MEMORY FUNCTION AFTER I.V. MIDAZOLAM OR INHALATION OF ISOFLURANE FOR SEDATION DURING DENTAL SURGERY

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SUMMARY

Memory function was assessed with a recognition memory test in 40 dental patients before and after sedation with i.v. midazolam or inhalation of isoflurane. The two groups were comparable, but there was a significant impairment of memory (P < 0.001) at the time of discharge for both words and faces after midazolam, but not after isoflurane.

KEY WORDS

Sedation is necessary for some patients having oral surgical procedures. I.v. midazolam is an established and effective method. As an alternative, inhalation sedation with isoflurane has been suggested as offering good sedation, flexibility of control and quicker recovery [1]. The amnesic effect of midazolam might be desirable for the procedure, but the duration of the impairment of memory is uncertain. A short duration of amnesia was suggested by Dundee and Wilson [2], whereas others suggested that a memory defect persisted for up to 5 h [3]. This duration of effect can cause concern when the patient is treated as an outpatient. As isoflurane gives quicker recovery it may cause less postoperative amnesia. We therefore assessed the amnesic effect of the two methods of sedation in dental outpatients at the time when the patients were ready for discharge.

PATIENTS AND METHODS

Ethics Committee approval for the study was obtained. We studied 40 patients requiring sedation for oral surgical procedures. Patients with serious medical disease, taking a psychotropic drug or with mask phobia were excluded. Explanation of the trial was given to the patients and written consent obtained.

It was arranged that, for a given patient, one anaesthetist administered the sedation while another made the pre- and postoperative assessments and memory tests. A blinded trial was impossible in view of the differences between the techniques. Observer blinding was precluded as the time criteria for discharge differed in the two groups. In addition, it would have been difficult to hide from an observer the signs of i.v. injection and a possible redness around the nose caused by the mask.

To ensure that there was a balanced number of each sex in each group, the two methods of sedation were used alternately in male and female patients.

The methods of administering the sedation, clinical assessments and monitoring during the procedures were the same as in a previous study [1], apart from two modifications. To obviate the slower induction of sedation found previously with isoflurane, 50% nitrous oxide was administered for the first 2-3 min. Recovery and discharge criteria were modified to incorporate the repeat memory tests described below.

Memory tests

A recognition memory test developed by Warrington [4] was used. The test consists of 50...
short words and 50 photographs of male faces printed individually on white cards and a set of two-choice recognition cards. For the purpose of our study we allocated the test cards randomly into two sets, each of 25 words and 25 photographs. One set was used before and the other after the sedation and dental procedure. To avoid potential bias from possible differences between the two sets of cards, they were used alternately, every two patients, as the initial preoperative assessment.

The patients were allowed 3 s to memorize each word or face. In the original test manual, the subject is required to respond "yes" or "no" according to whether he judged each word and face to be "pleasant" or "not pleasant". This was to ensure that the subject attended to each item. In a preliminary assessment, the use of "not pleasant" had been found unsatisfactory in nervous dental patients so, as an alternative, we requested the patient to read out each word and acknowledge each photograph within the 3-s period.

Memory retention was tested by two-choice recognition immediately after presentation of the 25 words and 25 photographs. Each of the original words was paired with a similar word and each photograph with another similar photograph. The patient was required to indicate the correct word or face from each pair. The score was the number of correct answers. The order of the words and faces presented in the retention test was not the same as that shown initially and the left or right position of the correct answer in each pair was also randomized.

The second memory retention test was given when the patient was ready for discharge. Patients in the midazolam group were detained a minimum of 1 h after the i.v. injection to meet the manufacturer's data sheet recommendations. Based on a previous study [5], the isoflurane group was detained for a minimum of 20 min after its discontinuation. As this period did not include the operating time, the discharge times for the midazolam and isoflurane groups were comparable.

In addition to these fixed minimum criteria, the patient was not discharged until assessed as "street fit" by postoperative recovery tests as follows. Ten minutes after operation, the patient sat up; if he was comfortable he tried standing. If he was steady, then a finger–nose test with the eyes closed was performed. Finally, if all the previous tests were complete, the patient walked 10 m in a straight line, turned and came back. Appropriate tests were repeated at 5-min intervals until all were completed successfully and recovery time was taken as this point. The tapping test used in the previous trial was omitted; although it had been of value in studies in volunteers [5], it was not thought to be of sufficient value to use as a routine postoperative assessment in patients.

As in the previous study, all patients were sent home with written instructions, accompanied by an escort and with a post-treatment questionnaire to be completed and returned later.

RESULTS

Six males and 34 females were included in the trial, three males and 17 females in each group. Twenty-five patients had extraction of wisdom teeth, nine had apicectomy, one a reduction of a tuberosity, one excision of a cyst and the remainder multiple extractions. The range of operations was comparable in the two groups.

