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Vitreous Fluid and/or Urine Glucose Concentrations in 1335 Civil Aviation Accident Pilot Fatalities*

ABSTRACT: During aviation accident investigations, vitreous fluid and urine samples from pilot fatalities are analyzed for glucose and blood for hemoglobin A_{1c} (HbA_{1c}) to monitor diabetic pilots and to discover other pilots with undiagnosed/unreported diabetes. The prevalence of elevated glucose concentrations in fatally injured pilots was evaluated by searching the Civil Aerospace Medical Institute's Toxicology Database for the period 1998–2005. Out of 1335 pilots involving 363 vitreous fluid, 365 urine, and 607 vitreous fluid and urine analyses, 43 pilots had elevated glucose in vitreous fluid (>125 mg/dL) and/or in urine (>100 mg/dL). Of the 20 pilots whose blood samples were analyzed, nine had >6% HbA_{1c}—four were known diabetics, and five were unknown diabetics. Urinary glucose levels were elevated in all 13 known hyperglycemic pilots. A considerable number of pilots (30 of 43) had elevated glucose and HbA_{1c} (5 of 20), suggesting undiagnosed/unreported diabetic conditions.

KEYWORDS: forensic science, forensic toxicology, vitreous fluid, urine, hyperglycemia, hemoglobin $A_{1c,}$ diabetes, aircraft accident investigation, Federal Aviation Administration

During aviation accident investigations at the Federal Aviation Administration's (FAA's) Civil Aerospace Medical Institute (CAMI), vitreous fluid and urine samples from pilot fatalities are analyzed for glucose (1–3). In those fatalities (cases) wherein glucose levels are elevated, blood hemoglobin A_{1c} (HbA_{1c}) is also measured (3,4). Concentrations of glucose >125 mg/dL in vitreous fluid and >100 mg/dL in urine are considered elevated (2). These glucose and HbA_{1c} analyses are conducted to monitor diabetic pilots to ensure that their disease was in control at the time of accidents and to discover other pilots with unreported diabetes. Such analyses of postmortem samples from aviation accident pilot fatalities are useful in determining whether hyperglycemia-induced performance impairment was the probable cause or a contributory factor in a particular accident.

At CAMI, vitreous fluid and urine glucose analysis was implemented on a routine basis in the beginning of 1998 and blood HbA_{1c} in the middle of 2001. However, information on the prevalence and causal effects of elevated glucose and HbA_{1c} in fatal civil aviation accidents is not documented. In this study, elevated glucose and HbA_{1c} in fatally injured civil aviators from whom biological samples were received at CAMI during 1998–2005 were evaluated by retrieving and analyzing necessary information from relevant databases. The possible causal effects of the elevated glucose and HbA_{1c} in the associated accidents were also retrieved during the database searches. The findings thus obtained are presented herein.

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Materials and Methods

Postmortem Biological Specimens

Autopsied biological samples (blood, urine, liver, kidney, vitreous fluid, and other body specimens) collected from fatally injured pilots of U.S. civil aviation accidents are submitted to CAMI for toxicological analyses for the investigation of aircraft accidents occurring within the jurisdiction of the United States (1,3). These aviation accidents entail accidents involving registered, as well as unregistered aircraft. Not all of the aviators involved in these accidents held airman medical and/or flying certificates required to legally pilot an aircraft. Collected postmortem samples are submitted to CAMI in the FAA's TOXBOX evidence containers (3). Submissions of the postmortem samples are coordinated through the FAA's Office of Accident Investigation by the National Transportation Safety Board (NTSB). The NTSB is responsible for investigating all U.S. civilian aircraft accidents.

