EFFECT OF ADRENALINE AND ALCOHOL ON SULPHADIAZINE LEVELS IN RAT BRAIN

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Summary: Adrenaline and alcohol facilitate passage of parenterally injected sulphadiazine into the brain of rats. While the effect of adrenaline was observed only at 15 min interval after drug administration, the effect of acohol was seen at 15 min and 30 min intervals.

Key words: sulphadiazine adrenaline alcohol blood brain barrier

INTRODUCTION

A number of papers have been presented in support of the concept that adrenaline may facilitate the passage of centrally acting drugs like barbiturates and amphetamine into the brain (7, 8) The present study was undertaken to determine the effect of adrenaline and alcohol on the penetration into the CNS of sulphadiazine which does not have an action *per se* on the CNS. Alcohol also increases the penetration of some substances into the brain (5).

MATERIALS AND METHODS

Albino rats of either sex weighing 80-120 *g* were used. They were allowed free access to food and water until the time of the experiment.

DRUGS : 1. Sulphadiazine sodium injectable (1:4) (M & B)
Dose—50 $\mu g/g$ of body weight.

2. Adrenaline bitartrate (1 : 1000) Burroughs Wellcome,
Dose—0.25 $\mu g/g$ of body weight.
This dose has been used by Mazel and Bush (7).

3. Alcohol (Glass distilled absolute ethyl alcohol diluted to a 10% soultion with distilled water)
Dose—1 *g/g* of body wight of absolute alcohol.

All the drugs were injected intraperitoneally. When two drugs had to be given to the same animal, the injections were made simultaneously.

Determination of brain sulphadiazine: At the predetermined time, the rat was decapitated and the brain was rapidly removed and weighed. The brain was homogenised in ice-cold

normal potassium chloride to make the volume upto 10 *ml*. Homogenisation was done in an electrically driven glass homogeniser. 2 *ml* of the homogenate were treated with 4 *ml* of 15% trichloracetic acid and filtered through a dry filter paper. The filtrate was analysed for its sulphadiazine concentration by the method described by Bratton and Marshall (2).

RESULTS

1. Animals given sulphadiazine alone served as controls and concentration of sulphadizine (Mean-S.D.) at different time intervals is given in Table I.

2. Animals given adrenaline plus sulphadiazine showed a significant rise in sulphadiazine concentration at 15 min after drug administration ($P<0.05$). The change in concentration at other time intervals was not significant (Table I).

TABLE I: Effect of adrenaline and alcohol on brain levels of suplphadiazine at various time intervals
Sulphadiazine concentration in *mg*/100 *g*
(±S.D.) of wet brain.

Treatment time (min after injection	*Sulphadiazine alone*	*Sulphadiazine +adrenaline*	*Difference from control*	*Sulphadizine +alcohol*	*Difference from control*
15	1.48±0.31 (6)	2.89±0.88 (6)	+1.41*	2.19±0.43 (6)	+0.71*
30	1.16±0.73 (8)	1.37±0.53 (8)	+0.21	2.00±0.45 (6)	+0.84*
60	2.25±1.13 (6)	2.15±0.39 (6)	—0.10	2.57±0.40 (6)	+0.32

N.B. : Number of animals in parentheses
*Significant by 't' test, $P<0.05$.

3. Animals receiving alcohol with sulphadiazine showed a significant rise in sulphadiazine levels in the brain at time intervals of 15 min and 30 min ($P<0.05$) (Table I).

DISCUSSION

The only significant change occurring in the adrenaline treated group of rats was an increased sulphadiazine concentration observed at 15 min interval after drug administration. The facilitatory effect of adrenaline on the penetration of some other substances like barbiturates, amphetamine and chloral into the brain has been reported (4, 7, 8). All these are neuroactive substances. It has been suggested by Young and Gordon (8) that the activity of neuroactive substances may be regulated by the circulating levels of catecholamines. The present work could imply a regulatory effect of adrenaline on the penetration of drugs other than neuroactive substances, as well.

Adrenaline is reported to have a generalized effect on other barrier systems as well (6). The effects reported in this paper may be a part of such generalized action.

A significant rise in the brain levels of sulphadiazine in the alcohol treated rats was observed at 15 min and 30 min time intervals. Alcohol has been reported to increase the permeability of several substances into the brains of rabbits and rats (3, 5).

The use of alcohol as a cerebral vasodilator has been recommended because of the dilatation of pial vessels observed in experimental animals under the influence of large doses of alcohol (1). This vasodilatory action may account for the increased passage of substances from blood vessels into the brain tissue.

Another possible explanation could be based on the toxic action of alcohol which may directly damage the endothelium of cerebral capillaries or of choroid plexus resulting in increased passage of substances into the brain. However, no histopathological changes were reported in the cerebral capillary walls under intoxicating doses of alcohol (5).

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