There was no statistical difference in the age or weight of the two groups (table I). The Corah anxiety score [6], and the visual analogue anxiety scores before and after the procedure were comparable, as were the durations of operations and the time to injection of local analgesia. The mean dose of midazolam was 5.5 mg (range 3–10 mg) and the concentrations of isoflurane after induction ranged from 0.4 % to 1.2 %. As in the previous trial, the recovery time was significantly shorter after isoflurane ($P < 0.05$;
AMNESIA AFTER SEDATION FOR DENTAL SURGERY

[Image of bar chart]

**FIG. 1.** Mean memory score (SEM) for words and faces before (□) and after (□) midazolam and isoflurane sedation. There was a significant reduction of both mean scores (**P < 0.001, Wilcoxon signed rank test) in the midazolam group, and the reduction in scores in the midazolam group was greater than that in the isoflurane group (P < 0.001, Mann-Whitney U test).

Mann–Whitney U test), but the time for induction of sedation was not significantly different.

Other general results mirrored those of the previous trial, both methods being equally satisfactory to the dental surgeon and patients. The incidence of postoperative side effects, assessed by a questionnaire, was similar in the two groups. Although 50% of the patients in the isoflurane group regarded the smell as pleasant, three reported the smell as unpleasant.

**Memory tests**

Eighteen patients recovered fully within the 60 min stipulated after the i.v. midazolam and their second memory tests were carried out at that time. In the remaining two patients, recovery was delayed and their second tests were given at 68 and 78 min. Similarly, 19 patients in the isoflurane group recovered fully and performed their second memory tests 20 min after ceasing to breathe isoflurane. One patient's recovery was delayed and the second test was carried out 30 min after discontinuation of the isoflurane.

There was a significant reduction in the mean memory scores after midazolam sedation, both for words and faces (P < 0.001 in each case; Wilcoxon signed rank test, Bonferroni correction). There was no significant change after isoflurane (fig. 1). The reduction in the mean scores in the midazolam group was also significantly greater than the change in the isoflurane group for both words and faces (P < 0.001 in each case; Mann–Whitney U test, Bonferroni correction).

The overall results of the presedation scores showed that the two test sets of 25 cards were comparable. The mean retention scores for words were 23.0 (SEM 0.4) for set 1 and 22.9 (SEM 0.4) for set 2, while for faces the scores were 21.0 (SEM 0.6) and 20.9 (SEM 0.7), respectively. The mean presedation score for faces was significantly less than that for words (P < 0.001; Mann–Whitney U test). The results of anxiety and memory tests showed no interrelationship.

**DISCUSSION**

With the decrease in demand for general anaesthesia during dental procedures, there has been an increase in the use of sedation techniques [7]. Ogg and his colleagues have drawn attention to the possible legal implications if patients are discharged with a defect of memory after day-case anaesthesia [8] and a similar concern for patients receiving sedation for dentistry indicates the need for studies of memory retention.

The learning and subsequent recall or recognition of words and diagrams have been used widely to test the effects of different psychoactive drugs on immediate memory [9]. The recognition memory test developed by Warrington [4] assesses
both verbal and non-verbal memory and the retention of both words and faces was affected equally after midazolam. Our study confirmed the ease of application of the test. None of the highly anxious patients we tested was distressed by the procedure.

Previous studies of benzodiazepines indicate that amnesia is usual, but they do not appear to be in complete agreement regarding the duration of the effect. In a study of the amnesic effect of diazepam, Clarke and his colleagues used both recall and recognition of words and found the amnesia to be marked for 10 min, then receding over 30 min [10]. Dundee and Wilson found that, after midazolam 5 mg i.v., the effect on memory impairment lasted 20 min [2]. However, Skelly and her colleagues, when comparing diazepam and midazolam, found there was a significant impairment of memory after 5 h with both drugs [3]. Although the prolonged effect found by the latter workers could be a result of more sensitive testing, it might be caused by a greater dose of drugs (mean diazepam 26 mg and midazolam 13 mg), as memory impairment is dependent on dose [11]. The higher dose of benzodiazepine used was consequent upon the use of the “Verrill technique” of dental sedation [12, 13]. In the present study a lesser dose of midazolam (mean 5.5 mg) gave adequate sedation and only one of the patients had the degree of ptosis described by Verrill. Even with this lesser dose, the amnesic effect still persisted for at least 1 h.

Isoflurane has been shown to be an effective alternative for dental sedation. Patients were assessed as street fit 10 min after treatment in one study [14] and in the present study we found no significant impairment of memory at the time of discharge, normally 20 min after operation.

In conclusion, patients may have a memory deficit at the time of discharge after dental sedation with midazolam. Any instructions for patients should be given before sedation and in written form, and verbally to the escort who accompanies the patient home. Isoflurane is an alternative technique for patients for whom a rapid return of memory is desired.

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REFERENCES