Biological Specimen Analyses

In addition to routine toxicological analyses of the submitted specimens following standard procedures of the CAMI Toxicology Laboratory, vitreous fluid and urine samples are analyzed for glucose and blood for HbA_{1c} (3–5). Glucose analysis is performed by a hexokinase method using a Du Pont Analyst Benchtop Chemistry Station (Du Pont Company Medical Products, Wilmington, DL). Blood HbA_{1c} is measured by a latex immunoagglutination inhibition using a DCA 2000+ Analyzer and DCA 2000 HbA_{1c} Reagent

Kit (Bayer Corporation, Elkhart, IN). The suitability of the method for measuring HbA_{1c} in postmortem blood samples has been established (4). The stability of HbA_{1c} was found to be consistent with previous studies of HbA_{1c} in postmortem whole blood (6–12). As HbA_{1c} is a fairly stable macromolecule, it has been proposed as an aid in the postmortem diagnosis of diabetes (6–12).

The glucose analysis in the Laboratory was implemented on a routine basis in the beginning of 1998 and the HbA_{1c} in the middle of 2001. The HbA_{1c} analysis was performed in those cases wherein vitreous fluid and/or urine glucose concentrations were elevated (2,4) and wherein suitable blood samples were available.

Database Search

Including glucose and HbA_{1c} analytical values, all toxicological results of civil aircraft accident pilot fatalities are electronically stored in a database maintained at CAMI in Oklahoma City, OK. The CAMI Toxicology Database was searched over an 8-year period (1998–2005) for pilot fatalities, from whom postmortem samples were submitted, and their vitreous fluid and urine samples were analyzed for glucose. Blood HbA_{1c} and toxicological findings were also retrieved from this database.

Additionally, the CAMI Toxicology Database search entailed the numbers of all U.S. civil aviation accidents and pilot fatalities, including the airman flying and medical certificates of those pilots and the flight categories of the associated accidents. Some additional information related to airman flying certificates and flight categories, along with the probable cause and contributing factors in the accidents, was obtained from the NTSB's Aviation Accident Database (Washington, DC). The cause and factors-related information included in the study is based on the findings reported in the NTSB Database through December 2006. Aviators that did not have airman medical and/or flying certificates were also part of the study.

Results

Pilot Fatalities and Accidents

During 1998–2005, postmortem samples from 2487 pilot fatalities were submitted to CAMI. This number of fatalities corresponded to the equivalent number of aviation accidents in which pilot fatalities had occurred, and their postmortem samples were toxicologically evaluated. Of the 2487 accidents, 2210 were of general aviation, 107 air taxi and commuter, 20 ultralight vehicle, and 32 public use categories (13). The remaining 118 accidents were associated with air carrier, agricultural, and other categories.

Elevated Glucose and HbA_{1c}

Vitreous fluid and/or urine specimens from 1335 (54%) of the 2487 pilot fatalities (cases) were analyzed for glucose in 1998–2005. In the remaining 1152 (46%) cases, vitreous fluid and urine samples were either not submitted, not available in sufficient amounts, or not of analytical quality to perform glucose analyses. Analyses of the 1335 cases consisted of 363 (27.2%) vitreous fluid, 365 (27.3%) urine, and 607 (45.5%) vitreous fluid and urine specimens. Although the majority of the glucose concentrations found in vitreous fluid and urine ranged from 0 to 99 mg/dL (Fig. 1), there were 26 vitreous fluid and 39 urine samples wherein the glucose concentrations were determined to be ≥100 mg/dL.

As given in Table 1, 43 pilots had elevated glucose in vitreous fluid (>125 mg/dL) and/or in urine (>100 mg/dL). In 29 of the 43 cases, both vitreous fluid and urine samples were analyzed—three had elevated glucose in vitreous fluid only, 19 in urine only, and seven in vitreous fluid, as well as in urine. In three cases, only vitreous fluid was received and analyzed. In 11 cases, only urine was received and analyzed. Glucose was found to be elevated in these 14 samples.

Of the 20 pilots whose blood samples were analyzed for HbA_{1c}, nine had >6% HbA_{1c}—four were known diabetics (HbA_{1c}: 7.1; 8.3; 10.8; and 12.4%) and five were not known diabetics (HbA_{1c}: 6.2; 8.2; 8.3; 8.6; and 13.0%). Urinary glucose concentrations were elevated in all 13 known hyperglycemic pilots.

Analytical toxicology failed to disclose the presence of drugs and/or ethanol in 26 of the 43 pilots. However, drugs were detected in the remaining 17 pilots. Drugs found were amitriptyline, amphetamines, atropine, β-adrenergic blockers, calcium channel blockers, H_1- and H_2-antagonists, lidocaine, midazolam, narcotic and non-narcotic analgesics, pentobarbital, and sildenafil.

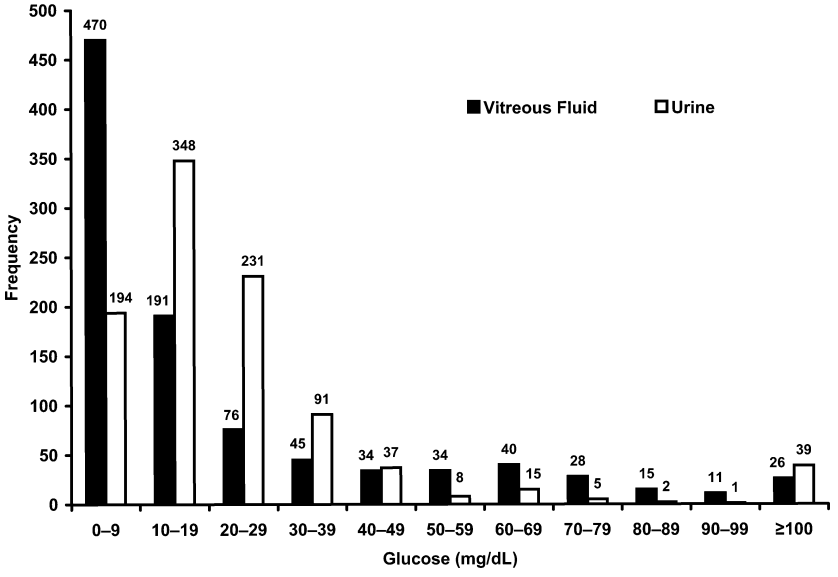

FIG. 1—*Frequency of glucose concentrations in vitreous fluid and urine specimens from the 1335 pilot fatalities.*

TABLE 1—*Glucose and HbA_{1c} concentrations and hyperglycemic medical history of 43 fatally injured pilots and their health and/or medical conditions as cause/factors in those civil aviation accidents (1998–2005).*

Pilots	Vitreous Fluid Glucose (mg/dL)	Urinary Glucose (mg/dL)	Blood HbA_{1c} (%)*	Hyperglycemic Medical History	Pilot's Health and/or Medical Conditions as the Cause/Factors in the Accidents as Determined by the NTSB
1998					
1	45	189	—[†]	Diabetes controlled by hypoglycemic drugs	—
2	12	3055	—	Glycosuria (low renal threshold)	—
3	147	65	—	—	—
4	256	8815	—	Diabetes controlled by diet	—
5	119	760	—	Diabetes controlled by hypoglycemic drugs	—
1999					
6[‡,§]	194	—	—	—	—
7	163	156	—	—	Factor: Pilot's incapacitation due to illegal substances
8	0	105	—	—	—
2000					
9	180	7182	—	Diabetes controlled by hypoglycemic drugs	—
10	42	165	—	—	—
11	—	1438	—	Diabetes controlled by diet	—
12[¶]	47	525	—	—	Cause: Pilot's impairment due to the use of unapproved medication
13	228	24	—	—	—
14	132	—	—	—	—
15	0	1175	—	Diabetes controlled by diet	Factor: Pilot's elevated glucose level
16	76	265	—	—	—
2001					
17	43	365	—	—	—
18	333	31	4.7	—	Cause: Pilot's incapacitation (cardiovascular)
2002					
19	230	1870	8.6	—	—
20	301	6050	12.4	Diabetes controlled by insulin and by oral hypoglycemic drugs	—
21	265	4487	8.2	—	Factor: Hypoxia
22	71	302	5.4	—	—
23	98	4700	10.8	Diabetes controlled by diet and by hypoglycemic drugs	—
24	11	162	8.3	—	—
25	—	1548	—	Diabetes requiring insulin and oral hypoglycemic medication	Cause: Pilot's incapacitation; Factor: The pilot and medical examiner providing false information on the pilot's medical applications
2003					
26	97	435	5.0	—	—
27	100	139	5.2	—	—
28	16	264	5.3	—	—
29	122	162	—	—	—
30	—	369	5.8	Diabetes controlled by hypoglycemic drugs	—
31	—	530	5.1	—	—
32[‡]	126	4700	13.0	—	—
2004					
33	0	1750	—	Diabetes controlled by diet	—
34	—	5700	—	—	—
35	174	—	6.2	—	—
36	—	5450	—	—	—
37	0	786	6.0	—	—
38	—	377	5.9	—	—
2005					
39	—	3350	7.1	Diabetes controlled by diet	—
40	—	2585	8.3	Diabetes controlled by hypoglycemic drugs	—
41	—	120	4.4	—	—
42	—	630	—	—	—
43	101	473	5.1	—	—

