LETTER TO THE EDITOR

MODIFICATION OF HEXOBARBITONE SODIUM-INDUCED HYNOSIS IN MICE BY BETA ADRENERGIC RECEPTOR BLOCKING AGENTS

Sir,

Beta adrenergic receptor blocking agents influence the functions of the central nervous system (CNS) in animals (1-5). The actions of these agents on the CNS are not related to their beta adrenergic receptor blockade (1). Proporanolol which possesses both sedative and anticonvulsant properties (3) potentiates hexobarbitone sodium induced hypnosis in mice (1). Since N-isopropyl-methoxamine (IMA) has been reported to reduce markedly the spontaneous motor activity (SMA) as well as methamphetamine induced increase in SMA (5), it was decided to study the effect of IMA on hexobarbitone sodium induced hyposis and compare it with propranolol and alprenolol.

The study was carried out in sixty albino mice (25-30 g) of either sex, divided into 3 groups. The room temperature was 31-33°C. These groups were further divided into sub-groups of 4 mice each. In each group, 4 mice served as controls. All groups of mice received an appropriate quantity of drug intraperitoneally ; controls received an equivalent volume of saline. Thirty min later, hypnosis was induced in all mice by hexobarbitone sodium (100 *mg/kg*, ip). Sleeping time was defined as the time interval in min between the loss and gain of righting reflex. The change in sleeping time was determined by calculating the percentage deviation from control values obtained within the same group and the dose-effect curves were plotted on a semilogrithm paper as percentage change in sleeping time against the dose of the drugs.

The drugs used were : (±) propranolol hydrochloride (ICI), (±) alprenolol hydrochloride (A.B. Hassale), N-isopropylmethoxamine hydrochloride (Burroughts & Wellcome) and hexobarbitone sodium (Bayer). All drugs were dissolved in distilled water and the doses employed refer to the salts.

Hexobarbitone sodium (100 *mg/kg*, ip) induced hypnosis for a duration of 31 ± 1.96 min (n = 12) in control mice. Prior administration of both propranolol and alprenolol potentiated hexobarbitone sodium-induced hypnosis in a dose-dependent way. The dose-effect curves for the percentage change in sleeping time were quite steep (Fig. 1). With both the drugs the sleeping time was prolonged over 50% at 20 *mg/kg* dose level.

The doses necessary to cause 100% increase in sleeping time were computed from Fig. 1; the values for propranolol and alprenolol were 31.25 *mg/kg* and 39.25 *mg/kg* respectively. The results are in agreement with those of Hermansen (1). However, values for propranolol and alprenolol reported by Hermansen (1) were 18 *mg/kg* and 16 *mg/kg* respectively. The higher values obtained, can be explained on the basis that the control mean value for hexobarbitone sodium-induced hypnosis (i.e. 31 ± 1.96 min) observed in the present study is higher than the value of 9-12 min reported by Hermansen (1), who however, used only a smaller dose (76 *mg/kg*).

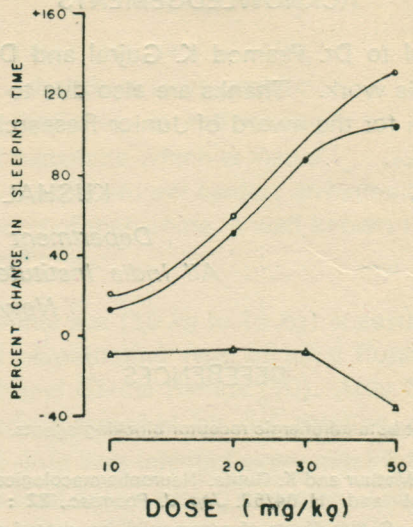

Fig. 1 : Effect of prior administration of beta adrenergic receptor blocking agents on hexobarbitone sodium induced sleeping time in mice.

O——O Propranolol
●——● Alprenolol,
△——△ IMA

On the other hand, the effect of IMA differed from propranolol and alprenolol since it reduced hexobarbitone sodium-induced sleeping time. The reduction in sleeping time which was not marked in smaller doses (< 30 *mg/kg*) was significant at 50 *mg/kg* dose and was the order of 35% ($P = <0.05$). IMA (100 *mg/kg*, i p) proved to be too toxic (more than 60% animals had shivering and death occured within 2-4 hr) and therefore, could not be employed. Such reduction in hexobarbitone sodium induced hypnosis has also been reported for DCI (1). In contrast to IMA, DCI produces significant increase in hexobarbitone sodium-induced sleeping time when used in smaller doses (1). Moreover, beta-adrenergic receptor blocking agents which reduce SMA, have also been reported to potentiate the pentobarbitone sodium-induced hynosis in animals (2). IMA which has also been reported to reduce SMA markedly and to block effectively the increase in

SMA (5) produced by methamphetamine not only failed to potentiate the hexobarbitone sodium-induced hypnosis but reduced the hexobarbitone sodium induced sleeping time. The mechanism (s) by which IMA reduced hexobarbitone sodium induced hypnosis necessitate further evaluation.

Thus the beta adrenergic receptor blocking agents modify hexobarbitone sodium induced hypnosis by mechanism(s) other than beta adrenergic receptor blockade.

ACKNOWLEDGEMENTS

The author is grateful to Dr. Pramod K. Gujral and Dr. A. Ramaswamy for their valuable help to carry out this work. Thanks are also due to the Indian Council of Agricultural Research, New Delhi for the award of Junior Research Fellowship.

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