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Cause and manner of death and phase of the blood alcohol curve

R.A. Lahti [a,*], J. Pitkäniemi [b,c], A.W. Jones [d], A. Sajantila [a,e], K. Poikolainen [b], E. Vuori [a]

[a] Department of Forensic Medicine, Hjelt Institute, University of Helsinki, Finland
[b] Department of Public Health, Hjelt Institute, University of Helsinki, Finland
[c] Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland
[d] Department of Clinical Pharmacology, University of Linköping, Linköping, Sweden
[e] Institute of Applied Genetics, Department of Molecular and Medical Genetics, University of North Texas Health Science Center, Fort Worth, TX, USA

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ABSTRACT

In a large number of forensic autopsies ($N = 28{,}184$) the concentrations of ethanol in femoral blood and bladder urine were determined and the urine-to-blood concentration ratios of ethanol were calculated. Based on the differences in ethanol concentration between urine and blood, the deaths were classified as having occurred during the absorptive, the peak or the post-absorptive phase of the blood–alcohol curve. Most people died in the post-absorptive phase, $N = 24{,}223$ (86%), whereas 1538 individuals (5.5%) were still absorbing alcohol and 2423 (8.6%) were at or close to the peak BAC at time of death. Both blood–alcohol concentration (BAC) and urine–alcohol concentration (UAC) were significantly higher in the post-absorptive phase ($p < 0.001$). The proportions of people dying in the absorptive and peak phases increased with advancing age. The cause of death (CoD) and manner of death (MoD) according to death certificates were compared with phase of the blood–alcohol curve using a multinomial regression model with and without making adjustment for possible effects of age, gender and BAC. The relative risk (RR) and relative risk ratios (RRR) showed some associations between CoD and phase of the blood–alcohol curve. Undetermined MoD was significantly higher in the absorptive phase compared with the post-absorptive phase (RRR = 2.12). Deaths related to esophagus, stomach and duodenum (RRR = 2.04) and alcoholic liver diseases (RRR = 1.85) were significantly higher at or close to peak phase compared to the post-absorptive phase. Road-traffic fatalities were more prevalent in the peak BAC phase (RRR = 1.33) and deaths by accidental falls were less in the absorptive phase (RRR = 0.58) compared with the post-absorptive phase. The phase of alcohol intoxication seems relevant to consider by forensic experts when alcohol-related deaths are investigated.

1. Introduction

Acute alcohol intoxication (drunkenness) denotes a clinical state in which cerebral functions are impaired by the actions of the depressant drug ethanol, which slows functioning of the brain [1]. Over-consumption of alcohol and drunkenness are common findings when unnatural deaths are investigated in clinical and forensic medicine [2,3]. Many studies verify that the signs and symptoms of alcohol intoxication and drunkenness are more pronounced at higher BAC, albeit with large inter-subject variations [4,5].

After drinking small doses of alcohol to reach fairly low BAC (<0.5 mg/g), people become more talkative and are less inhibited [4]. Drinking larger amounts of alcohol to reach higher BAC (>1.0 mg/g) leads to mental confusion and impairment of cognitive and psychomotor functioning. Massive amounts of alcohol resulting in very high BAC (>3.0 mg/g) leads to gross intoxication, stupor and risk of death from respiratory depression and circulatory collapse [6,7]. Also important for the clinical manifestations of drunkenness are the person's age, gender and previous drinking experience (habituation) so that tolerance develops [8].

Controlled drinking experiments verify that both subjective and objective measures of alcohol influence are more pronounced on the rising portion of the BAC curve compared with the declining BAC phase several hours post-drinking [9,10]. This phenomenon is referred to as acute tolerance or the Mellanby effect [11,12]. Euphoria and excitement are common on the rising phase of the BAC curve, which corresponds to a state of increasing drunkenness, whereas dysphoria and fatigue dominate on the post-absorptive

* Corresponding author at: Department of Forensic Medicine, Hjelt Institute, University of Helsinki, P.O. Box 40, Helsinki 00014, Finland. Tel.: +358 2941 27447.
E-mail address: raimo.lahti@kolumbus.fi (R.A. Lahti).

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phase during recovery from the acute effects of ethanol [13]. Whether a person is in the absorptive, peak or post-absorptive phase at time of death will depend on many factors, including drinking pattern, size of the last dose, intake of food and the time elapsed after end of drinking until the time of death.

Human experiments in which subjects drank a bolus dose of ethanol (0.5–1.25 g/kg) verify that BAC increases rapidly (rising phase of intoxication) before reaching a peak concentration in blood at 30–90 min after drinking [14]. However, the time to reach the peak BAC might be different under real-world drinking conditions when repetitive drinking occurs over several hours [15]. Regardless of the drinking pattern, the entire dose of alcohol seems to be fully absorbed by about 2 h after the end of drinking [16].

Most of the ethanol ingested (95–98%) undergoes oxidative metabolism in the liver and only a small fraction (2–5%) is excreted unchanged in urine and breath [17,18]. The principal enzyme responsible for metabolism of ethanol (alcohol dehydrogenase) is saturated with substrate when BAC passes 0.2 mg/g and ethanol is then eliminated from blood at a constant rate per unit time, as expected for zero-order kinetics [19]. The disappearance rate of alcohol from blood ranges from 0.10 to 0.20 mg/g/h for most people, although faster rates are commonly observed in heavy drinkers and alcoholics, owing to induction of a microsomal enzyme (CYP2E1) that occurs after a period of continuous heavy drinking [20].

