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The influence of the body mass index (BMI) on the volume of distribution of ethanol☆

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ABSTRACT

The volume of distribution of ethanol was already established in 1930s by Widmark. However, since then the average body composition has changed considerably. The effect of the body mass index (BMI) on the volume of distribution of ethanol was evaluated in this study. Fifty healthy volunteers (23 men and 27 women), with BMI-values between 16.0 and 36.0 kg/m^2, were asked to drink a dose of 0.4 g ethanol per kilogram body weight after an overnight fast. The ethanol content was measured by a fully validated headspace-GC-FID method. The volume of distribution of ethanol varied between 0.40 and 0.68 L/kg for women, and between 0.43 and 0.73 L/kg for men. For both sexes, the volume of distribution decreased with increasing BMI. Regression analysis resulted in the following equations: volume of distribution = $0.8202 - 0.0090 \times$ BMI for men ($r = 0.66$), and $0.7772 - 0.0099 \times$ BMI for women ($r = 0.78$). Population probability prediction interval limits were also calculated. In view of the current study, fixed values for the volume of distribution of 0.7 L/kg and 0.6 L/kg for men and women, respectively, often applied in legal blood alcohol calculations, are mainly suited to judge underweight or normal weight people, but not obese persons.

1. Introduction

Ethanol is one of the oldest and most studied molecules [1,2]. The relationship between a person's blood alcohol concentration (BAC), his impairment and the amount of alcohol consumed is important in forensic science. Already in 1930s, Widmark established the following relationship between the BAC (expressed in g/kg) and the administered dose [2]:

$$\mathrm{BAC}_0 = \frac{\mathrm{dose}}{\mathrm{rho} \times \mathrm{weight}} \quad (1)$$

where BAC_0 = extrapolated blood alcohol concentration (g/kg) at time 0 min, dose = amount alcohol (g), weight = body weight (kg), and rho = Widmark factor.

Widmark found a mean value for rho of 0.68 for men (range 0.51–0.86) and 0.55 for women (range 0.47–0.64) [2].

Rearrangement of this equation gives the following formula:

$$\mathrm{rho} = \frac{\mathrm{dose}}{\mathrm{BAC}_0 \times \mathrm{weight}} \quad (2)$$

which is quite similar to the definition of the volume of distribution (V_D) of ethanol:

$$V_D = \frac{\mathrm{dose}}{\mathrm{BAC}_0 \times \mathrm{weight}} \quad (3)$$

where V_D = volume of distribution of ethanol (L/kg), dose = amount alcohol (g), BAC_0 = extrapolated blood alcohol concentration (g/L) at time 0 min, and weight = body weight (kg).

The ratio between the Widmark factor and V_D is the density of blood, which is 1.055 kg/L on average [3]. The V_D is the theoretical volume that the total amount of administered drug would have to occupy to provide the same concentration as it currently does in blood, and can be calculated by extrapolation of the zero order elimination kinetics to the *Y*-axis [2,3] (Fig. 1).

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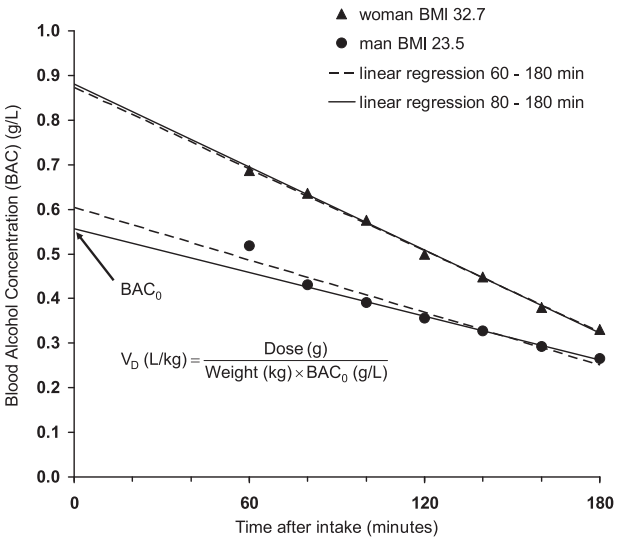

Fig. 1. Concentration–time profiles of ethanol in a healthy woman with BMI 32.7 kg/m^2 and a healthy men with BMI 23.5 kg/m^2 after drinking a 0.4 g/kg body weight dose of alcohol on an empty stomach in 1 min. BAC_0: extrapolated blood alcohol concentration (g/L) at time 0 min. The dashed and solid line are the linear regression analyses curves from 60 to 180 min and from 80 to 180 min post-drinking, respectively. The volume of distribution (V_D) is derived from this data as shown in the equation.

