Title: CHRONIC ALCOHOL INTAKE DOES NOT ALTER ANESTHETIC POTENCY OF THIOPENTAL IN RATS

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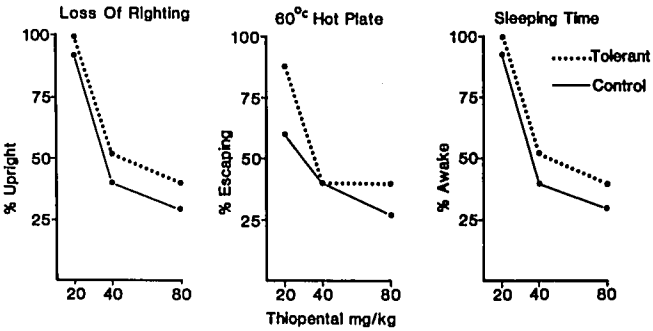
Introduction: It is widely accepted that chronic alcoholics are resistant to general anesthetics. However, such cross-tolerance between ethanol and specific anesthetics remains largely undocumented by systematic, controlled studies in either humans or animals. In this work we have investigated whether chronically ethanol-fed rats were also tolerant to a similar challange with thiopental.

Methods: Male Sprague-Dawley rats, housed two per cage, were allowed ad libitum access to a complete balanced liquid diet containing 6.54% ethanol as their only source of food and water for three weeks. Pair-fed controls were given the same diet except that dextrin was isocalorically substituted for the alcohol. Nine hours before testing, the diets were removed and the animals given free access to water. Ethyl alcohol 2.4, 3.2, and 4.0 gm/kg or thiopental 20, 40, and 80 mg/kg were injected intraperitoneally and the following observations made: whether or not righting reflex was lost, whether escape from a 60°C hot plate occurred within fifteen seconds, and whether the animals fell asleep. Sleep was considered to take place if the animals did not move from an 18 by 24 inch area within ten minutes. Ten rats were used at each dose for both experimental and control groups. The data were analyzed using the Fisher exact probability test; $p < .05$ was considered statistically significant. An additional group of ten rats were fed the alcohol-containing diet and venous blood samples, obtained by orbital puncture, were analyzed by gas chromatography for alcohol content. The samples were taken on the seventh day, at 9:00 A.M. and 4:30 P.M. on the fourteenth day and at midnight, 4:30 A.M., and 9:00 A.M. on the test day (day 21).

Results: All animals gained weight over the three week feeding period. At testing time there was no difference in the average weights of ethanol-fed and control rats. In the former group, average blood alcohol levels (mg/dl) were 155 at 9:00 A.M. on day 7, 107 at 9:00 A.M. and 186 at 4:00 P.M. on day 14, and 178 at midnight and zero at 4:30 A.M. on day 21 (testing began at 8:30 A.M.). The dose response curves for all three anesthetic responses to acute ethanol were shifted to the right in ethanol-fed rats compared with controls (data not shown). Differences between the two groups were significant at doses of 4.0 gm/kg for loss of righting, 2.4 gm/kg for hot plate escape and 4.0 gm/kg for sleep time. Although definite dose-dependence for those same effects were also seen with thiopental, differences in the dose-response curves between ethanol-fed and control groups were not significant.

Discussion: The dietary regimen used was nutritionally adequate and produced reliably high blood ethanol levels in ethanol-fed rats. Tolerance acquisition in the latter group was confirmed by the rightward shift in dose-response curves upon acute alcohol administration. The lack of such a shift with thiopental indicates that tolerance to ethanol was not associated with cross-tolerance to thiopental for effects related to induction, analgesia and duration of the anesthesia. Comparable findings were reported by Lee et al., who demonstrated no significant effect of chronic ethanol treatment on induction and maintenance responses to methohexital and thiopental[1]. Results of animal studies, thus, offer no support for altering thiopental doses in alcoholics.



Dose response curves for chronic alcoholic rats and pair fed controls given sodium pentothal and tested for loss of righting reflex, escape from a 60°C hot plate, and sleeping time. There is no significant differences between chronic alcoholic rats and controls.

References:

1. Lee P. et al., Effects of Alcoholism, Morphinism and Barbiturate Resistance on Induction and Maintenance of General Anesthesia. Can Anes Soc J 4:354-381, 1964.