SHORT COMMUNICATION

STUDIES ON THE EFFECT OF DIAZEPAM (VALIUM) ON NEUROMUSCULAR TRANSMISSION IN SKELETAL MUSCLES

By

S.R. DASGUPTA, N.M. RAY AND B.P. MUKHERJEE

Department of Pharmacology, Institute of Basic Medical Sciences, University College of Medicine, Calcutta University, Calcutta

Diazepam (7-chloro-1-methyl-5-phenyl-3H-1, 4-benzodiazepine-2(1H)-one) has recently been reported to be successfully used in spastic disorders (5) and also in convulsant disorders such as tetanus (1,3). It has also been reported to possess a strong antagonistic effect against spontaneous contractions and also contractions induced by various spasmogenic drugs in smooth muscles (4,2). It was, therefore, decided to study the effect of diazepam on neuromuscular conduction in skeletal muscles, the results of which are briefly reported hereunder.

Rat phrenic nerve-diaphragm preparation and frog sciatic-gastrocnemius preparation were used for these studies. Besides diazepam, chlordiazepoxide (CDP), an earlier analogue, was used for comparison.

With phrenic nerve-diaphragm preparation, it was observed that diazepam in a concentration of 20 *μg/ml* produced a forty per cent inhibition of neuromuscular transmission without any effect on direct muscular stimulation. With 40 *μg/ml.* however, the neuromuscular transmission was completely inhibited, and the response to direct muscle stimulation was also reduced by about twenty per cent. This neuromuscular blocking effect could not be antagonized by physostigmine. CDP, on the other hand, had no effect, either on neuromuscular transmission or on direct muscle stimulation even in a concentration of 50 *μg/ml.*

These concentrations of diazepam or CDP were insufficient to block peripheral conduction, when applied directly and kept in contact for 5 minutes on a length of the unsheathed nerve, in a frog sciatic-gastrocnemius preparation. But with a much higher concentration, viz. 2.5 *mg/ml*, the peripheral conduction was completely blocked by diazepam though not by CDP, indicating a local anaesthetic effect of diazepam in a very high concentration.

From these observations it is reasonable to infer that diazepam possesses a considerable blocking action on neuromuscular transmission in skeletal muscle, whereas CDP does not possess any such effect. Zbinden and Randall (6) have reported that diazepam, besides its anti-anxiety effect, also possesses a marked inhibitory action either on polysynaptic transmission within the spinal cord or on supraspinal structures (6). This probably is the rationale for the use of diazepam in the treatment of convulsant diseases like tetanus. Our findings provide a peripheral component to the muscle relaxant action of diazepam and also an additional pharmacological evidence in support of such therapeutic uses.

In vivo study is underway.

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