*HbA_{1c} analysis was implemented on a routine basis in 2001.
[†]No analysis.
[‡]Unregistered aircraft.
[§]Without medical and flying certificates.
[¶]Without medical certificate.

TABLE 2—*Aviation accident flight categories with elevated glucose and HbA_{1c} concentrations in pilot fatalities (1998–2005).*

Flight Categories*	Pilot Fatalities† Vitreous Fluid Glucose (>125 mg/dL)	Urine Glucose (>100 mg/dL)	Blood HbA_{1c} (>6%)‡
General aviation (Part 91)§	9	33	7
Air taxi and commuter (Part 135)	0	3	0
Ultralight vehicle (Part 103)¶	2	1	1
Public use**	1	1	1

*See reference (13).
†In seven fatalities (cases), glucose was elevated in vitreous fluid as well as in urine.
‡Blood HbA_{1c} analysis was implemented on a routine basis in 2001.
§Five pilots had elevated glucose in both vitreous fluid and urine.
¶Pilots flying unregistered aircraft were also included. One pilot had elevated glucose in both specimen types (vitreous fluid and urine).
**Used for the federal, state, and local government agencies. One pilot had elevated glucose in both specimen types.

Flight Categories

Of the 43 accidents, the highest number of 37 accidents were associated with general aviation flights, followed by three air taxi and commuter, two ultralight vehicle, and one public use flight. Under the general aviation category, vitreous fluid glucose was elevated in four pilots, urine glucose in 28, and vitreous fluid and urine glucose in five (Table 2). Of the nine pilots with elevated HbA_{1c} (>6%), seven were involved with general aviation flights and one each in ultralight vehicle and public use flights.

Airman Medical and Flying Certificates

Of the 43 pilots, one held First-Class, 21 Second-Class, and 18 Third-Class airman medical certificates. The other three pilots were without valid medical certificates. The pilot with the First-Class medical certificate was involved in a general aviation accident. Of the 21 Second-Class medical certificate holders, 17 were involved in general aviation accidents, followed by three in air taxi and commuter and one in public use accident. Out of the 18 pilots with Third-Class medical certificates, 17 were involved in general aviation and one in ultralight vehicle accidents. Of the three non-certificated pilots, two were involved in general aviation accidents and one in an ultralight vehicle accident. Except the First-Class pilot, all pilots with elevated glucose in vitreous fluid and/or urine and with elevated HbA_{1c} were holders of Second- and Third-Class medical certificates (Table 3). The majority of these Second- and Third-Class pilots had commercial and private flying ratings, respectively (Table 4).

TABLE 3—*Airman medical certificate categories with elevated glucose and HbA_{1c} levels in aviation accident pilot fatalities, 1998–2005.*

Medical Certificate Categories*	Pilot Fatalities† Vitreous Fluid Glucose (>125 mg/dL)	Urine Glucose (>100 mg/dL)	Blood HbA_{1c} (>6%)‡
First-Class	0	1	–§
Second-Class	8	19	4
Third-Class	3	16	5

*See reference (14).
†Three pilots without medical certificates are not included. There were seven pilots (six Second-Class and one Third-Class pilots) wherein glucose was elevated in vitreous fluid as well as in urine.
‡Blood HbA_{1c} analysis was implemented on a routine basis in 2001.
§No analysis.

