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The relationship between alcohol elimination rate and increasing blood alcohol concentration—Calculated from two consecutive blood specimens

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Abstract

In the period 1991–2005, a blood–alcohol concentration (BAC) analysis was carried out at the Institute of forensic medicine in Novi Sad including 2023 two consecutive blood specimens using the Headspace Gas Chromatography method. Cases with no alcohol concentration values, as well as cases where blood samples were taken within 1 h after the criminal act, were not taken into consideration. Following this rule, 1198 cases were considered in this study and all samples were grouped in 29 ranges of BAC_1 of $\Delta_{BAC} = 0.1$ g/kg, starting from 0.1–0.19 g/kg to 2.9–2.99 g/kg of absolute alcohol.

Gathered results and elimination curve differ from the zero-order model of elimination proposed by Widmark and point to an elimination process similar to a well-known Michaelis-Menten elimination kinetics model and its variants. Results reported in this study show dependence of alcohol elimination rate (β-slope) and BAC value. The analysis of β_{60}-slope versus BAC shows that a correlation between β_{60} (y) and BAC (x) has a logarithmic trend line. The value of alcohol elimination rate shows a slight increment with increase of BAC alcohol, with the mean value of $\beta_{60} = 0.221 \pm 0.075$ g/kg. Differences in values of β_{60} among consecutive intervals of $\Delta_{BAC} = 0.1$ g/kg are not significant ($p > 0.05$). When obtained samples were grouped into ranges of 0.5 g/kg each in these intervals β_{60} had the following values by range: 0.1–0.49 g/kg = 0.139 g/kg $\pm$ 0.035; 0.5–0.99 g/kg = 0.184 g/kg $\pm$ 0.043; 1–1.49 g/kg = 0.213 g/kg $\pm$ 0.052; 1.5–1.99 g/kg = 0.239 g/kg $\pm$ 0.058; 2–2.49 g/kg = 0.265 g/kg $\pm$ 0.073; 2.5–2.99 g/kg = 0.306 g/kg $\pm$ 0.096. Differences in values of beta slope among consecutive intervals of $\Delta_{BAC} = 0.5$ g/kg are significant ($p < 0.01$).

The elimination curve in the BAC interval 0.5–2.5 g/kg has a linear trend, while beta-slope (y)/BAC (x) correlation is given as $\beta_{60} = 0.15$ g/kg + (0.05 g/kg $\times$ BAC).

Retrograde calculation of the blood alcohol concentration in *tempore criminis* (BAC_{tc}) based on the determined alcohol concentration in the blood specimen (BAC_t) shows a statistically significant difference between BAC_{tc} calculated using a standard zero-order model versus corrected methodology. The higher the BAC_t and the longer the calculation time, the greater and statistically more significant ($p < 0.01$) is the difference between the calculated values of BAC_{tc}.

Keywords: Forensic medicine; Ethanol disappearance; Alcohol elimination; Disappearance rate (β-slope)

1. Introduction

Systematic research has already confirmed that alcohol is a significant cause not only of traffic accidents, but also of many other types of accidents and criminal acts. Forensic pathologists and toxicologists act in such cases as expert witnesses, with the task of determining blood alcohol concentration in ‘‘*tempore criminis*’’ (BAC_{tc}), either in retrograde manner, or on the basis of the dynamics of alcohol consumption. In our country BAC is calculated using the generally accepted Widmark equation and constant elimination rate – zero-order model (β_{60}-slope of 0.15 g/kg), regardless of the initial BAC, although the limitations of this model have been known for a long time.

A frequent occurrence of a phenomenon known in court practice as hip-flask defense, to us known as ‘‘cognac alibi’’ defense model [1], has led to establishing a practice of taking

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two blood samples from perpetrators of criminal acts within 60 min apart.

The results of the analyses indicated that there were no standard values for β-slope per hour. Some counsels adapted to this fact and, depending on whether it is more convenient for the defendant to have a lower (in traffic accidents) or higher alcohol concentration (in murder cases, for example) they usually ask the expert witness to use standard β-slope in one case, and in another the one obtained by analysis, arguing that this value is a fact. Such differences in approach, to which forensic medicine experts have objected more or less successfully, cause confusion in court and at the same time, disobey the principle of equality of citizens in the court of law.

These facts have influenced our decision to analyze the 15-year data, i.e. the values of β-slope in cases where two blood samples were taken.

