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UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
POSTGRADUATE DENTAL COLLEGE
SOUTHERN REGION OFFICE
2787 WINFIELD SCOTT ROAD, SUITE 220
JBSA FORT SAM HOUSTON, TEXAS 78234-7510
https://www.usuhs.edu/pdc

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Name of Candidate: Jonathan J. Dismuke

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Matthew B. Phillips, LTC, DC
DEPARTMENT OF ENDODONTICS, FORT GORDON
Committee Chairperson

GOODELL.KURT.BENEDICT.1246221606 Digitally signed by GOODELL.KURT.BENEDICT.1246221606 Date: 2023.06.30 15:47:38 -04'00' 30-Jun-2023

Kurt B. Goodell, LTC, DC
DEPARTMENT OF ENDODONTICS, FORT GORDON
Committee Member

DEPARTMENT OF ENDODONTICS, FORT GORDON
Committee Member

Symptomatic Irreversible Pulpitis Managed with Dexamethasone During Delayed Endodontic Treatment: A Case Series

CPT Jonathan J. Dismuke, DMD
LTC Joseph M. Dutner, DMD
LTC Matthew B. Phillips, DMD
LTC Kurt B. Goodell, DDS

ABSTRACT

BACKGROUND: Managing pain of endodontic origin is most often achieved via pulpotomy, pulpectomy, or nonsurgical root canal therapy in conjunction with postoperative analgesics. In the event endodontic treatment cannot be initiated promptly, an effective pain management protocol targeting reduction of inflammatory mediators is invaluable. Dexamethasone may provide an optimal approach to managing symptomatic irreversible pulpitis when endodontic treatment cannot readily be provided. Reasons for delayed treatment include but is not limited to: scheduling conflicts, lack of staffing support, inability to achieve profound anesthesia, difficult anatomy, or canal obstructions impeding adequate debridement. This article will review inflammatory pathways, as well as dexamethasone's mechanism of action to help facilitate discussion on its use for managing endodontic pain. A case series documenting dexamethasone's ability to adequately manage pain associated with symptomatic irreversible pulpitis during delay of endodontic treatment by one week demonstrates potential for this regimen.

METHODS: Three cases of symptomatic irreversible pulpitis were initially treated by long-acting local anesthesia and dexamethasone until endodontic treatment could be provided one week later. During the initial evaluation appointment, patients were administered 9mg of 0.5% Marcaine and one 4mg tablet of dexamethasone. Patients were provided two additional 4mg tablets, one to be taken before bed and the other upon waking. Patients were scheduled for endodontic treatment and followed up during that time to monitor the management of symptoms.

RESULTS: Each patient reported an adequate reduction of pain following completion of the dexamethasone regimen and lasting until NSRCT visit, however, one patient reported minimal rebound of cold sensitivity 48 hrs following first dose of dexamethasone.

CONCLUSIONS: Adequate reduction of pain associated with symptomatic irreversible pulpitis was observed in patients who were provided with a cumulative 12mg orally administer regimen of dexamethasone taken over 24 hours.

INTRODUCTION

Symptomatic irreversible pulpitis is an inflammatory condition of the pulp. If the tooth is to be retained, patient symptoms are most often managed via endodontic treatment in the form of a pulpotomy, pulpectomy, or non-surgical root canal therapy. The purpose of these procedures is to remove the inflamed pulp tissue (partially or completely) to alleviate symptoms. Studies indicate however that up to 80% of patients presenting with preoperative pain, will continue to experience symptoms following endodontic treatment (1). Therefore, management of patient symptoms continues postoperatively and is commonly treated with analgesic medications, such as ibuprofen and acetaminophen. Occasionally, situations arise when endodontic treatment cannot be readily provided, as was highlighted during the recent COVID-19 pandemic. Other situations include but are not limited to: scheduling conflicts and/or lack of staffing support, inability to achieve profound anesthesia, and difficult anatomy or root canal obstructions that impede adequate debridement (2). In such instances, glucocorticoids may offer an effective approach at alleviating symptoms caused by irreversible pulpitis until definitive endodontic treatment can be provided.

