Prospective audit: anterograde amnesic effects of IV sedation with midazolam in patients having oral surgery procedures

Précis

An audit measuring the anterograde amnesic effects of intravenous sedation with midazolam in a cohort of patients.

Abstract

Statement of the problem: Concerns were expressed over the level of sedation patients were receiving for oral surgery procedures, with many patients claiming to have had a recollection of the procedure despite receiving IV sedation.

Purpose of study: To determine if patients who are undergoing IV sedation with midazolam in the Oral Surgery Department in the Dublin Dental University Hospital (DDUH) and at the National Centre for Coagulation Disorders are being adequately sedated.

Material and methods: IV midazolam was administered by the sedationists incrementally. Data was collected through specific questionnaires at two different stages. These assessed patients' objective and subjective recollection of events following their procedure under IV sedation. The patients were asked specific questions immediately postoperatively and subsequently at their review appointment. This assessed the patients' objective and subjective recall of the procedure under IV sedation.

Result: Immediately postoperatively, 23% of patients had no recollection of the procedure, 55% had only partial recollection of the procedure, while 22% of patients recalled the procedure. One week postoperatively, total amnesia increased to 32%, partial amnesia reduced to 46%, while those recalling the procedure remained the same at 22%. While 78% of patients had some degree of amnesia of the procedure there were 22% who did not have amnesic effects from the sedative.

Conclusions: There is large inter-individual variation in response to IV sedation with midazolam regarding the anterograde amnesic effects. The reason why a certain proportion of patients have full recollection of the procedure needs to be fully investigated, and any confounding factors identified. Improving anterograde amnesia will provide us with the ability to ensure patient comfort, which is crucial to improving patient care.

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Introduction

The control of pain and anxiety is an integral part of dental treatment.[1] One of the most important goals for a clinician is ensuring patient comfort during a procedure and, as a result, IV sedation is often used as an adjunct to treatment. Sedation is the depression of a patient's awareness of the environment and reduction in their responsiveness to external stimulation,[2] thus enabling dental treatment to be carried out in those with a dental phobia, dental anxiety, or those who are undergoing an unpleasant procedure.[1] There is a continuum of sedation levels, and in dentistry our aim is to achieve sedation at a level between mild and moderate.[2] It is a commonly used technique to provide anxiolytics to patients undergoing oral surgery procedures.[1-4] Patients are reassured that following IV sedation with midazolam they will have reduced anxiety, and feel more comfortable and relaxed, enabling them to proceed with treatment more easily. They are also advised that the majority of patients do not remember the procedure (amnesia) afterwards, and this is one of the benefits of midazolam.[5-7] Midazolam has a fast-acting, short-lived sedative effect when given intravenously, achieving sedation within one to five minutes.[8] The effects of midazolam typically last for one hour but may persist for six hours, including the amnesic effect.[5,8] Midazolam is currently the sedative agent of choice as it is safe and predictable, and has been shown to have a quicker onset of action, providing more profound amnesia compared to other sedative agents.[5,6,9]

'Anterograde amnesia' is defined as a lack of recall of events, or the inability to create new memories,[5] from the time of administration of a drug onwards. This has been proven to improve patient comfort and satisfaction postoperatively,[7] and is an accepted pharmacologic action of a number of commonly used intravenous sedative agents.[5,8] Research has shown that midazolam has a more complete amnesic effect compared to other benzodiazepine drugs.[1,5-7,10,11] One study observed complete anterograde amnesia for over an hour following sedation with IV midazolam;[12] on the contrary, Dundee and Wilson observed that the majority of the amnesic effect had worn off after 20 minutes.[5] A double-blinded, randomised controlled trial observed that the anterograde amnesic effects are dose dependent, with increasing the dose of midazolam being associated with a higher degree of anterograde amnesia.[13] Similarly, a clinical trial by Miller *et al.* supports this finding. In this trial, those patients who were administered a low dose of midazolam (0.07mg/kg) did not have sufficient amnesia compared to those administered 0.10mg/kg or greater of midazolam, who displayed adequate amnesia.[14]

Aims and objectives

A significant number of patients claim to have full recollection of the oral surgery procedure despite receiving IV sedation. In order to ensure patient comfort and optimise patient care, a prospective audit was carried out to investigate the percentage of patients who have full and partial anterograde amnesia after receiving IV sedation with midazolam at the Dublin Dental University Hospital (DDUH) and the National Centre for Hereditary Coagulation Disorders. As it is difficult to measure subjective findings, we have included an objective test to assess the degree of amnesia.

