Title : PHYSOSTIGMINE REVERSAL OF DIAZEPAM SEDATION

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Introduction. Intravenous diazepam enjoys widespread use for outpatient surgical sedation Recovery times are variable, and delirium, prolonged sedation and central depression have been reported.[1,2] Case reports[1,3] suggesting physostigmine's ability to reverse diazepam delirium/overdose have led us to investigate the belief that physostigmine has an analeptic effect enabling it to hasten recovery from diazepam sedation.

Method. Oral surgical patients undergoing simple extraction under local anesthesia were studied. Twenty-one A.S.A. Physical Status Class I patients, after giving informed consent, were sedated with intravenous diazepam alone until Veril's eye sign (half-lid ptosis) was observed. The patients were randomly divided into a control group and experimental group receiving mean diazepam doses of 16.67 mg and 17.22 mg respectively. At the conclusion of a surgical procedure lasting no longer than 15 minutes, a solution of either 3 ml of normal saline or a 3 ml solution containing 2 mg of physostigmine and 1 mg of atropine was administered intravenously using a double blind technique. Two types of recovery assessment were employed. One involved psychomotor testing via a modified Bender-Gestalt test. The other involved independent subjective ratings of awakedness by the patient and (blind) by the surgeon, scored on a 0-10 measured scale. Psychomotor function was measured preoperatively, immediately postoperatively, and at five and fifteen minute intervals following injection of one of the solutions. In the psychomotor dot test, recovery score was based on a change in the mean number of dots missed from the preoperative to the three postoperative time periods. Data obtained was analyzed using a chi square test (X^2). A rating of subjective feelings of recovery was scored immediately postoperatively and again five minutes later after the administration of one of the solutions. Data retrieved from score differences in the subjective feeling assessment were evaluated in a two-tail Mann-Whitney U test to a $P < .05$ level of statistical significance.

Results. The Bender-Gestalt dot test, as expected, showed fewer missed in both control and experimental groups as the interval following surgery increased (Fig 1). However, when the groups were compared at each of the time periods, the total number of dots missed was not significantly different ($X^2 = 2.26$). In both patient self-assessment of recovery and the surgeon's (independent blind) assessment of recovery, participants in the control group scored significantly higher (more awake) on their rating scales than those in the experimental group. (U values obtained from the Mann-Whitney U test were $U \geq 26$ indicating a significant difference between the two groups.)

Discussion. Physostigmine has previously been shown to be effective in reversing the central anticholinergic action of such drugs as scopolamine.[5] If physostigmine were effective in hastening the recovery from sedation achieved with diazepam, it would be useful to any clinician providing outpatient anesthesia. However, our data indicate the physostigmine-atropine mixture did not speed recovery or improve psychomotor function significantly when compared with normal saline. These results suggest that, in contradiction to previous case reports, physostigmine's central analeptic effect may be specific for anticholinergic drugs. Indeed, when used in combination with atropine (as was necessary to avoid unpleasant muscarinic effects), physostigmine significantly delayed the subjective recovery process. The need to use atropine may have contributed a synergistic sedative effect[6] to an already diazepam sedated patient thus accounting for the observed increase in sleepiness and no difference in psychomotor performance in the groups receiving the physostigmine-atropine mixture.

References.

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CHANGE IN MEAN NUMBER OF DOTS MISSED FROM BENDER-GESTALT TEST

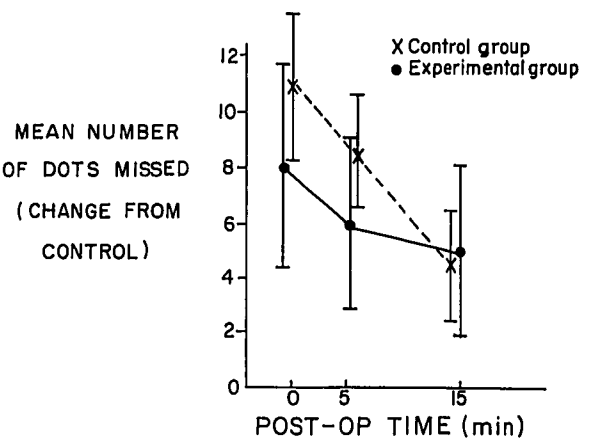

Figure 1