundmann et al. (1997) chose to give meperidine 5 minutes before the end of surgery. The incidence of shivering in the treatment group of the Horn et al. (1998a) study was 0% and 25% in the Grundmann et al. (1997) study. It should be noted that a larger initial dose of meperidine

was given in the Horn et al. (1998a) study, which makes it difficult to determine which factor was more influential in decreasing the incidence of postoperative shivering.

Hypothesis 2: Subjects in the UPAC control group will have a higher incidence of shivering than subjects in the control groups of studies that used conventional anesthesia machines.

The investigators found no statistically significant difference in the incidence of shivering in the control group of this study using the UPAC vs. the control group of the study by Horn et al. (1998a) using a conventional anesthesia machine. Data analysis showed that 47.6% of the subjects shivered in the control group (UPAC, no meperidine) compared to 40% in the control group (conventional machine, no meperidine) of Horn et al. (1998a), ($p = 0.623$). The second hypothesis was not supported by the data.

The differences in breathing systems between the UPAC and conventional anesthesia machines in theory, support the premise that there would be a difference in shivering. Physiologically, volatile anesthetic agents interfere with hypothalamic temperature regulation, allowing the body to cool more than normal. When general anesthesia is delivered using the Ohmeda UPAC, rebreathing of warmed gases does not occur because exhaled gases are not recycled. Each breath the subject takes is extracted from a reservoir bag and then drawn through the vaporizer. A greater degree of cooling of the respiratory tract should, therefore, lead to a lower core body temperature with the UPAC due to the fact that rebreathing of previously warmed gases does not occur. Rebreathing of previously warmed gas does occur with a conventional anesthesia machine.

According to Chinyanga (1984), during general anesthesia, the total respiratory heat loss is equivalent to 12% of the total body heat production at rest. When the subject is

ventilated with cool, dry gases, as happens with the UPAC, this potentially becomes an important source of heat loss (Chinyanga, 1984). No study was found to date that has addressed the heat loss associated with the Ohmeda UPAC, therefore, a comparison of heat loss using the UPAC with conventional anesthesia machines can not be made.

Contrary to Chinyanga (1984), simple thermodynamic calculations indicate that less than 10% of metabolic heat production is lost via the respiratory tract (Sessler, 1994). Because little heat is lost via respiration, even active airway heating and humidification minimally influences core temperature (Hynson and Sessler, 1992). Stone, Downs, Paul and Perkins (1981) showed an increase in temperature with active airway heating. However, Hynson and Sessler (1992) concluded that these results may have been due to artificial warming of the nasopharyngeal or esophageal temperature probes. This study's findings may accurately reflect previous research results, given the fact that humidification and heating of airway gases plays a minimal role in temperature loss.

Conceptual Framework

The conceptual framework for this study was derived from the science of physiology and pharmacology. Shivering occurs via two mechanisms: 1) volatile anesthesia agents interfere with the temperature regulating ability of the body, allowing the body to cool beyond its normal range and shiver upon the removal of the agent, and 2) through direct effects of volatile anesthetic agents on the brain and spinal cord. The pharmacological agent, meperidine, which has been shown in other studies to prevent postoperative shivering when using conventional anesthesia machines (Grundmann et al., 1997; Horn et al., 1998a) should also prevent postoperative shivering when using the UPAC drawover vaporizer. Statistical testing of this hypothesis indicated that no significant difference

could be found in the incidence of postoperative shivering in the group receiving meperidine and the group receiving the placebo.

Variables that could have impacted on thermoregulation and shivering were identified and monitored during the study. Age and gender in the control and treatment groups were evenly distributed without significant differences between the groups. However, an unexpected finding in this study was that subjects 30 years of age or less showed a statistically significant greater incidence of postoperative shivering than those over 30 years of age. Environmental factors such as operating room temperature and humidity, hemodynamic factors such as body temperature, mean blood pressure and heart rate, and surgical factors such as expired isoflurane concentration, total anesthesia time and the time the study solution was administered prior to extubation all were kept relatively constant between the two groups. Therefore, these variables should have little effect on the results of this study. Viewed in terms of the theoretical framework, the lone variable with any effect on shivering would be meperidine. Possible explanations for not finding significance are: 1) studies support meperidine does terminate shivering once it starts, 2) dose may be related to effectiveness, and 3) timing of administration should also be considered.