To better understand the added benefit glucocorticoids may have in managing pain of endodontic origin, an understanding of its etiology is required. Endodontic pain results from upregulation of host inflammatory mediators (3). The production and release of histamine, serotonin, bradykinin, prostaglandins, and leukotrienes both directly and indirectly mediate the pain response via increased vascular permeability and tissue pressure (4). Although the actions of inflammatory mediators vary, their culminating effect leads to reduction of pain thresholds, thereby lowering the stimulus required for activation of nociceptors in the dental pulp (5). Additionally, peripheral pain pathways change due to sprouting of nociceptor terminals with increased duration and acuteness of the inflammatory response (6). Therefore, an effective pain management protocol utilizing analgesics to address inflammatory pain is important, especially in the event of delayed endodontic treatment.

Various classes of drugs have been studied and used to treat endodontic pain, those of which include NSAIDs, acetaminophen, opioids, and steroids. Of these, NSAIDs and steroids have proven to be effective due to their anti-inflammatory action (7). Commonly prescribed NSAIDs cause inhibition of the cyclo-oxygenase (COX) enzymes, which converts arachidonic acid to prostaglandin endoperoxides (1). In contrast to the selective nature of NSAIDs, glucocorticoid steroids such as dexamethasone, have multiple sites of action within the matrix of inflammatory reactions. Glucocorticoids affect the acute inflammatory response by suppressing vasodilation, preventing the migration and phagocytic action of polymorphonuclear leukocytes, as well as inhibiting the production of prostaglandins (PGs) and leukotrienes through inhibition of both the COX and lipoxygenase inflammatory pathways (8).

Although anti-inflammatory medications help to treat patient symptoms, they do not address bacterial etiology causing the host inflammatory response. Extraction or endodontic treatment of the offending tooth is required. The goal of endodontic treatment is multifaceted, aiming to not only alleviate patient symptoms, but also to prevent and treat periapical pathology. Therefore, the success of endodontic treatment is directly influenced by adequate chemo-mechanical debridement prior to root canal obturation. To adequately perform endodontic treatment, an appropriate amount of time is needed to treat patients, in addition to the endodontic armamentarium. From a military perspective, herein lies the potential obstacle for providing prompt endodontic care to a symptomatic deployed soldier.

The dental corps' primary mission is the dental readiness of the Army patient population. Although this mission begins at home (CONUS) within established well-equipped dental clinics, it continues beyond the home front and follows soldiers into theater during deployment status. It's in this environment, where the dental mission transitions to operational dentistry, with the primary focus of emergency and essential dental care. While in theater, levels of dental support exist, which are defined by their capabilities and geographic location (FM 4-02 Army Health System). It's within this context, a soldier's dental treatment could be delayed and use of dexamethasone could be highly beneficial for managing endodontic pain from an inflamed vital pulp. The following cases describe use of dexamethasone for managing patients diagnosed with symptomatic irreversible pulpitis during the period of delayed endodontic treatment.

CASE 1

A 41-year-old African American female presented to the dental clinic for her scheduled operative appointment on tooth #14 that had been previously diagnosed with reversible pulpitis. The patient's chief complaint included, "significant discomfort following a biopsy completed last week and increase in sensitivity to cold in the upper left." The patient was seen by the OMS department the week prior for incisional biopsies on the buccal and gingival mucosa adjacent to teeth #14 and #19. Clinical examination at the time of the operative appointment revealed the patient had limited opening and the pulpal status of tooth #14 had developed into symptomatic irreversible pulpitis. The patient reported 8 out of 10 pain utilizing a visual analog pain scale (VAS). Due to the patient's clinical presentation and limited ability to open, the patient was provided block anesthesia (posterior superior alveolar) using 9mg of 0.5% Bupivacaine. Before departing the dental clinic, the patient was provided the first of three 4mg oral doses of dexamethasone. The remaining two doses were provided to the patient and instructions were to take 1 tablet at bedtime and the last upon waking the following morning, equating to a cumulative 12mg oral dose taken over 24 hours. The patient was scheduled for NSRCT one week later and followed up during that time to monitor symptoms. The patient reported the medication to be most effective during the first two days following the initial dexamethasone dose, however, pain remained at 2 out of 10 (VAS) until NSRCT was completed.

