Within-subject variability of alcohol pharmacokinetic parameters

DONALD NOEL SIMS[1], JAIMI BURNS[1] LISA YELLAND[2], AMY SALTER[2] and JASON WHITE[3]

1 Forensic Science SA, Australia

2 Department of Public Health, The University of Adelaide, Australia

3 Department of Clinical and Experimental Pharmacology, The University of Adelaide, Australia

AIMS: The objective of this study was to establish the degree of within-subject compared to between-subject variation in alcohol elimination and absorption rates. A further goal was to determine if within-subject variability is greater when there is a longer time between test days and to assess the impact of lower dose on within-subject variability.

METHODS: Twelve healthy male subjects participated in four study days over 12 weeks. Subjects received 0.44gkg-1 alcohol on study day 1 and 0.7gkg-1 on study days 2, 3 and 4 one hour after the completion of a standard breakfast. Study days 2, 3 and 4 were separated from study day 1 by 1, 10 and 11 weeks respectively. Blood samples were taken prior to drinking, at finish of drinking and at 10, 20, 30, 40, 55, 70, 90, 120, 150, 180, 240, 300 and 360 minutes after completion of drinking. Blood alcohol concentration measurements on these samples were made using gas chromatography and used to plot concentration-time profiles for each subject on each study day. Elimination and absorption rates were estimated using standard methods.

RESULTS: Within-subject variance accounted for approximately 44% of the total variance in elimination rates when dose was held constant and was not greatly influenced by the time between study days. Within-subject variance accounted for over 99% of the total variance in elimination rates when the time interval between testing was held constant and the dose was changed. The total variance in absorption rates was much greater than for elimination rates. Within-subject variance accounted for approximately 60% of the total variance in absorption rates when dose was held constant and was not greatly influenced by the time between study days. Within-subject variance accounted for over 99% of the total variance in absorption rates when the time interval between testing was held constant and the dose was changed. The within-subject variability in elimination and absorption rates was greater when the dose was changed but showed little change with changing time between study days.

CONCLUSIONS: Our results show the within and between-subject components of variation in alcohol pharmacokinetic parameters. Individuals' elimination rates are quite variable and show more variability with changes in dose. Thus a subject's elimination rate calculated from a single drinking trial has only limited use as information for the courts, particularly if conducted using a different dose than that associated with the offence. Few studies have assessed the significance of within-subject variation over time and so these findings could have an important impact on medico-legal issues related to alcohol pharmacokinetics.

KEYWORDS: *Alcohol, Pharmacokinetics, Variability, Within-subject.*

Corresponding author: sims.noel@saugov.sa.gov.au