Legal Medicine 17 (2015) 475–482

Contents lists available at ScienceDirect

Legal Medicine

journal homepage: www.elsevier.com/locate/legalmed

Comprehensive investigation of postmortem glucose levels in blood and body fluids with regard to the cause of death in forensic autopsy cases

Jian-Hua Chen *, Tomomi Michiue, Osamu Inamori-Kawamoto, Sayuko Ikeda, Takaki Ishikawa, Hitoshi Maeda

Department of Legal Medicine, Osaka City University Medical School, Asahi-machi 1-4-3, Abeno, Osaka 545-8585, Japan
Forensic Autopsy Section, Medico-legal Consultation and Postmortem Investigation Support Center (MLCPI-SC), c/o Osaka City University Medical School, Asahi-machi 1-4-3, Abeno, Osaka 545-8585, Japan

ARTICLE INFO

Article history:
Received 28 April 2015
Received in revised form 24 August 2015
Accepted 27 August 2015
Available online 3 September 2015

Keywords:
Forensic pathology
Postmortem biochemistry
Blood
Body fluid
Glucose
Ketone

ABSTRACT

The serum glucose level is regulated within a narrow range by multiple factors under physiological conditions, but is greatly modified in the death process and after death. The present study comprehensively investigated glucose levels in blood and body fluids, including pericardial fluid (PCF), cerebrospinal fluid (CSF) and vitreous humor, reviewing forensic autopsy cases ($n = 672$). Right heart blood glucose level was often higher than at other sites, and the CSF glucose level was the lowest, showing greater dissociation in acute/subacute death cases. The glucose level was higher in the diabetic (high HbA1c) than in the non-diabetic (low HbA1c) group at each site ($p < 0.01–0.0001$). Fatal diabetic ketoacidosis cases had evidently high glucose levels at each site; whereas in the non-diabetic group, blood glucose level was higher in fatal alcohol abuse, saltwater drowning, electrocution, cerebrovascular disease and sudden cardiac death due to ischemic heart disease. Fatal methamphetamine (MA) abuse, sepsis, malnutrition (starvation) and hypoglycemia due to antidiabetics showed markedly lower blood glucose levels. Ketones in bilateral cardiac blood and PCF were increased in diabetic ketoacidosis and fatal alcohol abuse as well as in most cases of hyperthermia (heatstroke), hypothermia (cold exposure) and malnutrition. These findings suggest that combined analysis of glucose, HbA1c and ketones in blood and body fluids is useful to investigate not only fatal diabetic metabolic disorders but also death processes due to other causes, including alcohol and MA abuse, as well as thermal disorders, sepsis and malnutrition.

1. Introduction

Serum glucose is regulated within a narrow range by multiple factors in physiological conditions, but the disorders involving hyperglycemia in diabetes mellitus cause serious complications, including systemic vascular disorder leading to ischemic heart disease, cerebrovascular disease and nephropathy, as well as severe metabolic disorders involving electrolyte disturbances [1–6]. Since these diabetic complications are often involved in the causes of sudden death or contributors to accidental casualties, postmortem diagnosis of diabetes mellitus is important in routine forensic autopsy [7–9]. In addition, hypoglycemia caused by misuse or abuse of antidiabetic drugs or in other pathological conditions may be related to unexpected or violent death [10,11]. Essential biochemical markers for a clinical diagnosis of hyperglycemia and hypoglycemia in diabetes mellitus and other metabolic disorders include serum glucose, hemoglobin A1c (HbA1c) and ketones [12–15]. In forensic biochemistry, previous studies suggested the usefulness of vitreous humor as postmortem material for glucose measurement to investigate metabolic disorders in diabetes mellitus since serum glucose level is modified in the death process and after death, while HbA1c is substantially stable [16–26].

Glucose metabolism may also be disturbed in other functional causes of death, including alcohol abuse and undernutrition or wasting illness, involving ketosis [5,26–31]. In addition, it is known that serum glucose is transiently elevated as part of mental and physical stress responses [32–38]. Thus, postmortem glucose level may be a useful indicator to investigate these causes and modes of death when diabetic disorders are excluded; although there are insufficient data for postmortem glucose levels in blood and body fluids with regard to the cause of death.

Against the above-mentioned background, the present study comprehensively investigated glucose and ketone levels in blood and body fluids, including pericardial fluid (PCF), cerebrospinal

* Corresponding author at: Department of Legal Medicine, Osaka City University Medical School, Asahi-machi 1-4-3, Abeno, Osaka 545-8585, Japan.
E-mail address: m2049040@med.osaka-cu.ac.jp (J.-H. Chen).

http://dx.doi.org/10.1016/j.legalmed.2015.08.004
1344-6223/

fluid (CSF) and vitreous humor (VH), reviewing forensic autopsy cases within 2 days postmortem, to examine their efficacy in diagnosis of the cause and mode of death.

2. Materials and methods

2.1. Autopsy materials

Biochemical data of serial medicolegal autopsy cases 0–100 years of age with a postmortem time within 48 h (n = 672: 473 males and 199 females) over a period of 7 years (2007–2014) were reviewed. Bilateral VHs and blood samples from bilateral cardiac chamber and external iliac vein, as well as PCF, CSF and urine, were collected using sterile syringes at autopsy; blood, PCF, CSF and urine were drawn after opening the body cavities. The serum was immediately separated by centrifugation, and all samples were stored at −20 °C until use.

The causes of death were classified on routine macromorphological, micropathological and toxicological bases, as shown in Table 1. Fatal hypoglycemia was defined based on circumstantial evidence of antidiabetic misuse and toxicological findings in consideration of low VH glucose level (<1.8 mg/dL), excluding other causes of death [5,39–41]. Diagnostic criteria of fatal liver dysfunction involving cirrhosis included pathological findings of advanced nodular fibrosis accompanied by diffuse hepatocyte degeneration and necrosis with marked cholestasis [42], supplemented with postmortem serum biochemical findings of low albumin, low cholesterol, low cholinesterase, and high bilirubin consistent with clinical features [43–45], excluding other causes of death. For these groups, case history as well as demographic, pathological, biochemical and toxicological data were collected from autopsy documents. Well-documented, clearly accountable cases were collected for all groups, to establish the cause of death, postmortem interval and survival time. The postmortem interval was defined as the time from the estimated time of death to autopsy. The survival time was the period from the onset of fatal insult to death.

2.2. Analytical procedure

Biochemical data reviewed in the present study were those of glucose, ketones, HbA1c, catecholamines and urinalysis. Measurement procedures were: a hexokinase-UV method for glucose (clinical peripheral venous reference interval, 70–109 mg/dL) [46], an enzymatic assay for ketones (clinical serum reference interval, 28–120 μmol/L) [47], a latex agglutination method for glycated hemoglobin (HbA1c: clinical reference interval, 4.6–6.2%) [48] and high-performance liquid chromatography for catecholamines, including adrenaline (Adr), noradrenaline (Nad) and dopamine (DA) [49–51]. VH ketone levels could not be examined due to small amounts of collected samples. Urinalysis was performed using a versatile urine analysis system, AUTION ELEVEN™ AE-4020 (Arkray, Inc., Kyoto, Japan).

Blood %carboxyhemoglobin (COHb) saturation was analyzed on a CO-oximeter system (Ciba Corning 270, New York, or Radiometer,

Table 1
Case profiles (n = 672).

Cause of death	n	Male/female	Age (years)		Survival time (hours)		With/without CPR	Postmortem time (hours)	
			Range	Median	Range	Median		Range	Median
Injury	197	159/38	0.4–100	58	0.1–24	3.0	125/72	5–48	21.7
Sharp instrument injury	42	33/9	27–91	58	0.1–16	0.5	24/18	5–40	20.2
Blunt injury	155	126/29	0.4–100	58	0.1–24	3.5	101/54	5–48	22.0
Acute mechanical asphyxiation	69	43/26	0.1–87	57	<0.5	–	0/69	8–46	23.3
Hanging and strangulation	56	35/21	0.1–87	57	<0.5	–	0/56	9–46	23.4
Others	13	8/5	0.4–79	63	<0.5	–	0/13	8–38	23.3
Drowning	34	21/13	1–96	65	<0.5	–	0/34	9–44	23.4
Fresh water	13	9/4	51–89	65	<0.5	–	0/13	13–44	32.1
Salt water	5	3/2	19–79	50	<0.5	–	0/5	23–31	31.0
Bath water	16	9/7	1–96	65	<0.5	–	0/16	9–41	23.9
Fatal methamphetamine abuse	15	12/3	33–62	44	0.5–24	6.0	5/10	7–42	27.7
Sedative-hypnotic intoxication	15	8/7	15–61	37	3–24	6.0	4/11	7–46	27.5
Fatal alcohol abuse	4	1/3	29–60	43	6	6.0	0/4	29–39	35.1
Other intoxications	13	9/4	14–75	45	0.2–24	6.0	4/9	18–31	26.8
Fire fatality	138	101/37	33–93	66	<0.5	–	0/138	7–46	18.6
COHb <60%	74	52/22	32–94	68	<0.5	–	0/74	7–40	19.6
COHb >60%	64	49/15	0.6–95	63	<0.5	–	0/64	9–46	17.7
Hyperthermia	22	12/10	0.6–95	65	2.5–24	6.0	9/13	11–47	29.1
Hypothermia	13	6/7	26–84	72	6–24	6.0	3/10	15–37	29.5
Acute ischemic heart disease	26	22/4	0.3–92	61	0.3–24	0.5	17/9	14–37	21.7
Chronic congestive heart disease	13	8/5	1–91	54	Unknown	–	7/6	13–45	20.0
Hemopericardium	7	6/1	0.6–72	64	0.3–3	0.5	6/1	13–30	21.8
Right ventricular cardiomyopathy	8	4/4	37–87	64	0.5–24	0.5	4/4	6–37	26.8
Pulmonary thromboembolism	5	2/3	31–54	39	0.4–10	3.0	4/1	9–36	31.3
Cerebrovascular disease	12	7/5	14–80	52	0.5–24	3.0	2/10	11–38	30.2
Fatal ketoacidosis	3	2/1	22–71	33	Unknown	–	1/2	24–38	29.0
Hypoglycemia	3	1/2	41–55	43	0.5–48	6.0	1/2	18–48	25.5
Fatal liver dysfunction involving cirrhosis	6	6/0	45–69	54	Unknown	–	2/4	13–30	19.3
Electrocution	3	3/0	23–65	33	<0.5	–	3/0	23–26	23.4
Sepsis	15	11/4	34–87	66	24–336	188	10/5	9–47	25.4
Malnutrition	7	2/5	21–92	66	Unknown	–	3/4	17–39	31.0
Pneumonia	44	27/17	0.1–91	8	Unknown	–	29/15	9–39	23.7
Total	672	473/199	0.1–100	60	0.1–336	0.5	239/433	5–48	23.2

COHb, carboxyhemoglobin; CPR, cardiopulmonary resuscitation.