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Association of Postmortem Blood Hemoglobin A_{1c} Levels With Diabetic Conditions in Aviation Accident Pilot Fatalities

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16. Abstract

Purpose. The Federal Aviation Administration's (FAA's) Office of Aerospace Medicine evaluates present and proposed medical certification standards for pilots. Under this responsibility, the FAA Civil Aerospace Medical Institute investigates the role of potential medical-or drug-related performance impairment in pilots. In previous research, abnormal glucose levels in vitreous humor (>125 mg/dL) and urine (>100 mg/dL) have been linked with diabetic conditions in pilots of fatal aviation accidents. Although these abnormal glucose levels identify pilots with elevated blood sugar at the time of death, they do not provide information on how well diabetes was controlled in these pilots. Since post-crash factors (trauma, stress, medical intervention) can dramatically affect blood glucose levels, a measure of long-term diabetic control was sought for postmortem specimens. **Methods.** Blood specimens from volunteers were collected and stored at room temperature for up to 52 days to mimic a postmortem condition. These specimens were analyzed for hemoglobin A_{1c} (HbA_{1c}) at selected time intervals during the 52-day period. Postmortem blood specimens from 34 aviation accident pilot fatalities were also analyzed. Some of these pilots had a known history of diabetes. **Results.** HbA_{1c} values in blood from volunteers did not significantly change for up to 52 days. The HbA_{1c} concentration in postmortem blood samples from pilots ranged from 3.9-10.5%. Only one pilot with a HbA_{1c} over 6.0% did not have a history of diabetes reported to the FAA. **Conclusions.** HbA_{1c} is stable in whole blood stored at room temperature for 52 days and appears to be stable in postmortem blood stored up to 84 days. HbA_{1c} above 6.0% was found to be generally correlated with a known history of diabetes and with the abnormal vitreous humor and urine glucose levels established previously. Elevated postmortem HbA_{1c} levels may be useful in supporting determinations of medical impairment/incapacitation in transportation accidents.

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Association of Postmortem Blood Hemoglobin A_{1c} Levels With Diabetic Conditions in Aviation Accident Pilot Fatalities

INTRODUCTION

Research into the use of hemoglobin A_{1C} (HbA_{1C}) began in the late 1960s and has continued to gain favor over the years for the diagnosis of diabetes mellitus (1-12). In fact, the analysis of HbA_{1C} has become a routine test for the diagnosis of diabetes and the monitoring of diabetic patients. The strong correlation found between elevated HbA_{1C} and diabetes (9) has made this analysis a very popular tool in the diagnosis and treatment of diabetics.

HbA_{1C} is formed through the irreversible reaction of glucose with hemoglobin at the NH_2-terminus of one or both beta chains of hemoglobin (4) and is reported as a percentage of the total hemoglobin present in the specimen. Normal non-diabetic individuals have HbA_{1C} levels between 3 – 6 % (11). The life expectancy of the red blood cell is 2 - 3 months. Therefore, HbA_{1C} will provide information on the patient's long-term success in treating their diabetic condition over the past 2 – 3 months.

A previous study has shown a correlation between diabetic pilots and elevated postmortem vitreous humor and urine glucose levels (2). This information has helped accident investigators assess the medical condition of the pilot at the time of the accident and allowed the Office of Aviation Medicine (OAM) to closely monitor medical certification standards concerning diabetic pilots.

Vitreous humor glucose levels can be influenced by several non-diabetic factors such as stress and medications. Therefore, it would be useful to know the HbA_{1C} level of the pilot to confirm the diagnosis of diabetes and help assess the pilot's prior control of the diabetic condition.

The analysis of blood collected from aviation accidents is complicated by the frequent delay of several weeks in receiving specimens. Autopsies are often delayed by difficulties in recovering bodies from remote accident sites, specimen collection, and sending samples to the laboratory. This delay in analysis requires that HbA_{1C} levels be stable in postmortem blood for extended periods of time. Earlier studies (4 – 8) have reported HbA_{1C} stability in postmortem blood collected and tested shortly after death. This study intends to examine the stability of HbA_{1C} in blood stored over an extended period of time.

MATERIALS AND METHODS

Materials

All reagents and blood specimens were allowed to reach room temperature prior to analysis. A 1 uL sample of thoroughly mixed whole blood specimen was placed into the glass capillary provided in the DCA 2000 Hemoglobin A_{1c} Reagent Kit and analyzed according to the manufacturer's operating instructions with a DCA 2000+ Analyzer and DCA 2000 Hemoglobin A_{1c} Reagent Kit (Bayer Corporation, Elkhart, IN).

Clinical Specimens

A blood sample was drawn from a known diabetic, and another sample from a non-diabetic individual. Blood was collected into tubes containing the anticoagulant EDTA and stored at room temperature. These specimens were analyzed over a period of 52 days. The collection time was noted, and analyses were performed at periodic intervals. This was done to demonstrate the stability of HbA_{1C} in blood stored at room temperature for an extended period of time.

Necropsy Specimens

Blood was collected by local pathologists, located near the accident site, in 10 mL gray top tubes containing 20 mg of potassium oxalate and 100 mg of sodium fluoride (Tri-Tech Inc., Southport, NC) from 34 pilots who had died in aviation accidents. Postmortem blood specimens from aviation pilots were aliquoted into tubes and frozen for analysis at a later date. HbA_{1C} was determined in postmortem blood samples, which were 7 to 84 days old.

RESULTS

Clinical Specimens

A blood specimen taken from a known diabetic subject had an average HbA_{1C} of 10.2 %, when tested over a period of 52 days with a 0.5 % standard deviation (n=12). A blood specimen taken from a non-diabetic subject had an average hemoglobin A1c of 4.9 % with standard deviation of 0.1 % (n=12) for the same period of time (Figure 1).

Necropsy Specimens

HbA_{1C} levels above 6% were found in 8 of the 34 postmortem cases analyzed (Table 1). A medical history of diabetes mellitus was found in 6 of the 8 cases with elevated HbA_{1C}. One case with a 10.5% HbA_{1C} had a medical history of glycosuria. Another pilot had a 6.7% HbA_{1C} level and no reported medical history of diabetes. Most of the elevated HbA_{1C} specimens analyzed were associated with elevated glucose levels in vitreous and/or urine.

DISCUSSION AND CONCLUSION

HbA_{1C} levels above 6% are generally correlated with a known history of diabetes. It may also be considered diagnostic of diabetes mellitus in post-mortem blood. Elevated postmortem HbA_{1C} levels, in combination with elevated glucose levels in vitreous

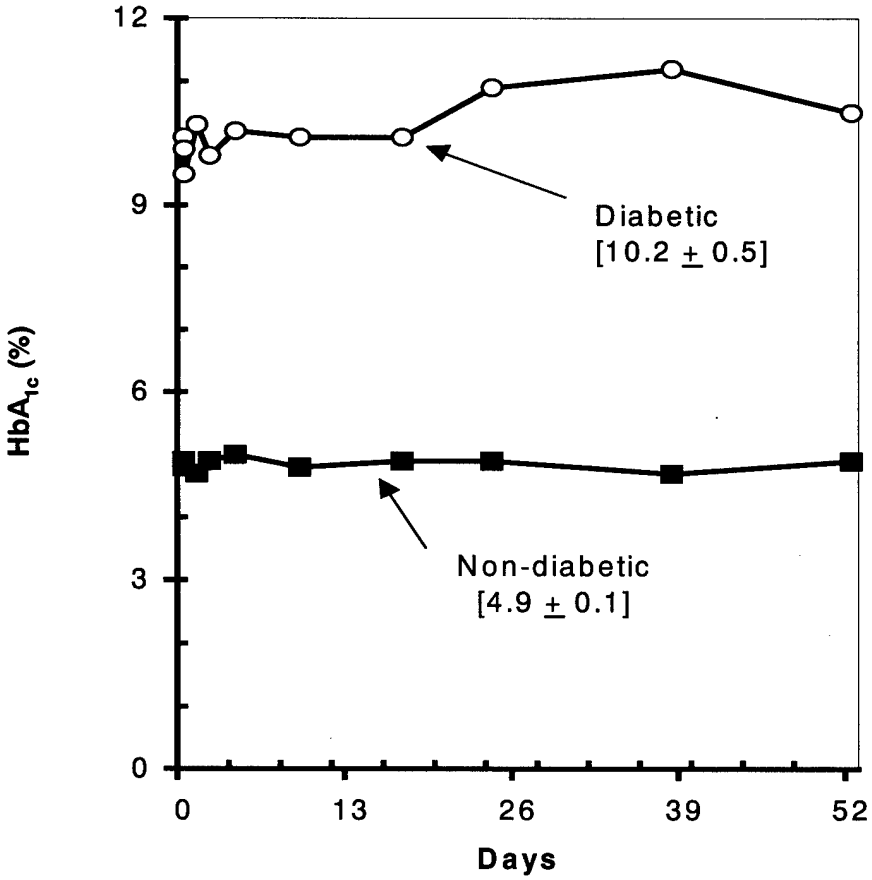

Figure 1. Comparison of Diabetic and Non-diabetic Subject HbA_{1C} Levels. HbA_{1C} was analyzed for 52 days. The diabetic blood sample had a 407 mg/dL glucose level on the first day of the test, and the non-diabetic blood sample had a glucose level of 92 mg/dL on the first day of the test.