CASE 2

A 36-year-old African American male presented to dental clinic for endodontic evaluation of tooth #14. The patient reported noticing a hole in his tooth several months prior while stationed in Korea and avoided cold food and drinks due to hypersensitivity. Pain was reported to be 7 out of 10 (VAS) and lingered when provoked by cold stimulus. Following sensibility testing, tooth #14 was diagnosed with symptomatic irreversible pulpitis and normal apical tissues. Clinical findings included a large cavitated lesion involving the mesial and occlusal surfaces of tooth #14. Due to the patient's schedule and unavailability for treatment that day, the patient was offered and received block anesthesia followed by administration of dexamethasone in the same manner as previously described in case 1. The patient was scheduled for treatment one week later and followed up during that time to monitor symptoms. The patient reported having continued cold sensitivity following the first dose of dexamethasone, however, significantly decreased following completion of the cumulative 12mg dose. The reported pain level remained at 1 out of 10 (VAS) until NSRCT was initiated and completed one week later.

CASE 3

A 37-year-old African American female referred from her general dentist for endodontic treatment of tooth #14. The patient presented to the endodontic clinic with the chief complaint, "I'm not sure which tooth it is, but it feels like it could be more than one. It hurts when I drink anything that's hot or cold or when I eat something sweet." Clinical findings included a resin restoration on tooth #14 that radiographically approximated the pulp chamber, and an occlusal amalgam on tooth #15 with mesial recurrent caries. The patient reported 5 out of 10 pain at rest, 10 out of 10 (VAS) when provoked by cold stimulus. Sensibility testing of tooth #14 produced an acute lingering response to cold (symptomatic irreversible pulpitis) with a normal periapex (normal apical tissues). Tooth #15 was diagnosed with reversible pulpitis and normal apical tissues. Due to the patient arriving late, she was offered and received block anesthesia and the dexamethasone regimen as previously described. The patient was monitored for one week until NSRCT was initiated. The patient reported experiencing nausea following the last dose of dexamethasone, however, symptoms were resolved with self-administered Tylenol. The patient stated that the cold sensitivity felt more manageable and reported her pain was reduced to a 2 out of 10 (VAS) until she was seen for her NSRCT appointment one week later.

DISCUSSION

Administration of dexamethasone does not preclude the need for endodontic treatment of teeth diagnosed with irreversible pulpitis, however, these cases highlight its ability to adequately manage pain during delay of definitive treatment. Review of glucocorticoid mechanism of action, in particular dexamethasone, helps to better understand its potential for short-term treatment of symptomatic irreversible pulpitis.

Among the class of synthetic glucocorticoids, dexamethasone has the greatest biological half-life (36-54 hours) and anti-inflammatory potency (1). Glucocorticoid mechanism of action results in the inhibition of inflammatory mediators via their effect on gene transcription. Glucocorticoids bind non-covalently with intracellular glucocorticoid receptors in target tissues, resulting in activation and translocation to the nucleus, allowing transcription of specific mRNA. This newly transcribed mRNA serves as the template for ribosomal synthesis of steroid-induced proteins(9). The net effect produces a decrease in the release of vasoactive and chemo-attractive factors, decreased secretion of lipolytic and proteolytic enzymes, decreased extravasation of leukocytes to areas of tissue injury, and decreased fibrosis(1).