The concentration relationships between ethanol in blood and bladder urine have been extensively studied in living and deceased persons [21,22]. For freshly produced (ureter) urine the UAC/BAC ratio is ~1.25:1, which corresponds to differences in water content of urine (~100%) compared with blood (~80%) [23]. However, urine is stored in the bladder until voided and during this time the BAC changes, either increasing during the absorptive phase or decreasing in the post-absorptive phase. Because of this temporal variation in BAC and UAC profiles, the concentrations of ethanol in blood and urine are shifted in time with UAC being lower than BAC during the absorptive phase and vice versa during the post-absorptive phase [24]. The UAC/BAC ratios of ethanol in the post-absorptive phase varies from 1.3 to 1.4:1 on average but might be higher depending on residence time in the bladder since the previous void [23].

The temporal variation in concentration–time profiles of ethanol in blood and bladder urine after drinking a bolus dose can be used to judge the position of the BAC curve (absorptive vs post-absorptive) when samples were taken [22]. The relationship between UAC and BAC under real-world drinking conditions has not been studied extensively, although a lot of information is available from samples obtained from drinking drivers, involving first and second voids [22,25].

This aim of this study was to investigate if an association existed between phase of alcohol intoxication (absorptive, peak or post-absorptive phase) and CoD and MoD according to official death certificates. To the best of our knowledge, this is the first time such a large forensic autopsy material has been subjected to this type of analysis.

2. Materials and methods

2.1. Death investigations in Finland

The police authorities in Finland investigate all sudden, unnatural and otherwise unexpected deaths in close co-operation with a forensic pathologist. The latter is responsible for performing the autopsy and collecting appropriate specimens for auxiliary tests, such as toxicology and histology. The range of drugs, chemicals and poisons analyzed depends on requests from the individual pathologists. In practice, BAC and UAC are routinely analyzed because ethanol abuse and ethanol intoxication is common in unnatural death investigations [26]. According to the Official Finnish Statistical Year Book, between the years 2000 and 2010 there were 48,000–51,000 deaths annually and of these 21–24% was subjected to a complete medico-legal autopsy.

The results of analytical toxicology provide important information when CoD and MoD are investigated by forensic pathologists. The legal drug ethanol tops the list of psychoactive substances identified in post-mortem toxicology in Sweden [27], Finland [28] and presumably in many other nations.

Head-space gas chromatography (HS-GC) was utilized to determine BAC and UAC. The method is accredited since 1997 and the concentration reported is the mean of four determinations done on femoral blood samples. The HC-GC instrument is fitted with two different stationary phases (columns) giving unique retention times for ethanol and furthermore, two different internal standards were used. Analytical toxicology in Finland is centralized to the Laboratory of Forensic Toxicology at the Department of Forensic Medicine (LFT-DFM), at University of Helsinki.

This retrospective study was done by searching a national forensic toxicology database covering the years 2000–2010. We located $N = 28{,}201$ forensic autopsies in which age, gender BAC and UAC results were available. Ethanol concentrations in blood and urine were determined by a well established HS-GC method described briefly above. The analytical cut-off concentration used to report ante-mortem drinking was BAC $\geq$ 0.20 mg/g (20 mg/100 mL or 0.02 g%), which helps to exclude cases when small amounts of ethanol might have been produced after death. If the dead bodies showed obvious signs of putrefaction or were already embalmed these were omitted as were deaths when the age of the deceased was not known.

The remaining 28,184 autopsies were categorized according to the likely stage of alcohol intoxication at the time of death based on concentrations of ethanol in blood and urine. Deaths in the absorptive-phase of the BAC curve were defined as those when BAC > UAC by 0.1 mg/g or more. Deaths occurring at or close to the peak BAC were defined as those when BAC and UAC were the same or within ±0.1 mg/g of each other. Most deaths occurred in the post-absorptive phase of the BAC curve when UAC was greater than BAC by 0.1 mg/g or more.

2.2. Cause and manner of death

Information about CoD and MoD was obtained from the LFT-DFM database and these were classified as natural death (diseases), accidental death, suicide, homicide or undetermined. When CoD was natural, these fatalities were grouped according to World Health Organization (WHO) International Classification of Diseases, 10th Revision (ICD-10) as follows:

Diabetes and other disorders of glucose regulation (E10–E16); alcoholism and other types of "-isms" (F10–F19); epilepsy and status epilepticus (G40, G41); hypertensive diseases (I10–I15); ischemic heart diseases (I20–I25); alcoholic cardiomyopathy (I42.6); pulmonary embolism, cardiac arrest and arrythmias, heart failure, diseases of veins (I26, I46–I51, I80–I89); cerebrovascular diseases (I60–I69); bronchopulmonary infections (J10–J42); diseases of esophagus, stomach and duodenum (K20–K31); alcoholic liver diseases (K70); and acute pancreatitis and alcohol-induced chronic pancreatitis (K85, K86.0).

The accidental deaths were further subdivided into poisoning (of any kind), traffic accident, fall injuries, either on same level or from a height, drowning (submersion), and suffocation. The few other types of accidental death were omitted.

2.3. Statistical analysis

The existence of a relationship between CoD and phase of alcohol intoxication was determined by a multivariate analysis