AMER. J. DRUG & ALCOHOL ABUSE, 1(1), pp. 107-110 (1974)

Propranolol and Alcohol Consumption in the Rat

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ABSTRACT

Recently some investigators have reported that propranolol antagonizes the psychopharmacological effects of heroin and alcohol. Others have proposed that propranolol may control the compulsive craving for opiates. We conducted an experiment in which we studied the effects of three different doses of propranolol on alcohol intake in rats. Our results indicate that propranolol is not effective in reducing alcohol consumption in rats.

Propranolol is a well known beta-adrenergic blocking agent which rapidly penetrates the brain tissues [1]. Clinical use of the drug has been primarily restricted to the treatment of cardiovascular disorders [2].

Recently, a great deal of interest has been generated by the potential use of propranolol in the treatment of alcoholism and drug abuse. Grosz [3-5] has reported that the intake of heroin after propranolol actually precipitates major symptoms of withdrawal. He reports that propranolol blocks the euphoric effects of heroin and, most important, that it abolishes the compulsive craving for the opiate.

The influence of propranolol on the depressant effects of ethanol has been studied by Smith *et al.* [6]. These workers found that the return to the righting reflex in mice after ethanol ingestion was shortened considerably by low doses of propranolol. Smith and Hayashida [7] reported that administration of 1 mg/kg of propranolol antagonized the respiratory

depression and narcosis brought about by 3 g/kg of ethanol. These authors concluded that propranolol blocks the depressant effects of ethanol.

A recent study by Carlsson and Johansson [8] demonstrated that propranolol has a stress-relieving effect on various symptoms of alcoholics. However, a report by Tryer [9] indicates that propranolol has no effect in the treatment of withdrawal symptoms of alcoholics. Furthermore, he states that propranolol may indeed increase alcohol intake.

Because of past contradictory reports, we undertook to study the effects of propranolol on ethanol consumption in rats.

METHODS

The subjects were 20 male Long Evans hooded rats, 10 weeks old and weighing 250-300 g at the start of the experiment. The animals were housed individually in rat cages. The room temperature was kept at 76°F and the 12-hr day and night cycle was maintained by an automatic timer. The animals were always given food and water ad lib.

Alcohol preference was measured with the use of a two-bottle method, which is a modification of a previously described procedure [10]. The animals were simultaneously offered a choice between plain water and a solution of 95% ethanol prepared volumetrically with tap water. The fluids were contained in two 100 ml inverted graduated bottles that were fitted with steel spouts which protruded into the cage. The bottles were placed randomly and their positions were interchanged daily to eliminate error due to position or bottle preference. Fresh solutions of alcohol and water were placed in the bottles daily.

For the baseline period, measurement of alcohol preference and consumption was established by increasing the concentration of alcohol solution each day in a stepwise fashion as follows: 3, 4, 5, 6, 7, 9, 12, 15, 20, and 25%. Only one concentration of this ascending series was offered per day for the 10 days of baseline. The daily fluid consumption was recorded at 9 a.m., 11 a.m., and 2 p.m.

Subsequent to the baseline period, half the animals (N = 10) were randomly assigned to the experimental group, the other half to the control group. In the experimental group, animals were injected subcutaneously with 1 mg/kg of propranolol hydrochloride daily, for a period of 10 days in conjunction with the ascending series of alcohol concentration; the control group was treated similarly, except that the animals were injected with an equivalent dose of 0.9% saline.

After this sequence, all animals were provided with only food and water ad lib for a period of 3 days. A similar sequence was then started in which the experimental animals received 5 mg/kg of propranolol for another 10 days. Finally, after another rest period of 3 days, the last sequence began, in which the experimental animal received 10 mg/kg of propranolol and the control animal received an equivalent amount of saline.

RESULTS

Statistical analysis of the voluntary consumption of ethanol during baseline procedure showed no significant difference between the experimental and control groups. A repeated measurement analysis of variance was carried out in order to compare alcohol consumption between the experimental and control groups across all ethanol concentrations. No significant differences were obtained between the propranolol-treated animals and the saline-treated animals for all recordings (9 a.m., 11 a.m., 2 p.m.). The failure of propranolol to change alcohol consumption was found with all three doses of propranolol as can be seen in Table 1.

It should be noted that the data were also analyzed in terms of a ratio or proportion of alcohol to water consumed. Again, our statistical analysis did not yield any significant differences between the experimental and control groups.

Table 1. Daily Consumption of Alcohol by Concentration (mls)

Propranolol Dose	3%	4%	5%	6%	7%	9%	12%	15%	20%	25%
1 mg/kg										
Experimental group	37	39	39	30	27	31	29	20	17	7
Control group	39	37	41	36	24	30	25	22	12	5
5 mg/kg										
Experimental group	35	29	36	31	22	24	27	18	9	4
Control group	37	34	36	32	20	25	19	14	12	8
10 mg/kg										
Experimental group	31	34	32	30	29	26	16	17	11	9
Control group	34	36	30	29	28	22	19	16	12	6

DISCUSSION

Our findings indicate that propranolol has no significant effect on ethanol preference and consumption in rats. It is possible that the so-called anticraving effects of propranolol can only be observed in physically dependent organisms. The lack of a significant effect in our present study might be accounted for by the fact that our animals were not physically dependent on alcohol. Furthermore, it is also possible that the beneficial effects of propranolol are quite specific to man and may not be present in the rat.

While it has been demonstrated that propranolol can inhibit the central depressant actions of ethanol in animals, our results raise serious doubts about the anticraving effects of propranolol which have been claimed in connection with alcohol.

ACKNOWLEDGMENT

This study was supported by NIMH Grant AA 01231. Propranolol was generously donated by Henry L. LeMien, Jr. of Ayerst Laboratories.

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