Table 1. HbA_{1C} and glucose data collected in this study. All glucose data reported in mg/dL. Interval between death and analysis is reported in days. Medical refers to medical history of the individual: NO = No medical history for abnormal glucose levels; PA = Passenger no medical history on file; PM = Pilot no medical history on file; DI = Diabetic; EM = Emergency medical treatment; GL = Glycosuria or low renal threshold; SU = surface accident, no medical history on file.

Case Number	Urine Glucose	Vitreous Glucose	Accident Date	Date of Result	Interval (days)	Medical	HbA_{1C} (%)
199800208001	3055	12	05-Jul-98	19-Aug-98	45	GL	10.5
199800290001	8815	256	25-Sep-98	17-Nov-98	53	DI	8.5
199910012001	1221		03-Jun-99	08-Jul-99	35	DI	8.0
199900049001	38	97	22-Mar-99	12-Apr-99	21	DI	7.5
199800186001	189	45	26-Jun-98	18-Aug-98	53	DI	6.6
199800332001	760	119	04-Dec-98	13-Jan-99	40	DI	6.4
199800134001	28	43	26-May-98	18-Aug-98	84	DI	6.1
199900208001	29		20-Aug-99	30-Aug-99	10	DI	5.6
199800301001	11	0	12-Oct-98	18-Nov-98	37	DI	5.0
199900181001		109	07-Aug-99	16-Aug-99	9	DI	4.5
199900037001	65	113	08-Mar-99	19-Mar-99	11	EM	4.7
199800216001	65	147	31-Jul-98	18-Aug-98	18	EM	4.6
199900047001		194	10-Mar-99	12-Apr-99	33	EM	4.6
199800289001	24	10	10-Oct-98	17-Nov-98	38	EM	3.9
199800251001		0	12-Sep-98	25-Sep-98	13	EM	3.9
199800335001	18	105	04-Dec-98	13-Jan-99	40	NO	6.7
199900030001	67	66	20-Feb-99	01-Mar-99	9	NO	5.8
199800328001	12	0	21-Nov-98	13-Jan-99	53	NO	5.4
199800212001	14	0	31-Jul-98	18-Aug-98	18	NO	5.1
199800305001	18	0	02-Nov-98	18-Nov-98	16	NO	5.0
199900053001	0	0	03-Apr-99	12-Apr-99	9	NO	4.9
199800333001	0	0	29-Nov-98	13-Jan-99	45	NO	4.8
199800265001	42	102	26-Sep-98	17-Nov-98	52	NO	4.8
199800229001	87	10	12-Aug-98	01-Sep-98	20	NO	4.8
199800188001	29	66	10-Jul-98	18-Aug-98	39	NO	4.7
199800317001	14	0	12-Nov-98	13-Jan-99	62	NO	4.6
199900017001	13	0	26-Dec-98	05-Feb-99	41	NO	4.5
199900067001	12	0	22-Apr-99	11-May-99	19	NO	4.4
199900040001	15	0	13-Mar-99	12-Apr-99	30	NO	4.3
199800209001	0	0	26-Jul-98	18-Aug-98	23	NO	4.2
199900162001	12	0	17-Jul-99	27-Jul-99	10	NO	4.2
199800217001	17	0	02-Aug-98	18-Aug-98	16	NO	4.2
199900083001	20	0	04-May-99	11-May-99	7	NO	4.0
199900012002	14	13	22-Jan-99	23-Feb-99	32	PA	4.2

and/or urine, could be useful in supporting determinations of medical impairment/incapacitation in transportation accidents.

HbA_{1C} levels are stable in a clinical whole blood specimen stored at room temperature for 52 days (Fig. 1) and appear to be stable in necropsy whole blood stored up to 84 days. This finding is consistent with early reports on HbA_{1C} in postmortem whole blood.

The pilot originally diagnosed with glycosuria was most likely a diabetic, considering the 10.5% HbA_{1C} found in the pilot's blood and the 3055 mg/dL of glucose found in the urine. Research has shown a 3% increase in HbA_{1C} levels above normal (>8%) "generally indicate that mean plasma glucose concentrations have been well over 2000 mg/L" (200 mg/dL) during the past 2-3 months (4).

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