MEDLINE Abstract

Pharmacokinetics and pharmacodynamics of triazolam after two intermittent doses in obese and normal-weight men.

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This study was designed to determine whether differences in alpha-1 acid glycoprotein and free drug concentrations result in an altered response to triazolam. Twelve normal-weight and 12 obese adult male subjects received intravenous doses of triazolam, 0.5 mg, on two occasions separated by 1 week. There was a small difference in the alpha-1 acid glycoprotein concentrations between groups but no difference in free fraction of triazolam. There was a longer terminal half-life (t1/2 beta) in the obese subjects (3.16 +/- 0.87 vs. 3.83 +/- 1.24, p = 0.0098). Overall, week 1 data revealed no difference in effect between normal and obese subjects. However, response data reveal a pattern of increased sensitivity with the second exposure to triazolam. For example, area under the effect curve (AUEC) on all tests was significantly greater in week 2 for both groups of subjects. For a memory test and sedation from 0 to 12 hours, AUEC/free AUC ratios were significantly greater in week 2 for all subjects. The obese had a higher ratio on week 2 than on week 1 for all psychomotor tests and sedation (0 to 4.5 hours; $p < 0.05$). The results of modeling psychomotor impairment-concentration data pooled by group for each week continue the pattern: week 1 data are similar between the obese and normal-weight subjects. Although EC50 values are up to 15% lower in week 2 for the normal-weight subjects, EC50 values are as much as 66% lower in week 2 for the obese, where a lower EC50 indicates greater sensitivity. Logistic regression of the recognition data is consistent with these results.(ABSTRACT TRUNCATED AT 250 WORDS)

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