TABLE 4—*Airman flying ratings with elevated glucose and HbA_{1c} concentrations in aviation accident pilot fatalities, 1998–2005.*

Airman Flying Ratings*	Pilot Fatalities† Vitreous Fluid Glucose (>125 mg/dL)	Urine Glucose (>100 mg/dL)	Blood HbA_{1c} (>6%)‡
First-Class medical certificate-holding pilots			
Airline transport	—	1	—§
Commercial	—	—	—
Private	—	—	—
Second-Class medical certificate-holding pilots			
Airline transport¶	3	4	2
Commercial**	5	12	2
Private	0	3	0
Third-Class medical certificate-holding pilots			
Airline transport	—	1	—
Commercial	0	2	1
Private††	3	13	4

*See reference (14).
†Two pilots without medical and flying certificates and one pilot without medical certificate are not included.
‡Blood HbA_{1c} analysis was implemented on a routine basis in 2001.
§No analysis.
¶Two pilots had elevated glucose in vitreous fluid and in urine.
**Four pilots had elevated glucose in vitreous fluid and in urine.
††One pilot had elevated glucose in vitreous fluid and in urine.

With respect to flying ratings, 19 pilots held private, 16 commercial, and seven airline transport certificates. One pilot was non-certificated. Of the 19 private pilots, 18 were involved in general aviation accidents, while one in an ultralight vehicle accident. In the 16 commercial pilots, 12 were involved in general aviation, three in air taxi and commuter, and one in public use accidents. All seven pilots with airline transport pilot certificates were involved in general aviation accidents.

Pilot Medical History and Accident Cause/Factor

Out of the 43 pilots, 14 had an aeromedical history of hyperglycemia—one had renal glycosuria (low renal threshold) and 13 known history of diabetes (Table 1). According to the medical histories, diabetes should have been controlled by diet in five pilots, by hypoglycemic drugs in five, by diet and hypoglycemic drugs in one, and by insulin with oral hypoglycemic drugs in two. The remaining 29 pilots did not have history of hyperglycemia.

Of the 43 accidents, health, medical condition(s), and/or use of medication(s)—authorized or unauthorized—of aviators have been established by the NTSB to be the cause or a factor in five accidents.

1. In one accident, the elevated glucose level of the pilot was a factor. This pilot had a history of diabetes that should have been controlled by diet. The pilot's urinary glucose concentration was 1175 mg/dL. No drugs and ethanol were found in this case.
2. In three accidents, incapacitation of the pilot was the probable cause or a contributing factor.
   a. The pilot of the first accident had elevated urine (156 mg/dL) and vitreous (163 mg/dL) glucose levels, with no reported history of diabetes. The NTSB determined that a factor in the accident was the pilot's incapacitation due to illegal substances. Toxicological analysis revealed amphetamine and methamphetamine in the pilot's blood, urine, and brain.

b. The NTSB determined the cause of the second accident to be "Incapacitation of the pilot (cardiovascular) resulting in his inability to fly the airplane." In addition to autopsy findings of "Fresh posteroseptal myocardial infarction; stenotic coronary atherosclerosis," the toxicological examination revealed that hydrocodone, dihydrocodeine, and hydromorphone were present in the urine. The pilot's glucose levels were 333 mg/dL in the vitreous and 31 mg/dL in the urine, with no reported history of diabetes.
c. The NTSB established the cause of the third accident to be the incapacitation of the pilot, with a contributing factor being the pilot and the Aviation Medical Examiner (AME) providing false information on the pilot's medical applications. The NTSB stated that the pilot had multiple serious medical conditions, including congestive heart failure; coronary heart disease, requiring angioplasty and bypass surgery; and diabetes, requiring insulin and oral hypoglycemic medication. However, neither the pilot nor his AME reported his medical conditions to the FAA, which was known to both individuals at the time of application. The pilot's urinary glucose level was 1548 mg/dL.

