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Original communication

Intra-individual and inter-individual variation in breath alcohol pharmacokinetics: Variation over three visits

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ABSTRACT

Eleven male and 7 female student subjects underwent serial Breath Alcohol Concentration (BrAC) measurements after being given alcohol as 13% white wine (5.7 ml/kg for males and 4.7 ml/kg for females) in a fasting state on three separate occasions. BrAC versus time curves were constructed for each subject and the values of peak BrAC (C_{max}), theoretical BrAC extrapolated at zero time (Co), time taken to reach peak (T_{max}) and rate of elimination (ß) from breath were recorded directly from the curves. Average Intra-individual variation for each individual between the 3 visits (for males and females, respectively) was 5.6% and 8% for Co, 12% and 13% for C_{max}, 42% and 37% for T_{max} and 11% and 13% for ß. Inter-individual variation (for males and females) was 7.5% and 13% for Co, 16% and 15% for C_{max}, 43% and 46% for T_{max} and 21% and 15% for ß. Average elimination rates in males (5.3 μg/100 ml breath/h, range 4–7.7) and females (5.6 μg/100 ml breath/h, range 4–7) were not significantly different. Widmark factors calculated by various established mathematical methods were 0.71–0.81 in males and 0.59–0.68 in females, higher than the originally quoted mean experimental levels.

1. Introduction

Measurement of alcohol concentration in blood and breath is of major medico-legal importance with respect to drink-driving offences. An excellent recent review of many studies on blood alcohol kinetics has been provided by Jones.[1] Many of the more recent studies have involved measurement of breath alcohol concentration (BrAC) since this is the primary evidential specimen in most jurisdictions, its measurement is less invasive than blood sampling and because BrAC is thought to correlate well with blood alcohol concentration (BAC).[2] Breath samples have been found to show similar or lower variations than blood, both within and between subjects.[3]

Numerous factors may affect the rate and extent of alcohol absorption and its rate of elimination. Alcohol absorption rate is dependent upon the concentration of alcohol in the beverage consumed and upon carbonation of any mixers used.[4] Taking food with alcohol has been shown to both reduce the peak blood alcohol level achieved and enhance the rate of alcohol elimination.[5–8] Conversely, other studies demonstrated a slightly lower rate of alcohol elimination from breath after food.[9–11] The peak level achieved after food may only reach two thirds of the level achieved after fasting.[11]

Several studies have demonstrated significantly higher rates of alcohol elimination in females than in males.[13–15] We have previously failed to demonstrate any significant difference between the sexes.[16] Even breathing technique has been found to affect BrAC measurements.[17–19]

In Australia, alcohol drinking experiments can be performed when intoxicated drivers challenge blood alcohol concentration evidence based on mathematical assumptions relating to elimination rate.[20] Elimination rate may be determined experimentally several months after an alleged offence making natural variability in breath alcohol elimination rate, especially intra-individual variation, of great medico-legal significance.

Calculation of blood alcohol concentration (BAC) at any material time is usually based on the Widmark equation: $C_0 = A/p.r$,[21] where C_0 = theoretical BAC at zero time, assuming complete instantaneous absorption and distribution; A = amount of alcohol ingested (in grams); p = body weight (kg); r = Widmark Factor (W.F.), the

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fraction of the body mass in which alcohol would be present if it were distributed at concentrations equal to that in the blood;

The alcohol level at any given time is given by $Ct = C_0 - \beta$ t, where C_t = BAC at time t minutes; β = elimination rate (mg/100 ml/h) and t = time elapsed in minutes.

Widmark's original research in 1932 proposed average values for the Widmark Factor (r) of 0.68 for 20 males and 0.55 for 10 females.[21] Mathematical models which include anthropological data such as sex, height, weight and build will improve the estimation of Widmark Factor. Experiments using students, who have a lean body mass, tend to give higher than average values.[11,16]

In drinking experiments, the Widmark Factor (r) can be estimated by rearranging the Widmark equation since the alcohol dose is known and a value of C_0 can be extrapolated back from the linear portion of the experimental BAC or BrAC curve. At its simplest, use of the Widmark equation depends on knowledge of the subject's weight and sex and on how much alcohol was consumed at a former time. In forward calculations, where the BAC likely to be achieved following consumption of a known amount of alcohol is calculated, the principal factor contributing to error is the uncertainty concerning the volume of distribution or Widmark Factor. In retrograde or back calculations, where the BAC likely to have existed at an earlier time is estimated from a measured level, the principal factor contributing to error is the individual's rate of elimination. Back calculation of alcohol concentrations to the time of an offence have usually involved conversion of BrAC to BAC as elimination rates in breath have only recently been established.[15] However, the BAC/BrAC conversion factor (Q) is itself subject to great variations since Q appears to be inversely proportional to BrAC.[18,19,22] In the UK, where the legal limits for driving are 80 mg/100 ml blood and 35 μg/100 ml breath, the value of Q used in mathematical conversions is 2286 (=80/0.035).