Additional Findings

In addition to the primary and secondary hypotheses, the investigators evaluated the differences in age, body temperature change, expired isoflurane concentration, gender, time of meperidine administration to time of extubation, operating room temperature and humidity at time of induction and the total anesthesia time. An unexpected finding was that subjects > 30 years old shivered less than those ≤ 30 years old ($p = 0.033$). However,

no statistical significance was found when trying to relate these results to whether the subjects received meperidine or not ($p = 0.100$).

This unexpected finding is not supported by most current literature or theories of thermoregulation. Although thermoregulation in the older adult is similar to that in younger adults, in the older person there may be a reduction in metabolic rate, skeletal muscle mass, voluntary activity, and subcutaneous fat (Chinyanga, 1984). In a cold environment, the older person, whose metabolic rate and muscle mass are somewhat reduced, produces less body heat and loses relatively more heat to the environment than a younger person because the mechanisms of heat conservation are less effective (Chinyanga, 1984). This should result in a lower core temperature in the older subject than in a younger one following similar surgery, therefore the logical conclusion would be an increase in the incidence of shivering in older subjects rather than a decreased incidence.

In support of this conclusion, Vaughan, Vaughan and Cork (1981), found that elderly subjects (> 60 years old) had a significantly lower temperature ($p < 0.05$) than younger subjects following surgery. Because subjects of the current study were less than 60 years old, a comparison could not be made to this study. There was, however, one study that supported this additional finding. Volgelsang (1991) found less postoperative shivering in subjects greater than thirty-six years old ($p < 0.0001$). She concluded that her results might have been due to the younger subjects having healthier nervous systems and therefore, they displayed more sensitivity to the anesthetic agent.

Regardless of age, Vaughan, Vaughan and Cork (1981) found that hypothermic subjects shivered significantly more than did normothermic subjects ($p < 0.05$). In direct

contrast, Volgelsang (1991) found no difference in temperature between subjects who developed postoperative shivering and those who did not ($N = 533$, $p > 0.10$). Horn et al. (1998a) found no difference in temperature postoperatively between those who developed postoperative shivering and those that did not. As shown in the theoretical framework, this may be a result of the volatile agent's direct effect on shivering. In this study the subjects demonstrated little difference in change of body temperature between the control (0.975° F) and treatment (0.972° F) groups and, therefore, limited the effect that temperature changes might have on shivering.

Expired isoflurane concentrations were analyzed because of the relationship between volatile agents and shivering. There were no significant differences found between the subjects who shivered and those that did not ($p = 0.315$). The study's conceptual framework demonstrates the shivering pathways of volatile anesthetic agents by: 1) interfering with the temperature regulating ability of the body, allowing the body to cool below its normal interthreshold range, and 2) through the direct effects of the volatile anesthetic on the brain and spinal cord. As the core temperature cools, the anesthetic agent blocks the normal rewarming processes mediated by the hypothalamus from occurring. These effects quickly disappear as the agents are removed after surgery and anesthesia is discontinued. Once the suppressing effect of the agent is gone, shivering is triggered as the body attempts to raise its reduced core temperature. Volatile anesthetics may also directly trigger shivering, perhaps as a result of the body's process of emerging from anesthesia, with the spinal cord awakening prior to the brain's full recovery. This allows spinal reflexes uninhibited by the brain to be manifested and cause a shivering-like response (Cohen, 1960; Stoen and Sessler, 1990). Expired isoflurane concentrations

in the control (mean = 0.981%, SD = 0.258) and treatment (mean = 1.10%, SD = 0.243) groups were kept fairly constant in this study. By doing so, the researchers limited the effect that any difference in the concentrations might have on postoperative shivering.

Previous studies have found differences in females and males responses to meperidine. Pauga et al. (1984) found that when subjects in the meperidine treatment group changed from 15 males and 12 females to 9 males and 10 females, the percentage of subjects who did not shiver changed from 88.9% to 95%. Based on this change, they hypothesized that females responded better than males to the treatment of postoperative shivering with meperidine. Pozos, Israel and McCutcheon (1987) also found women responded to meperidine better than men. This study did not support these findings. Males and females were equally distributed between the control (male 43%, female 57%) and treatment (male 45%, female 55%) groups. No statistical differences were found in the control or treatment groups between those who shivered and those who did not shiver ($p = 0.221$) when gender was analyzed.

Total anesthesia time was also analyzed to determine if increased anesthesia time had any effect on postoperative shivering occurrence. No significant differences were found between the control and treatment groups in total anesthesia time (range 35-275 minutes).

Lastly, the difference in mean time of the administration of meperidine to the time of extubation between subjects who shivered and those who did not shiver was examined. The researchers wanted to ensure meperidine would be at its peak as the subject was extubated and transported to the PACU. Meperidine has an onset of < 5 minutes, with a peak effect in 5 – 20 minutes and a clinical duration of 2 – 4 hours. The mean time between administration of meperidine and extubation in those that shivered was longer

(33.55 minutes) than for those that did not shiver (23.5 minutes). While there was a 10-minute difference in these mean times; statistical significance was not found between the two groups. It is possible that those subjects who shivered had passed the peak effect time of meperidine and therefore tended to shiver more. However, both groups were well within the 2 – 4 hour duration of action of meperidine.

Study Strengths

There were several strengths of this research study. One of the most important strengths was the use of a protocol, which monitored the extraneous variables related to shivering. Our findings showed that extraneous variables were kept relatively constant between the subjects, which limited the effect that any difference might have had on shivering. The study utilized a quasi-experimental design with manipulation of the independent variable and the use of a control group. Without a control group, (a group that does not receive the meperidine treatment) it is impossible to separate the effects of normal physiologic temperature regulation from those of the treatment (Polit and Hungler, 1995). The study was double blinded; the investigators, as well as the subjects were blinded to which solution was given which helped to control a source of bias in this research. The pharmacy randomly selected, using sample power version 1.2 (SPSS, Inc), whether the subject received the treatment or control solution. A small group of primary investigators obtained consent and conducted the research. For consistency and reliability, a single Genius® thermometer, calibrated by biomedical engineering, was used for temperature measurement. Also, the same Ohmeda UPAC was used for every subject. Similar surgical procedures were performed on relatively healthy subjects as seen in previous research. A large sample size of 50 subjects was obtained from a

homogeneous population. A very low attrition rate of 6% demonstrated tight control of the protocol and a good design. Environmental factors such as temperature and humidity were kept constant for all the subjects. The investigators developed and used a video to teach PACU nurses proper identification of shivering criteria and obtained 100% interrater reliability between the PACU nurses.

Study Limitations

The findings should be viewed with caution due to the selection bias for the sample. These were: 1) convenience sample, 2) using a predetermined dose of meperidine, and 3) exclusion of ASA III & IV, large abdominal surgery and mechanically ventilated subjects.

The investigators utilized a convenience sample with random assignment to the treatment or control group. The sample was chosen from a large southeastern medical center. Of the potential subjects that presented for surgery, only those that consented for the study were enrolled. The use of convenience sampling limits the generalizability of the results to all populations. The researchers utilized a set total dose of meperidine (25mg) instead of using a mg/kg dosing regimen. This might have resulted in some subjects not receiving an adequate dose of meperidine to alleviate postoperative shivering.

This study included only subjects of ASA category I and II, which limits the generalizability of the results to similar populations. This was done to limit extraneous variables that could interfere with obtaining a clear understanding of the relationship of meperidine to shivering. Subjects with disease processes and/or states in which temperature regulation was altered or potentially abnormal were excluded from the study.

Because the UPAC is not designed to be used with a ventilator, subjects were kept spontaneously breathing or hand ventilated, therefore, mechanically ventilated subjects were excluded. Subjects that were scheduled for large abdominal surgeries were also excluded from this study. Large abdominal surgeries are generally associated with decreases in core body temperature and require external heating devices to be used intraoperatively. The use of external heating devices would interfere with the design of the study because body temperature would be artificially maintained or supported.

