

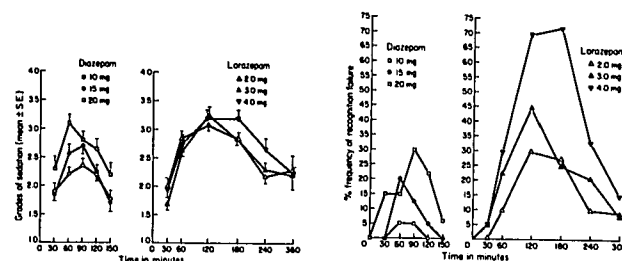
Date :  
 Title : ORALLY ADMINISTERED DIAZEPAM AND LORAZEPAM.  
 SEDATIVE AND AMNESIC EFFECTS.  
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**Introduction.** Diazepam and lorazepam are among the most common oral premedicants used in this country. Their sedative and anxiolytic effects are well recognized. Although both are believed to produce marked anterograde amnesia, these impressions are based on studies done after intravenous administration. Obviously, the blood levels, pharmacological effects and their time course would vary considerably with different routes of administration. Dundee et. al. (1979) were the only ones who referred to the time course of the amnesic action of these two drugs given orally at two dose levels but their study was restricted to 90 minutes after the medication. So they did not observe the peak nor the duration of the amnesic effect of the larger doses. Most other authors have based their conclusion of the amnesic effects of these agents on one or two observations after the administration of the agent. Thus, the true time course of the amnesic effect has never been established after oral administration of diazepam and lorazepam at different doses.

**Methods.** 150 healthy adult patients between the age of 18-55, 50-100 kg, of either sex, ASA class I or II scheduled for elective surgery participated in the study. None of the patient were mentally retarded nor had a prior history of psychological disorder. Drug dependant individuals were excluded. A full explanation of the procedure was given to each patient the day before the operation. Three doses of diazepam (10, 15 and 20 mg) and three doses of lorazepam (2, 3 and 4 mg) were studied. The dispensing of the drugs was done randomly but not blindly (because of the known difference in the pharmacokinetics of the two agents). A single dose of the assigned premedication was given orally in the morning. No other medication was given during the study period. At five pre-determined times after the medication (see figure) each patient was visited and the grade of sedation (on a scale of 1-5) was observed. At each time the patient was shown a large memory card (black and white sketch of an animal or object) and was asked to identify it. Thus, a maximum of five different cards were shown to each patient at various time intervals, but the cards were randomized within the group. There were 20 cases in each group to start with; but in the lorazepam group, in a number of cases the last cards could not be shown because of the unexpected early operation. To compensate for this, in a number of cases, the study actually started 2-3 hours after the drug administration to make up for the lost cases and to bring N=20 at each time of observation. All data were pooled for each time of observation. Because of this overlap of two sets, we could actually have six observations at each dose level, which also explains why we needed 150 patients instead of 120. Either general, regional or combination anesthesia was used. Twenty-four hours after the operation each patient was visited and was asked about his/her memory of the para-operative events. He/she was also asked to first recollect and then recognize the memory cards from a bunch of similar cards. Failure of both "recollection"

and "recognition" was considered amnesia due to the pre-medication.

**Results.** The six groups were comparable in respect of age, sex, height and weight. All patients remembered receiving the medication (no retrograde amnesia). The grade of sedation was clearly dose dependent in the diazepam group but all doses of lorazepam produced good sedation for a long time (Fig.). Diazepam 10 mg. produced virtually no amnesia (peak effect 5%) at any time, this justifies our not using a placebo in the study. Even diazepam 15 and 20 mg. produced low incidence of amnesia (peak of 20 and 30% respectively). By two and one-half hours, the frequency was less than 10% in all the three groups of diazepam. In the lorazepam group however, the peak effects were close to 30, 45 and 75% in 2, 3 and 4 mg. groups respectively. The latency and the duration of these effects were also quite long (Fig.). The grades of sedation and incidence of amnesia were not parallel.



**Discussion.** As expected, orally given diazepam, 10 mg. does not produce significant amnesia. Even at higher doses the amnesic frequency of diazepam is less than that produced by scopolamine 0.6 mg.<sup>2</sup> However, oral lorazepam has significant amnesic effects especially in 3 and 4 mg doses. The peak, latency and duration of amnesic effect of 3 mg. is comparable to the effect of scopolamine 0.6 mg., but the effects are significantly higher with 4 mg. lorazepam. This knowledge should enable the anesthesiologists to select the appropriate oral premedication given at appropriate doses and time depending on the need of preoperative sedation and supplemental intraoperative amnesia.

#### References.

1. Dundee, J.W., et.al.: Comparison of actions of diazepam and lorazepam. *Brit. J. Anaesth.* 51:439-445, 1979.
2. Dundee J.W. and Pandit, S.K.: Anterograde amnesic effects of pethidine, hyosine and diazepam in adults. *Brit. J. Pharmacol.* 44:140-144, 1972.