2. Material and methods

Following a strict protocol, the blood samples were collected at the same location, at the Department of emergency medicine of the Clinical Center in Novi Sad, Serbia. The specimens (3 mL of blood) were collected directly into plastic tubes containing 30 mg of sodium fluoride. Each tube was marked with an identification code, sealed, properly stored and sent to the Toxicology Laboratory of the Institute of forensic medicine. A police voucher accompanied every specimen, containing the name of the suspect, time of arrest and time of blood sampling. The police kept the suspects under constant surveillance, from the time of arrest to the time of blood sampling. Therefore, consumption of alcohol after arrest was practically impossible.

In the period 1991–2005, in 2023 cases two consecutive blood specimens' analyses were performed at the Institute of forensic medicine in Novi Sad. Two blood specimens were taken from each suspect with a 30–60 min interval. The cases with no alcohol concentration values, as well as cases where blood samples were taken too soon (within 1 h) after the criminal act, were not taken into consideration. Following this rule, 1198 cases were considered in this study.

Blood analyses were performed using an exact and precise methodology—Headspace Gas Chromatography (*Hewlett Packard*). Data on blood alcohol concentration at first (BAC_1) and second sampling (BAC_2), the time of first (t_1) and second (t_2) blood sampling were analyzed.

In 84% of cases ($N = 1005$) the second sample was taken within 60 min. The apparent alcohol elimination rate was calculated using the following formula:

$$\beta_{60} = BAC_1 - BAC_2.$$

In 16% of cases ($N = 193$) the second sample was taken 30–59 min later, and the elimination rate (β-slope) was calculated using the following formula:

$$\beta_{60} = (BAC_1 - BAC_2) \times \left[\frac{60}{t_2 - t_1}\right].$$

Statistical analysis was performed by calculating mean values of alcohol concentration, standard deviation and median within 0.1 g/kg and 0.5 g/kg intervals.

3. Results

The calculated blood alcohol concentration in the first sample (BAC_1) was between 0.1 g/kg and 2.99 g/kg of absolute alcohol, with the mean of 1.442 g/kg, whereas in the second sample (BAC_2) it was 1.227 g/kg. All samples were grouped in 29 ranges of BAC_1 of 0.1 g/kg, starting from 0.1–0.19 g/kg to 2.9–2.99 g/kg. The arithmetic mean value (Fig. 1) and standard deviation of the alcohol elimination rate were calculated for each group. The β-slope value ranged between 0.054 g/kg and 0.648 g/kg, depending on the BAC with the mean value of 0.221 g/kg $\pm$ 0.075 (S.D.).

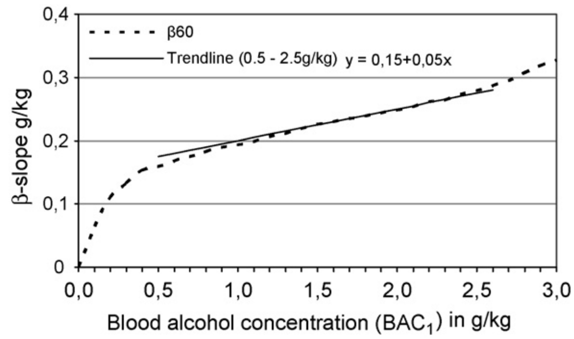

Fig. 1. Mean values of β_{60}-slope within the range of 0.1 g/kg per group (dashed), and linear trend line for interval 0.5–2.5 g/kg (continual line).

Apart from that, all samples were sorted into six additional groups within 0.5 g/kg of blood alcohol concentration range. The mean value, standard deviation and median of the alcohol elimination factor were calculated for each group (Table 1).

It is shown on the alcohol elimination curve that there is a linear beta-slope increase in the 0.5–2.5 g/kg interval. Data analysis in this interval has shown that correlation between beta-slope (y) and BAC_1 (x) has the following relationship: $y = 0.15 + 0.05x$ (Fig. 1), i.e.:

$$\beta_{60} = 0.15\,\mathrm{g/kg} + (0.05\,\mathrm{g/kg} \times \mathrm{BAC}).$$

In other words, for any increase of the BAC value by $\Delta_{BAC} = 0.1$ g/kg beta-slope averagely increases by $\Delta_{\beta_{60}} = 0.005$ g/kg.