Conclusions

Based on the results of this study 25 mg meperidine iv does not significantly reduce postoperative shivering with the use of the UPAC anesthesia system. However, the investigators did see a clinical decrease in the number of subjects that shivered (31% treatment vs 47.6% control). Previous research does support the effectiveness of meperidine administered intraoperatively to decrease the incidence of postoperative shivering.

There was not a significant difference in the incidence of postoperative shivering with use of the UPAC anesthesia system compared to a conventional anesthesia system. There was, however, an unexpected finding in the > 30 years age group. This group shivered less than expected when compared to the ≤ 30 year age group. Further research is warranted to determine if there is an age related difference in the incidence of postoperative shivering.

Implications for Nursing Anesthesia Practice

Although the findings of this study do not support the use of 25 mg meperidine intravenous given intraoperatively to decrease the incidence of postoperative shivering,

meperidine has been shown to be a safe, effective and simple method to alleviate postoperative shivering in past research (Macintyre et al., 1987). Previous research has also shown meperidine to be an effective way to prevent shivering before it begins (Grundmann et al., 1997; Horn et al., 1998a). In austere conditions where the UPAC is regularly used, limited space is available for external warming devices. Meperidine is not only convenient and inexpensive, it alleviates shivering and decreases pain, which in turn decreases metabolic demands and preserves homeostasis.

Recommendations

This study used meperidine iv intraoperatively to decrease postoperative shivering with use of the UPAC anesthesia system. No previous study was found in the literature which used meperidine prophylactically while using the UPAC anesthesia system. Although the results were not statistically significant, a clinical pattern was seen. Previous research studies have shown iv meperidine to be effective when administered intraoperatively to decrease postoperative shivering (Grundmann et al., 1997; Horn et al., 1998a). Because meperidine has been proven to be a simple, effective and safe method to alleviate shivering after it has already begun (Burks et al., 1980; Macintyre et al., 1987), future studies using meperidine intraoperatively with use of the UPAC system are warranted.

The investigators would recommend using a larger dose of meperidine, a mg/kg dosage regimen, or multiple treatment groups with differing doses of meperidine. Administration of meperidine at a time interval closer to the end of surgery should be investigated. A future study could use multiple study sites, which could allow for a larger sample size. The role that temperature plays in the occurrence of postoperative shivering

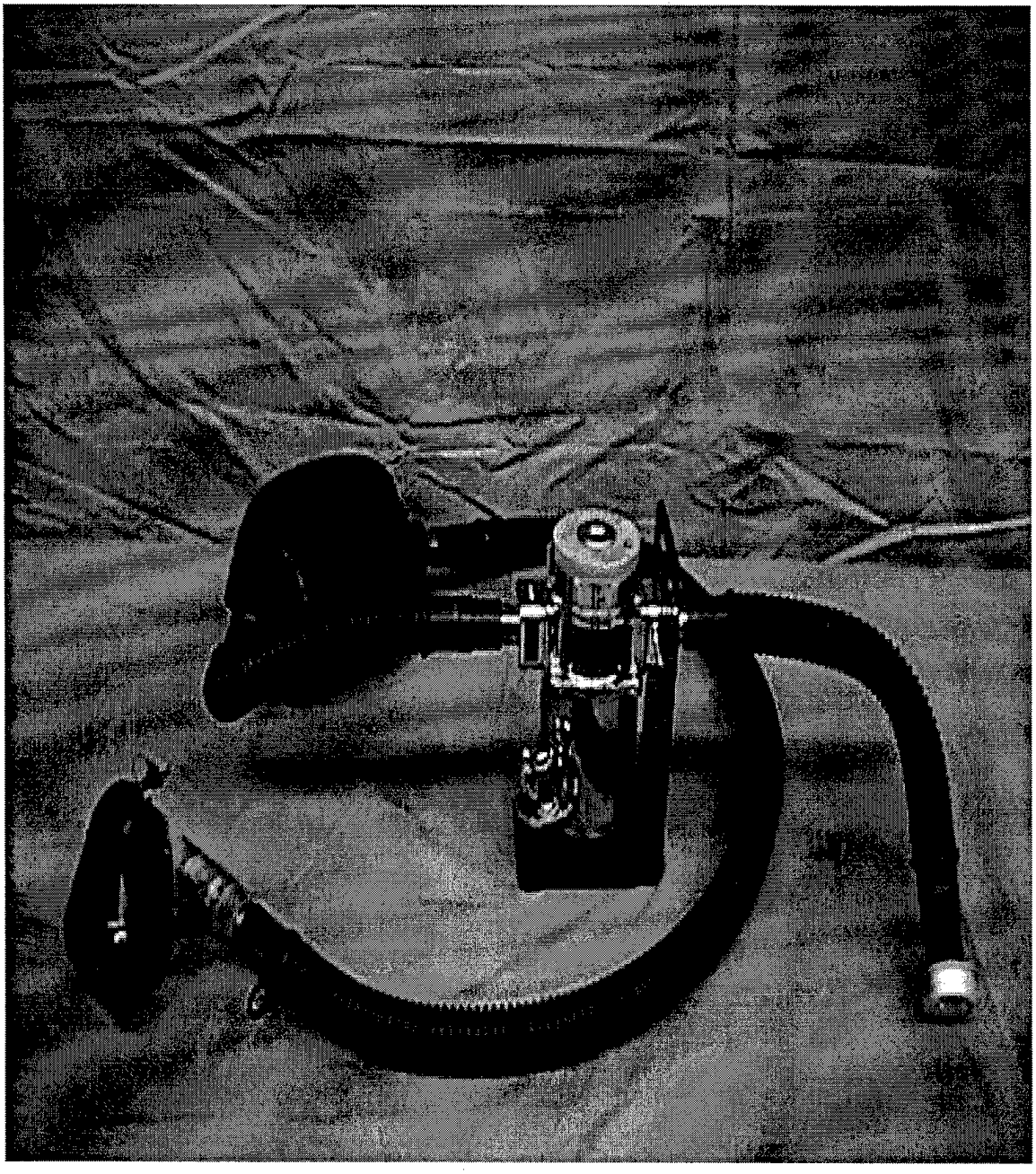
needs to be investigated. Also, dividing the groups according to gender to see if meperidine affects men and women differently could be studied.

Summary

This study compared the incidence of postoperative shivering after general anesthesia when using the Ohmeda UPAC in subjects given meperidine 25 mg iv intraoperatively to subjects receiving a placebo. The study also compared the incidence of postoperative shivering in the control group, to the control group of a study using a conventional anesthesia machine. Although statistical significance was not found in either case, older subjects (> 30 yrs) were found to shiver less than younger subjects (≤ 30 yrs). Additional research is recommended with the Ohmeda UPAC to investigate higher dosage regimens, timing of meperidine administration, and possible differences in gender responses to meperidine.

APPENDIX A

Ohmeda Universal Portable Complete (UPAC) Drawover Vaporizer



OHMEDA Universal Portable Anesthesia Complete (UPAC) System

APPENDIX B

American Society of Anesthesiologists (ASA) Classification

ASA Classification

Status	Disease State
I	No organic, physiological, biochemical or psychiatric disturbance
II	Mild to moderate systemic disturbance that may or may not be related to the reason for surgery
III	Severe systemic disturbance that may or may not be related to the reason for surgery
IV	Severe systemic disturbance that is life threatening with or without surgery
V	Moribund patient who has little chance of survival but is submitted to surgery as a last resort (resuscitative)
E	Any patient in whom an emergency operation is required

Note. Adapted from information in American Society of Anesthesiologists: New classification of physical status. Anesthesiology, 24, 111. (1963).

APPENDIX C

Data Collection Tool

Data Collection Tool

Instructions: Please complete this form and put inside the patient's study folder. Place the study folder in the box labeled "Study Packets and Anesthesia Buck Slips" located in the PACU.