There are several competing variables which affect the rate of absorption, distribution and elimination of alcohol. The present study involved student volunteers and was designed to assess the degree of variation in breath alcohol concentrations over three visits.

2. Materials and methods

Subjects were student volunteers who were given a full written explanation of the procedure and asked to complete a detailed health questionnaire which included details of any medical conditions, prescribed drugs, and normal drinking and smoking habits. If deemed suitable, informed consent for participation was obtained from each subject. The experimental work was carried out in 2007–08 with ethical approval granted by the Tayside Committee on Medical Research Ethics.

Eleven male and 7 female subjects underwent serial BrAC measurement on three occasions. The visits were typically a few days apart but often irregularly spaced. For each subject, visits were usually at the same time of day, most often early evening. Volunteer subjects were asked to refrain from food and drink for a minimum of 6 h prior to attending each experiment. A small drink of water was allowed within the fasting period, if required. On the first visit weight and total body water (%) were recorded on electronic body composition scales (Tanita BC-570 Innerscan Family Body Composition Monitor). Height was measured to within 1 cm. Subjects completed a questionnaire detailing their usual drinking habits and recent alcohol, food and cigarette consumption. A breath sample was then screened for alcohol to ensure subjects were free of alcohol prior to commencement.

On each visit, fasted subjects were given an ethanol loading dose as white wine of 13% alcohol by volume (abv). Males were given 5.7 ml/kg wine and females were given 4.7 ml/kg. The loading dose was calculated using Forrest's method to give a target BAC of 80 mg/100 ml (equivalent to 35 μg/100 ml breath) in males and 70 mg/100 ml in females.

For each subject, the alcohol dose was calculated by rearranging the Widmark equation:

Alcohol Dose (g) = (Target Blood Alcohol Concentration (mg/100 ml) × Body Weight (kg) × r) ÷ 100

Widmark Factor (r) was calculated from simple anthropological data (height in cm (H), weight in kg (W) and Body Mass Index (W/H^2)) according to the method published by Forrest[23]:

Fat as a percentage of body weight in males = (1.34 × BMI) − 12.469

Fat as a percentage of body weight in females = 1.371 × BMI − 3.467

Total Body Fat (TBF) in males = ((1.34 × BMI) − 12.469) × W/100

Total Body Fat (TBF) in females = ((1.371 × BMI) − 3.467) × W/100

Total Body Water (TBW) = 0.724 × (W − TBF)

r = TBW/(W × 0.8)

The loading dose ranged from 34 to 50 g in males and from 26 to 43 g in females. The actual volume of 13% white wine given (ml) = Alcohol dose (g) ÷ (0.79 × 0.13), where 0.79 is the specific gravity of alcohol (g/ml) and 0.13 represents the alcohol content of the wine by volume (13% abv).

This bolus was consumed uniformly over a 15 min period. BrAC measurements were performed on a Camic Datamaster Breath Analyser System, commencing 5 min after completion of drinking. The machine was set up to replicate the evidential breath testing cycle. Two breath alcohol measurements were taken in immediate succession, the second breath sample being blown immediately upon completion of the purging process after the first breath sample analysis. In practice this gave paired samples within 2 min of each other. All BrAC results are the average of these two measurements which were always within 2 units (micrograms/100 ml) of each other (data not shown). Serial measurements were repeated at 10 min intervals for 180 min. Throughout each experiment, subjects remained seated but were allowed to play computer games, read magazines and to chat quietly. Smoking was not permitted.

Widmark factors were calculated for each subject according to the mathematical methods published by Watson et al.,[21] Forrest,[23] Seidl et al.,[24] Ulrich,[25] calculated from the Total Body Water measurement (measured on body composition scales) and from experimental values of C_0 extrapolated from the BrAC-time curves, using the Widmark equation.

Watson's method[21] for estimating total body water in an individual is based on age in years (for male subjects only), Weight in kg (W) and Height in centimetres (H):

TBW (males) = 2.447 − (0.09516 × Age in years) + (0.1074 × Height) + (0.3362 × Weight)

It is claimed that a simplified version is almost as accurate: