Intragastric self-administration of alcohol by rats: A dose-effect comparison

TOREEN E. WERNER, STANLEY G. SMITH, and W. MARVIN DAVIS
Department of Pharmacology, University of Mississippi, University, Mississippi 38677

Rats were implanted with a trans-esophageal intragastric cannula and allowed access to saline and three different dosages of ethyl alcohol (EA). Dosages of EA employed were 25, 50, and 100 mg/kg/infusion. All subjects readily self-administered the EA at all dosages in a dose-related fashion. The greatest number of infusions was taken by the lowest dosage group, while the least number of infusions was taken by the highest dosage group. For the amount self-administered, the reverse order was observed; rats in the highest dosage group had the highest intake of drug, while those in the lowest dosage group self-administered the least amount.

The intragastric (IG) drug self-administration methodology has provided a much needed alternative to oral "drinking" technique. The IG cannula bypasses the orosensory receptors and delivers a drug solution directly to the stomach. In this manner, drugs such as alcohol, which are not readily consumed by lower animals, can be more easily studied. To date, most published reports are demonstrations that some orally aversive compounds are readily self-administered by this method (Altschuler, Weaver, & Phillips, 1975; Gotestam, 1973; Marfaing-Jollat, Pruvost and Le Magnen, 1974; Smith, Werner, & Davis, 1975). The only study to provide additional information was one examining the lower end dose-effect of alcohol (Smith, Werner, & Davis, 1976a). These data indicated that increases in dose, to 3.0 mg/kg, resulted in increases in numbers of infusions and amount self-administered. Theoretically, the numbers of infusions should peak and then decrease with increases in unit dose. Therefore, to provide data on the upper range of intragastric alcohol's dose-response effects, the following research was instituted.

METHOD

Subjects

The subjects were adult male rats of Sprague-Dawley descent. Twenty rats were employed for this experiment, with five animals per group. All animals were drug naive at the beginning of the experiment. Food and water were available ad lib in both the home cage and experimental chamber throughout the experiment.

Apparatus

The rats were implanted with chronic esophageal intragastric cannulas, which passed from the esophagus subcutaneously to an exit on the upper back (for details, see Smith, Werner, & Davis,

1975). At the back, the catheter was attached to an external harness. The harness was then connected to a length of spring-wrapped plastic tubing which joined a leak-proof swivel at the top center of the chamber. The opposite end of the swivel was connected by vinyl tubing to an infusion pump which delivered .092 ml of .9% saline or EA solution in 1 sec each time it was activated. The experimental chambers, clear plastic cylinders 24 cm high and 25 cm in diameter, contained a response lever, food, and water. Each chamber was lighted and enclosed in a ventilated sound-attenuated compartment. Leverpresses were registered on electromechanical counters, and all programming was accomplished via solid state electronic circuitry.

Procedure

The subjects were placed in the test chambers, attached to the injection system and allowed a 1-h period for adaptation to the chambers. Following adaptation, the operant level of leverpressing was determined for a 10-h period, during which each response was followed by an intragastric infusion of saline. Superimposed on the infusion interval was a buzzer presentation of equal duration. On each of the subsequent 5 days, a 10-h acquisition period was run, with all conditions identical to those of the first day except that subjects were allowed access to 0 (saline), 25, 50, or 100 mg/kg/infusion of ethyl alcohol. Each dosage group consisted of five individual animals. Statistical comparisons between groups refer to data on Day 5.

RESULTS

Figure 1 shows the mean number of infusions taken by different treatment groups. It can be seen that the 0 (or saline) dose group did not maintain self-administration behavior. Note also that the greatest number of infusions was taken by the lowest treatment group (25), followed in decreasing order by the 50- and 100-mg/kg/infusion groups. The number of infusions for all doses of EA, 25, 50, and 100 mg/kg/infusion, significantly exceeded the infusions of saline ($p < .05$). However, the number of infusions did not differ significantly among the three EA groups ($p > .05$).

Figure 2 shows the amount of drug self-administered for all groups. The greatest amount of EA was taken by the highest dosage group (100 mg/kg/infusion), followed in decreasing order by the 50-, 25-, and 0-mg/kg/infusion

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Figure 1. Mean number of infusions of intragastric alcohol taken at different unit doses.

Figure 2. Mean amount (mg/kg) of intragastric alcohol self-administered at different unit doses.

groups. Statistical analysis shows that all EA groups differed significantly. Intake by the 100-mg/kg group exceeded that of both the 50-mg/kg ($p < .05$) and 25-mg/kg ($p < .01$) groups, but the later two groups did not differ significantly from one another.

DISCUSSION

Previous alcohol self-administration research with the intragastric route has indicated that increases in unit dose up to 3.0 mg/kg/infusion, highest dose studied, produce increases in number of infusions and amount self-administered (Smith et al., 1976a). The above research examined only lower range dose effects. The present research was an attempt to provide data on

upper range dose effects. These data indicated that increases in the dose of alcohol to 25 mg/kg/infusions produced the largest number of infusions taken, while further increases in dose resulted in a dose-related decline. The amount self-administered increased with increase in unit dose. Results for numbers of infusions and amount self-administered are similar to those reported for morphine via the same route (Smith, Werner, & Davis, 1976b).

With morphine and alcohol, increases in unit dose at the lower range produced increases in number of infusions taken and amount self-administered. Increases in unit dose at the upper range produced a decrease in number of infusions taken with an increase in amount self-administered. If potency comparisons were made between morphine and alcohol, the highest dose of morphine studied, 10 mg/kg/infusion, resulted in numbers of infusions very similar to those obtained for the highest alcohol dose studied, 100 mg/kg/infusion. While species, sex, experimental environments, and methods were identical for both studies, the time factor allows possible occurrence of historical incidence variables, i.e., temperature, etc., and exact quantification comparisons are not possible. Yet it is clear that upper dose morphine effects are far more potent than alcohol in a self-administration paradigm.

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