General Information

A. Subject #:_____ **B.** Date of Surgery:_____

C. Ambient OR Temperature:_____°C

D. Humidity:_____%

Patient Information

A. Age:_____ **B.** Gender: Male Female

C. ASA: I II

D. Procedure:_____

Intra-operative Information

A. Baseline Vital Signs: HR:_____BP:_____RR:____SaO_2:____TEMP:_____°C **B.** Time of induction: _____

C. Fentanyl _____ug **D.** Propofol_____mg **E.** Succinylcholine_____mg

F. Mivacurium_____mg **G.** Isoflurane Concentration: Insp %_____ End Tidal %_____

H. Toradol: NO YES If Yes, then _____mg **I.** Time Study Solution was administered: _____

J. Vitals Signs at time of Study Solution administration: HR:_____BP:_____RR:____SaO_2:____TEMP: _____°C

K. Time of extubation: _____ **L.** Total Anesthesia Time:_____min

Post-operative Information

A. Vital Signs:

	Initial: HR: _____	BP: _____	RR: _____	SaO_2: _____	Temp: _____°C
15min:	_____	_____	_____	_____	_____
30min:	_____	_____	_____	_____	_____
45min:	_____	_____	_____	_____	_____
60min:	_____	_____	_____	_____	_____

B. Shivering Criteria (Check box YES or NO for each category)	YES	NO
1. ECG Artifact----------	☐	☐
2. Palpable Mandibular Vibration----------	☐	☐
3. Visible Fasciculations of the Head, Neck or Trunk----------	☐	☐
4. Generalized Shaking of the Body With or Without Teeth Chattering ----------	☐	☐
Shivering (Check YES if 2 Criteria Were Met) ----------	☐	☐

Post-operative Medications

A. Demerol (total)_____mg **B.** Morphine (total)_____mg

If you have questions or need assistance completing this form, please contact:

CPT Wilcox (Pager)-0766
CPT Baughan (Pager)-0765
or
Call Anesthesia Classroom 787-7005/787-3087

APPENDIX D

Informed Consent Form

VOLUNTEER AGREEMENT AFFIDAVIT

For use of this form, see AR 70-25 or AR 40-38; the proponent agency is OTSG

PRIVACY ACT OF 1974

Authority: 10 USC 3013, 44 USC 3101 and 10 USC 1071-1087

Principle Purpose: To document voluntary participation in the Clinical Investigation and Research Program. SSN and home address will be used for identification and locating purpose.

Routine Uses: The SSN and home address will be used for identification and locating purposes. Information derived from the study will be used to document the study; implementation of medical programs, teaching, adjudication of claims, and for the mandatory reporting of medical condition as required by law. Information may be furnished to Federal, State and local agencies.

Disclosure: The furnishing of SSN and home address is mandatory and necessary to provide identification and to contact you if future information indicates that your health may be adversely affected. Failure to provide the information may preclude your voluntary participation in this investigational study.

PART A - VOLUNTEER AFFIDAVIT

Volunteer Subjects in Approved Department of the Army Research Studies

Volunteers under the provisions of AR 40-38 and AR 70-25 are authorized all necessary medical care for injury or disease which is the proximate result of their participation in such studies.

I, _____ SSN _____having full capacity to consent and having attained my _____ birthday, do hereby volunteer/give consent as legal representative for_____ to participate in the research study, " The effect of intraoperative administration of 25mg Demerol (meperidine) on postoperative shivering," under the direction of CPT Ryan Wilcox, CPT Thomas Baughan, LTC Patricia Harrington, MAJ Cynthia Griffith, and MAJ Mark Schierenbeck conducted at Eisenhower Army Medical Center.

The implications of my voluntary participation/consent as legal representative; duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by CPT Ryan Wilcox or an associate.

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights/the right of the person I represent on any study-related injury I may contact the Center Judge Advocate (706) 787-4097 or the Clinical Research Protocol Coordinators on the 12th floor, Eisenhower Army Medical Center (Bldg 300), Ft. Gordon, GA (706) 787-4273.

I understand that I may at any time during the course of this study revoke my consent and withdraw/have the person I represent withdrawn from the study without further penalty or loss of benefits; however, I/the person I represent may be required (military volunteer) or requested (civilian volunteer) to undergo certain examinations if, in the opinion of the attending physician, such examinations are necessary for my/the person I represent's health and well being. My/the person I represent's refusal to participate will involve no penalty or loss of benefits to which I am/the person I represent is otherwise entitled.

Initials of volunteer _____
(or guardian for minor volunteer)

PART A(2)-ASSENT VOLUNTEER AFFIDAVIT (MINOR CHILD)

I, _____, SSN _____, having full capacity to consent and having attained my _____ birthday, do hereby volunteer for _____ _____to participate in the research study " The effect of intraoperative administration of Demerol (meperidine) on postoperative shivering," under the direction of CPT Ryan Wilcox, CPT Thomas Baughan, LTC Patricia Harrington, MAJ Cynthia Griffith, and MAJ Mark Schierenbeck conducted at Eisenhower Army Medical Center.

The implications of my voluntary participation; the nature, duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconvenience and hazards that may reasonably be expected have been explained to me by CPT Ryan Wilcox or an associate. I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights/the right of the person I represent on study-related injury I may contact the Center Judge Advocate (706) 787-4097 or the Clinical Research Protocol Coordinators on the 12th floor, Eisenhower Army Medical Center (Bldg 300), Ft. Gordon, GA (706) 787-4273.

I understand that I may at any time during the course of the study revoke my consent and have the person I represent withdrawn from the study without further penalty or loss of benefits; however, the person I represent may be requested to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for their health and well-being. The person I represent's refusal to participate will involve no penalty or loss of benefits to which they are otherwise entitled.

PART B - EXPLANATION OF WHAT IS TO BE DONE

The study that you are being asked to participate in involves research which looks at the effectiveness of meperidine (Demerol) to prevent shivering after surgery. Shivering after surgery can make you feel uncomfortable, increase your body's oxygen requirements and increase the risk of reopening your wound. Studies have shown that Demerol can stop shivering when given after surgery. The purpose of this study is to determine if the addition of 25mg of Demerol, administered during surgery, will prevent shivering after surgery. This will help anesthesia care providers to better control shivering after surgery and its effects on you. The potential benefits to you are that Demerol may decrease your chance of shivering, decrease your pain, and increase your comfort level after surgery. Potential risks of Demerol include drowsiness, pruritis (itching), allergic reaction, difficulty breathing, and hypotension (decreased blood pressure). You will be closely observed for complications after surgery related to general anesthesia.

If you choose to participate in this study, you will be randomly assigned, as in tossing a coin, to one of two groups. You will have a 50% chance of being in one of the two groups. If you are assigned to the experimental group you will receive 25mg Demerol (1cc) via the catheter that is in your vein which was started before surgery. If you are assigned to the control group you will receive 1cc of a placebo (0.9% normal saline) via your iv catheter. A placebo is a pretend treatment with no drug in it. Neither you, the physician, nor the investigators will know whether you are receiving the Demerol or the placebo. In case of an emergency, the pharmacy will be contacted to determine which treatment you received. During the period after surgery, you will be monitored in the post anesthesia care unit and be treated for any discomfort that you may experience regardless of your group assignment. Your chart will be marked identifying you as a participant in the study.

This study will be conducted by graduate students in the U.S. Army Graduate Program in Anesthesia Nursing (as identified above) under the supervision of a faculty member or the phase II site director. The Demerol or normal saline will be administered by a staff nurse anesthetist, or student nurse anesthetist under the supervision of faculty.

Initials of volunteer _____
(or guardian for minor volunteer)

Your participation in this study is entirely voluntary. You may withdraw from participation in this study at any time. Should you choose to withdraw, you will incur no penalty or loss of benefits to which you are otherwise entitled. Refusal to participate in the study will not alter your surgical or anesthesia care, nor will it alter any future care that you may receive. If at any time it is determined that it is not in your best interest to continue in this study, you will be withdrawn from the study.