One of the synthesized steroid-induced proteins is lipocortin 1. Lipocortins prevent the synthesis of arachidonic acid, blocking the synthesis of both COX and lipoxygenase products, including PGs, leukotrienes, and thromboxane(9). Glucocorticoids affect the innate immune response via inhibition of cytokine production, specifically interferon γ, granulocyte/monocyte colony-stimulating factor (GM-CSF), interleukins 1, 2, 3, 6 (IL-1, IL-2, IL-3, IL-6) and tumor necrosis factorα (TNFα) (10). Bradykinin, a strong pro-inflammatory mediator with multiple actions (vasodilation, vascular permeability, leukocyte chemoattraction, and nociceptor activation) is often associated with pain. A study by Hargreaves & Costello demonstrated the reduction of bradykinin via the administration of glucocorticoids (11). It is the synthesis of kinase II (ACE) induced by glucocorticoids that leads to a reduction of bradykinin. An additional protein synthesized by glucocorticoids, vasocortin, has shown to have the effect of suppressing edema, an action not seen with NSAIDs(12).

As with any medication, there are precautions for the administration of dexamethasone. Potential drug interactions associated with glucocorticoids involve those that are metabolized in the liver via CYP3A. CYP3A inducers may increase the metabolism of dexamethasone leading to reduced efficacy, while CYP3A inhibitors may decrease the rate of metabolism leading to toxicity (13). Glucocorticoids are contraindicated for patients with systemic fungal infections and known hypersensitivity to the drug. Patients with medical conditions including ulcerative colitis, pyogenic infection, diverticulitis, peptic ulcer, renal insufficiency, hypertension, osteoporosis, pregnancy, diabetes mellitus, ocular herpes, acute psychosis, and history of tuberculosis should be cautious with the use of steroids (1). Avascular necrosis (osteonecrosis) is a condition that results in the collapse of bone structure, leading to significant clinical morbidity, including progressive joint pain and loss of function. Although the most common cause of avascular necrosis is due to trauma, it has been associated with corticosteroid use. The risk of corticosteroids on the development of osteonecrosis is dependent on daily dose, cumulative dose, maximum dose, route of administration, and underlying disease states (14). The potential for adverse effects is typically only seen at supraphysiological doses given over a long-term period, usually more than two weeks. In an *in vivo* study by Czerwinski et al., it was found that single large doses (2 mg/kg) of dexamethasone (10-25 times the amount advocated for endodontic pain) did not produce harmful side effects (15). The short-term (24 hour)

dosages of dexamethasone used within this case series remained well below even those found to be safe by Czerwinski.

A study by Liesinger et al, evaluated the effect of variable dosages of dexamethasone on posttreatment endodontic pain. Their findings revealed dosages between 0.07 to 0.09mg/kg that were provided via intraoral intramuscular injection were most effective within an 8 hour range (16). Therefore, given dexamethasone's pharmacodynamics and half-life, a protocol consisting of 4mg tablets that was to be taken orally every 8 hours for an accumulated 12mg dose was implemented. Oral administration was chosen as the preferred route in effort to both simplify and ensure systemic absorption.

Previous clinical trials have varied regarding routes of administration, in addition to combining glucocorticoids with other analgesics and antibiotics (2,4,8,16–32). Methods for administering include intracanal, intramuscular, supraperiosteal, intraligamentary (PDL), intraosseous, and oral. Intracanal placement of glucocorticoids has shown to be efficacious in the reduction of inflammatory pain but requires initiation of endodontic treatment and does not ensure systemic absorption of a given dosage. Conversely, the remaining routes help to ensure systemic absorption and better evaluate pain reduction of a predetermined dosage. Additionally, studies evaluating pain reduction following administration of a corticosteroid without initiation of endodontic treatment, provides a purer representation of drug efficacy.

In the event of delayed endodontic treatment, glucocorticoids may provide equitable reduction of pain caused by inflammation. Isett et al. conducted a prospective, randomized, double-blind study evaluating pulpal concentrations of prostaglandin E2 (PGE2) and interleukin-8 (IL-8) in untreated teeth with irreversible pulpitis, following IO injection of Depo-Medrol. Forty patients diagnosed with symptomatic irreversible pulpitis were randomly assigned to receive either 1 ml of Depo-Medrol (40 mg) or 1 ml of sterile saline placebo. No endodontic treatment was rendered and teeth were extracted at 1 or 3 days following IO injection for harvesting of the pulpal tissue. Analysis of PGE2 and IL-8 showed a significantly lower concentration of PGE2 compared to the saline group at day 1. There was no significant difference between groups by day 3 (26). In a double-blind, randomized study conducted by Gallatin et al., the direct effect of glucocorticoid administration alone without any initiation of endodontic was evaluated for reduction of patient symptoms. Patients presenting with irreversible pulpitis with moderate to severe pain were randomly divided to receive either intraosseous injection of Depo-Medrol (40mg) or 1mL sterile saline. Patients were then provided ibuprofen and Tylenol #3 and completed a 7-day questionnaire on pain. The results of this study showed that patients who received an intraosseous injection of Depo-Medrol reported significantly less pain and took significantly fewer pain medications (2). In another randomized clinical trial, patients with acute irreversible pulpitis were treated either by intraosseous methylprednisolone injection or pulpotomy treatment. At the one-week follow-up, patients who received an intraosseous injection of methylprednisolone reported less pain throughout the 7 days compared to the

pulpotomy treatment group (21). This study's conclusion indicated methylprednisolone to be more effective than pulpotomy at relieving acute pulpitis symptoms (21).

Although non-surgical root canal therapy is the first-line treatment for the management of symptomatic irreversible pulpitis, there are instances in which endodontic treatment is delayed. As previously discussed, such situations include scheduling conflicts, lack of staffing support, inability to achieve profound anesthesia, difficult anatomy, or root canal obstructions that impede adequate debridement due to time constraints. Given the dynamics of Army dentistry and the patient population it serves, additional obstacles often found in a deployed setting may prevent timely endodontic treatment. Therefore, research directed at identifying the most effective pain protocol, especially one that mitigates the use of narcotics, not only contributes to civilian practice but is invaluable for the activated soldier population. The cases presented here, as well as the clinical trials discussed, demonstrate the beneficial effect corticosteroids have on reducing pain of endodontic origin. There are, however, inherent limitations to this case series and areas where further investigation would contribute and enhance the level of available research.

When interpreting the results of clinical trials evaluating corticosteroid efficacy, it's important to consider the study protocol. Most studies evaluate reduction of post-operative pain following initiation of endodontic treatment. Postoperative pain will invariably be reduced following adequate endodontic treatment, regardless of which class analgesic is administered. This reduces the statistical power of endodontic clinical trials for detecting active analgesics over time, otherwise known as the floor effect (1). Additionally, it's difficult to interpret studies utilizing intracanal placement of corticosteroids due to multiple factors: variable dosage, time to reach the site of action in periapical tissues, assuming the canal is patent (1). As stated in the article by Marshall, prospective randomized trials focused on systemic administration without endodontic treatment are needed to truly evaluate the direct effect of active analgesic (1).

The studies conducted by Gallatin, Isett, and Bane provide good examples of protocols that enable the analysis of dexamethasone alone without initiation of endodontic treatment. Although these studies utilized a predetermined systemic dose, each protocol administered dexamethasone via the same intraosseous route. As previously stated, IO injection requires an adjunctive delivery system (Stabident or X-tip system) to obtain access through denser cortical bone and into the medullary space. In the absence of such a system, oral administration of dexamethasone offers a simplified and predictable route for systemic delivery of a predetermined dose. To our knowledge, no randomized control trial has evaluated the efficacy of orally administered dexamethasone in reducing endodontic pain during delay of endodontic treatment.

CONCLUSIONS

In this case series, adequate reduction of pain associated with symptomatic irreversible pulpitis

was observed in patients who were provided with a cumulative 12mg orally administer regimen of dexamethasone taken over 24 hours. Dexamethasone may provide an optimal approach to managing symptomatic irreversible pulpitis when endodontic treatment cannot readily be provided. Future research should include prospective randomized trials involving dexamethasone administration without endodontic treatment to further evaluate efficacy and increase level of evidence.

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