SHORT COMMUNICATION

THE INTERACTION OF BARBITURATES AND ANALEPTICS

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Summary: The interaction of pentobarbitone sodium with three analeptics viz. micoren, pentylenetetrazol and methedrine was studied in mice. Micoren prolonged pentobarbitone sleeping time. Pentylenetetrazol shortened the sleeping time. Methedrine also shortened the sleeping time, but clonic convulsions of mild to severe intensity were noticed 45-60 minutes after the drug injection.

Key words : barbiturates analeptics

INTRODUCTION

The place of analeptics in the treatment of barbiturate poisoning remains a controversial one. Use of nikethamide is recommedned in the event of excessive depression following the use of central depressants (3). It has also been suggested that when respiratory paralysis due to barbiturates supervenes, amphetamine or micoren may be used (2).

Botting *et al.* (1) have shown that nikethamide potentiates the action of pentobarbitone sodium in mice and have strongly suggested that it is contra-indicated in cases of respiratory depression due to barbiturate intoxication. It was thought, therefore,worth assessing the value of a few other analeptics in this situation.

MATERIALS AND METHODS

Albino mice of either sex weighing between 20-40 *gms* were selected for the study. All the drugs were administered intraperitoneally. Pentobarbitone sodium was given in the dose of 4.5 *mg*/100 *gm* body weight. Ten minutes after this, the analeptic was administered. The dose of the analeptic chosen was such that when given alone it produced minimal hyperactivity in mice for 15-20 minutes, the animals becoming normal thereafter.

The analeptics administered were as follows :—

1.	Micoren	—	8 *mg*/100 *gm*
2.	Pentylenetetrazol	—	3 *mg*/100 *gm*
3.	Methedrine	—	0.25 *mg*/100 *gm* and 0.5 *mg*/100 *gm*

The sleeping time was determined in the control (pentobarbitone sodium treated) a analeptic treated (analeptic administered ten minutes after the dose of pentobarbitone sodiu mice.

RESULTS AND DISCUSSION

The righting reflex in mice was lost between 3-6 minutes of administration of pentob bitone sodium. The sleeping time of the micoren treated mice (134.41±16.79) was almost t and half times that of the control (55.48±8.36). Once the righting reflex was regained, th showed normal behaviour.

The mean sleeping time of the pentylenetatrazol treated mice (31.85±6.07) was only h that of the controls (63.50±9.97). They too showed normal activity once the righting reflex w regained.

The sleeping time of methedrine treated (0.5 *mg*/100 *gm*) mice (36.85±6.00) was nea one and half times less than that of controls (81.08±7.32). All the mice showed mild to sev clonic convulsions 15-30 minutes after regaining the righting reflex.

A lower dose (0.25 *mg*/*kg*) of methedrine was tried to minimise the incidence of convu ions. Methedrine treated (0.25 *mg*/100 *gm*) mice slept (39.64±7.91) almost the same time that of the controls (34.36±3.82). 50% of these mice also showed occasional jerky movem or very mild clonic convulsions 15-20 minutes after regaining the righting reflex.

The results are shows in the following Table.

Analeptic and dosage used	*Sleeping time in minutes (± SE)*		*P. Value*
	Control animals	*Analeptic treated animals*	
Micoren 8.0 *mg*/100 *gm*	55.48 (18) ±8.36	134.41 (19) ±16.79	<0.01
Pentylenetetrazol 3.0 *mg*/100 *gm*	63.50 (17) ±9.97	31.85 (19) ±6.07	<0.01
Methedrine 0.5 *mg*/100 *gm*	81.08 (19) ±7.32	36.85 (20) ±6.00	<0.01
Methedrine 0.25 *mg*/100 *gm*	34.36 (19) ±3.82	39.64 (19) ±7.91	>0.5

The figures in the parentheses indicate the number of mice in each group.

The potentiation of the sleeping time of pentobarbitone sodium by micoren could be due to two reasons. Firstly, the analeptic or its metabolite could act as depressant in mice. Secondly, micoren could inhibit the metabolism of the barbiturates. As indicated earlier, the dose of micoren chosen was such that it produced increased spontaneous movements or hyperactivity in mice for 20-25 minutes. Hence, the possibility that it or its metabolite acts as depressant seems to be out of question. It is possible that micoren inhibits those microsomal enzyme systems which determine the metabolism of barbiturates and thus prolongs the barbiturate sleeping time.

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