3 In the last accident, the NTSB attributed the pilot's impairment due to the use of unapproved medication as the cause. The pilot's glucose levels were 525 mg/dL in the urine and 47 mg/dL in the vitreous. The pilot had no reported history of diabetes. Toxicological analysis revealed the presence of propoxyphene, amitriptyline, and diphenhydramine in the blood.

In 36 accidents, health, medical condition(s), or use of medications by aviators was not determined by the NTSB to be the cause or a factor. Two accidents were not investigated by the NTSB.

Discussion

Postmortem vitreous fluid and urine can be used for glucose analysis to establish diabetes (2,15). Concentrations of glucose >125 mg/dL in vitreous fluid and >100 mg/dL in urine are considered as elevated glucose levels (2,4) and are thus indicative of hyperglycemia. As initial rapid decrease in vitreous humor glucose levels has been reported after death (15–18), a vitreous glucose concentration of ≤125 mg/dL would not necessarily suggest a normal glucose level at the time of death. However, glucose values >125 mg/dL in vitreous fluid and/or >100 mg/dL in urine would certainly be indicative of hyperglycemia. In addition to renal glycosuria and diabetes, elevation of glucose could be related to transient hyperglycemia associated with trauma, stress, and/or medical intervention. For diabetics, the elevated glucose does not provide information on how well the disease had been controlled, but long-term diabetic controls can easily be established by measuring HbA_{1c} in postmortem blood samples (4). Postmortem blood HbA_{1c} values >6.0% correlated well with a known history of diabetes and with the elevated vitreous fluid and/or urine levels in pilots (2,4). Therefore, such elevated postmortem HbA_{1c} values would suggest that diabetes was not properly controlled by the patients (pilots). In addition, some pilots did not know or they did not report to the authorities that they had diabetes. Depending upon the measurement method, clinical ranges of HbA_{1c} vary. Clinically, HbA_{1c} is 3–6% in non-diabetics and 6–9% in controlled diabetics (6,19), although target is <7% HbA_{1c} for diabetic patients and interventions are suggested at HbA_{1c} >7% for difficult-to-control diabetics (20).

Only 3.2% of the 1335 pilots found to be hyperglycemic suggested a very small number of associated aviation accidents. The urinary glucose findings in 13 (30%) of the 43 pilots were consistent with their aeromedical history of diabetes—this number did not include the pilot who had renal glycosuria (low renal threshold). Blood HbA_{1c} analyses of four of the 13 known diabetic pilots revealed that their disease was not well controlled, as their HbA_{1c} values were >6.0%. Furthermore, there were a considerable number of pilots (30 of 43) whose vitreous fluid and/or urine glucose concentrations were elevated and were not known to be hyperglycemic (or diabetic) and blood HbA_{1c} analysis of 15 of the 30 non-diabetic pilots indicated that diabetes in five aviators was not in control, as the HbA_{1c} levels were >6.0% (2,4).

The highest number of pilots with elevated glucose held Second-Class medical certificates, followed by pilots with Third-Class medical certificates. These two groups of pilots were correspondingly rated as commercial and private pilots. The observation of the majority (86%) of the 43 glucose-associated accidents found to be of the general aviation category was consistent with the observations reported in previous studies (5,21–24).

Of the two pilots with known diabetic conditions, elevated glucose was a factor in one accident. Incapacitation of the pilot as the cause of the second accident may not necessarily be attributed to only hyperglycemia. The incapacitation might have been the resultant of the medical conditions, hyperglycemia, hypertension, and ulcer, as postmortem toxicology also disclosed the presence of metoprolol and ranitidine in the pilot.

Overall, the findings from this study revealed that the disease of the diabetic pilots was not in control at the time of accidents. In addition, there were a considerable number of pilots with elevated glucose and HbA_{1c} concentrations, suggesting undiagnosed and unreported diabetic conditions. Therefore, greater attention is necessary in controlling diabetes by aviators in coordination with Aviation Medical Examiners.

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