Ethanol distributes into the total body water (TBW) compartment without binding to plasma proteins and solubility in fat and bone is negligible [4]. Hence, the V_D for ethanol is significantly influenced by the proportion of fat to lean body mass (LBM) [5], although very frequently fixed values for V_D of 0.7 L/kg for men and 0.6 L/kg for women are used in blood–alcohol calculations [5].

An attempt to individualize Widmark's factor by calculating the TBW based on the gender, age, height and weight was made in 1982 by Watson et al. [6]. The calculations were later fine-tuned by Gabe [7]. Another possibility is to take into account the body mass index (BMI), which is the weight (in kg) divided by the square of the person's height (in m). Theoretical calculations and hypothetical nomograms based on the BMI have been published [8,9], although empirical evidence has not been presented.

Jones [4] published the BAC time courses of two individuals (a man with low BMI and a women with high BMI) after the intravenous administration of 0.4 g ethanol per kilogram body weight. He stressed the need to investigate the V_D over a wide range of BMI values given that the average body composition has changed considerably since 1930s with obesity becoming a major health problem.

This study presents the alcohol pharmacokinetics in 50 volunteers, both men and women, evenly distributed over 5 BMI classes, ranging from BMI 16 to 36. The V_D of ethanol for each person is calculated, and the influence of the BMI on the V_D is evaluated.

2. Experimental

2.1. Volunteers

This study was approved by the Institutional Review Board of the Ethics Committee of Ziekenhuis Netwerk Antwerpen, Belgium (E.C. Approval N° 3755). Fifty healthy volunteers, both men and women, with BMIs varying between 16.0 and 36.0, were selected from a large database of SGS Life Science Services (Antwerp, Belgium). The study protocol was explained and exclusion criteria (younger than 18 years, pregnancy, renal or hepatic failure, history of alcohol abuse, consumption of more than 21 drinks per week or severe nicotine dependence) were highlighted. Individual length and weight was determined and the following instructions were given: minimal abstinence of alcohol, food and beverages other than water from 48, 8 and 8 h, respectively, prior to study entry. All volunteers gave informed written consent.

2.2. Drinking experiment

The drinking experiment took place in the SGS Life Science Services, Research Unit, Stuivenberg (Antwerp, Belgium). On study entry, volunteers were measured and weighed again (Tanita balance type TBF-300A, AIRPEC Medical Devices cv/sc, Hever-Boortmeerbeek, Belgium). Women were asked to undergo a urinary screening pregnancy test, and men to empty their bladder. Predose glycemia was determined by finger-prick (Accu-Chek, Roche Diagnostics Belgium, Vilvoorde, Belgium) and a 4 mL whole blood sample was collected in a sodium fluoride/dipotassium oxalate tube (Terumo Venosafe VF-054SFX, Terumo Europe N.V., Leuven, Belgium). Subsequently, the volunteers were asked to drink a dose of 0.40 g ethanol per kilogram body weight in 1 min as a 20.0% (w/v) ethanol solution in water. Blood samples were collected after 60, 80, 100, 120, 140, 160 and 180 min. Volunteers were asked not to eat anything before the end of the experiment and to drink only moderate amounts of water starting from 60 min after alcohol intake. Blood samples were stored at 4 °C in the dark.

2.3. Chromatographic analysis

The ethanol concentration in the whole blood samples was measured within 1 week by a routinely used fully validated headspace-GC-FID method (Agilent 7697 A Headspace Sampler and Agilent 6890 GC-FID), which complies with the Belgian law within the framework of medico-legal blood–alcohol analyses [10] and for which the laboratory routinely takes part in proficiency test schemes. All samples were analysed in duplo.

3. Results

3.1. Volunteers

The study group consisted of 23 Caucasian men and 27 Caucasian women, divided over 5 BMI-classes: class 1, BMI 16.0–19.9; class 2, BMI 20.0–23.9; class 3, BMI 24.0–27.9; class 4: BMI 28.0–31.9; class 5: BMI 32.0–35.9. Their descriptive statistics are summarized in Table 1 and full details can be found in Supplementary File 1. None of the female volunteers tested positive on the pregnancy test.

Supplementary material related to this article found, in the online version, at http://dx.doi.org/10.1016/j.forsciint.2014.04.036.

3.2. Predose BAC and glycemia

Alcohol was not detected in any of the predose samples (limit of detection: 0.015 g/L). Glycemia was lower than 125 mg/dL for 47 out of the 50 participants. The glycemia was 132, 142 and 144 mg/dL for 3 males with BMIs of 33.6, 33.6 and 29.3, respectively. One admitted not to have complied with the fasting rule, and therefore, his data (AN42 – Supplementary File 1) were omitted from the study. Full details can be found in Supplementary File 1.

3.3. Amount of alcohol ingested

The density of the 20.0% (w/v) ethanol solution in water was 0.9635 g/mL. All volunteers succeeded in drinking the amount of alcohol within 1 min. The tare of the glass was weighed before