I understand that my entitlement to medical and dental care and/or compensation in the event of injury is governed by federal laws and regulations. If I have any questions about my rights or if I believe I have received a research-related injury, I may contact the Eisenhower Army Medical Center Protocol Coordinator at (706) 787-4273 or CPT Ryan Wilcox, Principal Investigator at (706) 787-7005. I understand that participation in this study does not alter my ongoing benefits as a military beneficiary, and I will continue to receive any needed medical treatment should I experience illness or injury as a result of this study. In the event of physical injury resulting from the investigational procedures, the extent of medical care provided is limited and will be within the scope authorized for DoD health care beneficiaries. Needed medical treatment does not include domiciliary (home or nursing) care.

Participants in this study are encouraged to ask questions. You may ask your anesthesia care provider, or you may direct your questions to the principle investigator, CPT Ryan Wilcox or his associate. If you have any questions about the ethical, legal, or social aspects of this study, you should contact the Clinical Investigations Division, Eisenhower Army Medical Center, at (706) 787-4273. The results of this study will be provided to you upon request.

Any information that you may provide in this study that identifies you, will remain strictly confidential and will not be disclosed. Information gained because of your participation in this study may be publicized in the medical literature, discussed as a teaching tool, or used to generally advance medical science. Information from this study may be used as part of a scientific publication in professional journals, but you will in no way be personally identified. A copy of this form will be given to you upon request.

You are deciding whether or not to participate in this study. If you sign the form it means you have decided to volunteer after reading and understanding all of the information on this form. You will not be paid to participate in this study. You will be given a copy of this form upon request.

I do ❑ do not ❑ (check one & initial) consent to the inclusion of this form in my outpatient medical treatment record.

<table>
<tr><td>SIGNATURE OF VOLUNTEER</td><td>DATE</td><td colspan="2">SIGNATURE OF LEGAL GUARDIAN</td></tr>
<tr><td rowspan="2">PERMANENT ADDRESS OF VOLUNTEER</td><td colspan="3">PRINTED NAME OF WITNESS</td></tr>
<tr><td>SIGNATURE OF WITNESS</td><td colspan="2">DATE SIGNED</td></tr>
</table>

Initials of volunteer _____
(or guardian for minor volunteer)

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VITAE

Ryan Wilcox was born on April 27, 1971, in the town of Devils Lake, North Dakota to the parents of Jim and Patricia Wilcox. He attended high school at Devils Lake Central High. He was involved in wrestling, football, JROTC (junior reserve officer corps), science club and the National Honor Society. His interest in the Army earned him a ROTC scholarship, which he attended the University of North Dakota for a year, then transferred to the University of Iowa. There, in December of 1994, he earned a Baccalaureate of Science in Nursing, commissioned a second lieutenant in the Army Nurse Corps and was a distinguished military graduate. March 1995, he went on active duty and attended Officers Basic course at Fort Sam Houston (FSH), Texas. His first duty assignment was on a cardiac step-down unit at Brooke Army Medical Center, FSH, Texas. A second assignment on the neurological/trauma Surgical Intensive Care Unit lasted three years before he was accepted into the U.S. Army Graduate Program in Anesthesia Nursing.

Thomas Gerald Baughan was born in Montgomery, West Virginia on December 26, 1959, the son of Gary Wayne and Shirley Jane Baughan. After completing his work at Devola Christian School, Marietta, Ohio, in 1978, he attended Bob Jones University and West Virginia Institute of Technology. In 1984, he moved to Wilson, North Carolina and worked for Cox Industries until 1991, when he began attending Barton College. In 1993 he graduated from Barton College and received the degree of Bachelor of Science with a major in Nursing. He has since been employed as a nurse in the United States Army Nurse Corps where in 1998 he entered the US Army's Graduate Program in Anesthesia Nursing. In 1985, he married Francis Michelle Shumate of Glen Ferris, West Virginia. Together they have a daughter, Karyn Michelle, born in 1986, and three sons, Thomas Gerald II, born in 1987, Clark Emory, born in 1993 and Gary Holt, born in 1994.

This thesis was typed by the investigators