According to presented data, it could be concluded that if there is an β_{60} increase depending on BAC increase, the elimination time needed for $\Delta_{BAC} = 0.1$ g/kg is not always the same, but decreases with increased BAC, which could be described by the following equation:

$$\Delta_t = \frac{0.1\,\mathrm{g/kg}}{0.15\,\mathrm{g/kg} + (0.05\,\mathrm{g/kg} \times \mathrm{BAC}_t)}.$$

Calculated Δ_t values in different BACs in 0.1 g/kg intervals are shown in Fig. 2. It is shown that correlation between Δ_t (y) and BAC_1 (x) has a linear trend:

$$\Delta_t = 0.6 - 0.1 \times \mathrm{BAC}_1.$$

Table 1
Values of β_{60}-slope within range of 0.5 g/kg per group

BAC range (g/kg)	Number of cases	Mean value (g/kg)	S.D.	Median (g/kg)
<0.5	147	0.139	0.035	0.142
0.5–0.99	229	0.184	0.043	0.181
1.0–1.49	226	0.213	0.052	0.206
1.5–1.99	261	0.239	0.058	0.235
2.0–2.49	185	0.265	0.073	0.249
2.5–2.99	110	0.306	0.096	0.279
0.1–2.99	1198	0.221	0.075	0.209

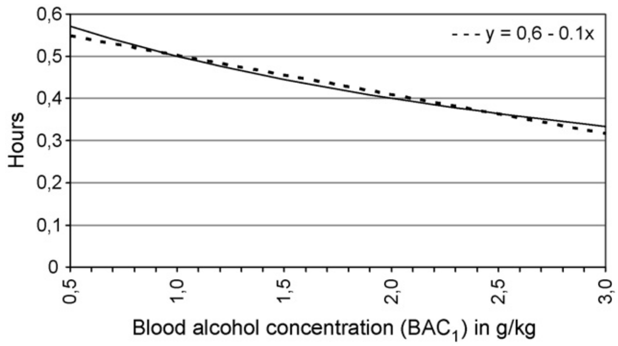

Fig. 2. Elimination time within the range of 0.1 g/kg in different values of BAC.

4. Discussion

The use of the generally accepted zero-order model of ethanol elimination, first proposed by Widmark in forensic expertise, has been routinely applied, although the limitations of this model have been known for a long time.

Previous researches of the pharmacokinetic disposition of ethanol metabolism in biological systems were mainly based on experiments on both humans [2–14] and animals [15–17]. Mean values differed both in animals and humans, depending on the quantity of alcohol intake by kilogram of body mass and way of application (ingestion versus intravenous injection). Discrepancies in reported results clearly show a difference in alcohol elimination as a function of BAC, although they are closer to Widmark's mean values in studies performed on human subjects, probably because smaller quantities of alcohol were used in experiments (mostly 0.5–1 g/kg of body mass).

Results reported in this study show dependence of β-slope and BAC value. The curve shape is similar to the non-linear pharmacokinetic curve, which has a mathematic interpretation proposed by Michaelis-Menton [18] equation for enzyme kinetics. The analysis of alcohol elimination rate (β_{60}) versus BAC shows a hyperbolic shape plot. A correlation between beta-slope (y) and BAC (x) has a logarithmic trend line (Fig. 3). This is especially true for elimination of lower alcohol concentration from blood (BAC up to 0.5 g/kg), where a significant difference ($p < 0.05$) between intervals of 0.1 g/kg has been established. Above this value, differences in values of alcohol elimination rates among consecutive intervals are not significant ($p > 0.05$). The beta slope shows a slight increment with increase of BAC, which was also confirmed by other researchers [10]. When obtained samples were grouped into ranges of $\Delta_{\mathrm{BAC}} = 0.5$ g/kg (Table 1) differences in values of beta slope among consecutive intervals are significant ($p < 0.01$).

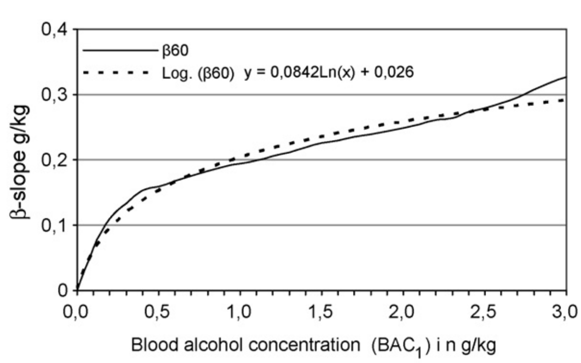

Fig. 3. Mean values of β_{60}-slope within the range of 0.1 g/kg per group (continuous line), and trend line (dotted).

