

Toxicity of ethanol barbiturate mixtures

We feel that Smith & Herxheimer (1969) may have misunderstood the objectives of our initial study on the ethanol-barbiturate interaction (Wiberg, Coldwell & Trenholm, 1969). Our experiments were not designed to establish whether the interaction was additive or synergistic. If this had been our purpose we would have used an experimental design similar to that recently described by Gebhart, Plaa & Mitchell (1969).

The information available from newer techniques should be used for a better comprehension of the mechanisms of drug interaction. Our studies of the ethanol-barbiturate interaction have now progressed far beyond the report referred to above (Coldwell, Wiberg & Trenholm, 1970; Trenholm, Maxwell & others, 1970; Wiberg, Trenholm & Coldwell, 1970). Thus, (1) ethanol (3 g/kg, i.p.) with barbiturates markedly reduces blood pressure with concomitant reduction in urine formation and renal clearance of barbiturates; (2) ethanol produces a dose-related decrease in body temperature (as much as 2–3°), an effect which would be expected to decrease the hepatic metabolism of barbiturate and ethanol; (3) ethanol depresses the respiration rate and lowers the blood pO₂ levels, an effect which would be expected to reduce ethanol and barbiturate metabolism; (4) pentobarbitone enhanced the activity of purified rat liver alcohol dehydrogenase but retarded the metabolism by liver slices; (5) ethanol is more toxic in older rats (12–14 months) and there is an increased sensitivity to ethanol-barbiturate mixtures; (6) ethanol alters the distribution of barbiturates in body compartments. The distribution pattern for barbiturates was studied in the presence and absence of ethanol for some seventeen different organs and tissues and several changes were noted.

Magnussen (1968) has noted that in oral dosing, with ethanol-barbiturate mixtures, there is an optimal ethanol concentration of between 5–10% which facilitates barbiturate absorption. Decreased barbiturate absorption was found when ethanol concentrations exceeded 10%.

Such information has convinced us that the use of the terms “additive” or “synergistic” do not help to clarify our understanding of the ethanol-barbiturate toxicity. Obviously, there are inherent dangers associated with the combined use of ethanol and barbiturates which must be repeatedly brought to the attention of the public.

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