Large studies on alcohol elimination using the two blood sample method are scarce. A major limitation of this method is that the validity of results depends on the liability and accuracy of persons registering the time of sampling, which opens the question of sampling validity. However, a great number of samples minimize possible errors. The next weak point of this kind of study is that at the time of first sample taking the examinee may still be in the phase of absorption of previously consumed alcohol. In order to exclude such cases, we analyzed only cases where at least one hour passed from the time of alcohol consumption and blood sampling. Nevertheless, we cannot exclude the possibility that some suspects did not fully enter the elimination phase at the time of blood sampling. In other words, they might be considered as being in the plateau phase of the BAC profile versus time curve, which is the case in subjects who consume great quantities of food with drinks of lower alcohol concentration.

In the Netherlands, an analysis was carried out by Neuteboom and Jones [19] using the two consecutive blood sample method in 1314 drunken drivers. The reported mean alcohol elimination rate was 0.22 mg/mL/h, which is not different from mean values obtained in our study ($\beta_{60} = 0.221$ g/kg). In the study of 1090 double blood samples, Jones and Andersen [20] found an overall mean alcohol elimination rate of 0.191 mg/mL/h, while other researchers reported lower mean values: Lund [21]—mean value of 17 mg/mL/h, and in several German studies [22] based on double blood sampling, the mean value of alcohol elimination rate was 0.18 mg/mL/h.

Using a capacity-limited model, similar to the Michaelis-Menton model for enzyme kinetics, Holford [23] calculated the maximum rate of ethanol elimination of 8.5 g/h/70 kg-equivalent to the blood ethanol elimination rate of 230 mg/L/h, while Wilkinson et al. [24] found the average $V_{\max}$ of 0.232 mg/mL/h. This is in concordance with the mean value reported in our study.

Our study, as well as other published reports, shows that the value of the elimination parameter per hour may be extremely high: in small number of cases it was 0.4–0.6 g/kg/h, and the maximal reported value was 0.648 mg/mL/h, whereas higher rates seem to be associated with higher initial BAC. Generally speaking, significant variations were found in alcohol elimination rates within one range of BAC of 0.1 g/kg, for example in BAC_1 1.4–1.49 g/kg the value of β_{60}-slope ranged 0.14–0.353 g/kg.

Studies of ethanol pharmacokinetics show that there are numerous factors affecting alcohol elimination [25]. In a number of papers, sex differences in blood alcohol elimination rate have been reported. Experiments conducted by Taylor et al. [12] and by Seidl et al. [26] showed faster alcohol elimination

Table 2
Comparison of the retrograde calculated BAC_{tc} vs. β_{60} = 0.15 g/kg (row a), β_{60} = 0.15 g/kg + 0.05 g/kg × BAC (row b), with corrected factor of time (Δ_t) needed for elimination of Δ_{BAC} = 0.1 g/kg (row c)

BAC_t (g/kg)		BAC_{tc} g/kg vs. time (h)											
		0^{15}	0^{30}	0^{45}	1^{00}	1^{15}	1^{30}	1^{45}	2^{00}	2^{15}	2^{30}	2^{45}	3^{00}
0.5	a	0.538	0.575	0.613	0.650	0.688	0.725	0.763	0.800	0.838	0.875	0.913	0.950
	b	0.544	0.588	0.631	0.675	0.719	0.763	0.806	0.850	0.894	0.938	0.981	1.025
	c	0.545	0.590	0.637	0.684	0.731	0.778	0.826	0.875	0.923	0.973	1.024	1.075
1.0	a	1.038	1.075	1.113	1.15	1.188	1.225	1.262	1.300	1.337	1.375	1.412	1.450
	b	1.050	1.100	1.150	1.200	1.250	1.300	1.350	1.400	1.450	1.500	1.550	1.600
	c	1.051	1.103	1.155	1.207	1.261	1.315	1.369	1.422	1.477	1.535	1.592	1.649
1.5	a	1.538	1.575	1.613	1.65	1.688	1.725	1.762	1.800	1.837	1.875	1.912	1.950
	b	1.556	1.613	1.669	1.725	1.781	1.838	1.894	1.95	2.006	2.063	2.119	2.1750
	c	1.558	1.615	1.671	1.728	1.788	1.850	1.913	1.975	2.038	2.000	2.163	2.226
2.0	a	2.038	2.075	2.113	2.15	2.188	2.225	2.262	2.3	2.337	2.375	2.412	2.450
	b	2.063	2.125	2.188	2.251	2.313	2.375	2.438	2.500	2.563	2.625	2.688	2.750
	c	2.066	2.128	2.191	2.255	2.318	2.384	2.448	2.514	2.586	2.657	2.729	2.800
2.5	a	2.538	2.575	2.613	2.65	2.688	2.725	2.762	2.799	2.836	2.873	2.910	2.947
	b	2.569	2.637	2.706	2.775	2.844	2.912	2.980	3.048				
	c	2.571	2.643	2.714	2.786	2.860	2.935	3.010					

rates in women, while Jones and Andersen [20] found that the mean value of beta-slope among females was 0.214 mg/mL/h compared with 0.189 mg/mL/h in males. In our study, no gender differences were established, because the number of investigated women was extremely small (0.5%).

Experimental results of several investigators show that chronic alcohol consumption also affects the elimination rate [3,4,13], i.e. that the rate of ethanol elimination increases with drinking experience. This finding may be the consequence of high individual activity of liver alcohol oxidizing system, or simultaneous distribution and alcohol equivalence between blood and tissue water [11,20].

The results reported in this study are in concordance with results of recent studies using the same methodology. However, these results raise the question of their implications in forensic practice, since they cannot simply be ignored. How big a mistake can a forensic medicine expert make by using standard values of β-slope [8,19,25]? To answer this question, we performed retrograde calculation of BAC_{tc} using three different methods in the interval of BAC_t = 0.5–2.5 g/kg, on every 15 min, the time frame of 3 h:

(a) First, BAC_{tc} was calculated using zero-order model and known formulas for retrograde calculation of BAC_{tc} on the basis of BAC_t found in the blood specimen taken within certain time interval after critical event $BAC_{tc} = BAC_t + (\beta \times t)$, as well as using standard value of elimination factor β_{60} = 0.15 g/kg (Table 2, row a).

(b) Consecutively, aforementioned equation has been modified by corrected beta-slope value β_{60} = 0.15 g/kg + (0.05 g/kg × BAC):

$$BAC_{tc} = BAC_t + [0.15\,\mathrm{g/kg} + (0.05\,\mathrm{g/kg} \times BAC_t)] \times t,$$

followed by calculation according to the same initial values (Table 2, row b).

(c) The main concern of the third applied method was that the time interval needed for the elimination of Δ_{BAC} = 0.1 g/kg is not always the same, but decreases as the BAC increases. In the first step the beta-slope for BAC_t value has been calculated, followed by the time period (Δ_t) needed for the BAC change of Δ_{BAC} = 0.1 g/kg. The whole procedure has been repeated for the new value of BAC_t + 0.1 g/kg within certain time interval (Table 2, row c).

Obtained results have shown that there is a statistically significant difference ($p < 0.05$) in the cases of initially low BAC_t (0.5 g/kg) values, where retrograde calculation ((a) versus (b)) was applied. However, observed relative difference is not high. The difference between methods (b) and (c) is not statistically significant ($p > 0.05$).

In the cases of high BAC_t (2.0 g/kg) values, difference in calculated values of BAC_{tc} obtained by method (a) versus method (b) is statistically significant ($p < 0.01$) and within the first hour could be found at the level of the second decimal point, after which it could be seen at the first decimal point (0.3 g/kg maximal). Difference in calculated BAC_{tc} between methods (b) and (c) is not statistically significant ($p > 0.05$).

5. Conclusion

Results reported in this study demonstrated dependence of β-slope and BAC value. The elimination curve in the BAC interval 0.5–2.5 g/kg has linear trend and for any increase of the BAC value by Δ_{BAC} = 0.1 g/kg beta-slope increases on average by $\Delta_{\beta_{60}}$ = 0.005 g/kg.

Reported results show that there is a statistically significant difference between BAC_{tc} values calculated using standard versus corrected method. The higher the BAC_t and the longer the calculation time, the greater and statistically more significant ($p < 0.01$) is the difference between the calculated values of BAC_{tc}.

Beta-slope correction using time factor (Δ_t) necessary for elimination of $\Delta_{BAC} = 0.1$ g/kg could be neglected, due to the fact that found difference is fairly low (third and second decimal point), and it could not possibly influence forensic and psychiatric expert witness' testimonies, regarding the influence of the established blood alcohol concentration on sensory functions.

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