Materials and method

Benchmark/standard

To date there are currently no set standards for the percentage of patients that should experience anterograde amnesia following IV sedation with midazolam. For the purpose of this audit, the benchmark of 90% was used. This was an estimate from previous studies; however, these trials were not in the field of dentistry. This estimate was obtained from a double-blind, randomised controlled trial and case studies assessing anterograde amnesia in patients having IV midazolam for other procedures.[13,15] The randomised controlled trial had a confounding factor in that patients were having general anaesthetic (GA) following administration of the IV midazolam; however, their amnesia was assessed on the events prior to their GA.

Inclusion criteria

Patients with an American Society of Anesthesiologists (ASA) category of I and II, in the age group of 18-80 years, of either gender, undergoing oral surgery procedures consecutively under IV sedation with midazolam between January and March 2015 in the DDUH day theatre and The National Centre for Hereditary Coagulation Disorders were included in the study.

Exclusion criteria

Patients who fell into ASA categories III and IV, patients who were on narcotics, or those who were unable to communicate or had intellectual disabilities, were excluded. Patients who did not attend their review appointment were also excluded, as they did not fulfil the timeline requirement.

Materials

Questionnaire forms consisting of four questions were devised by the authors for data collection immediately postoperatively (**Appendix 1**) and at the review appointment (**Appendix 2**).

Method and data collection

This audit was approved by the DDUH Audit Committee. The sedationists were informed about the audit and gave their consent to participate. All consecutive patients who attended the oral surgery department and who met the inclusion criteria were informed about the audit. Written informed consent was obtained from those who were taking part. The necessary training was provided to all

Appendix 1: Questionnaire used for data collection immediately postoperatively.

Patient name	MRN
Today's date	Surgeon

1. Do you remember getting the local anaesthetic (injection)? (Y) (N)
2. Do you remember the procedure? (Y) (N)
3. Do you remember being asked to remember a word? (Y) (N)
4. Do you remember the name of the fruit you were asked to remember? (Y) (N)

Appendix 2: Questionnaire used for data collection at the review appointment.

Patient name	MRN
Today's date	Surgeon

1. Do you remember getting the local anaesthetic (injection)? (Y) (N)
2. Do you remember the procedure? (Y) (N)
3. Do you remember being asked to remember a word? (Y) (N)
4. Do you remember the name of the fruit you were asked to remember? (Y) (N)

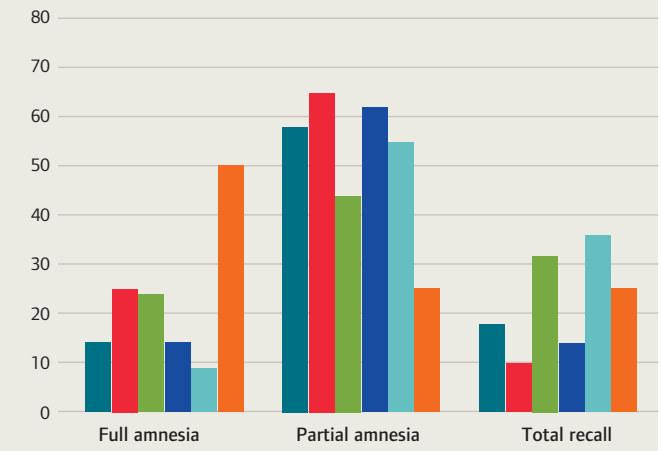

FIGURE 1: Immediate postoperative questionnaire results.

Operator A: A total of 28 patients were included in the audit. Immediately postoperatively, only 14% had full amnesia, and 58% had partial amnesia.

Operator B: A total of 20 patients were included in the audit. Immediately postoperatively only 25% had full amnesia, and 65% had partial amnesia.

Operator C: A total of 25 patients were included in the audit. Immediately postoperatively only 24% had full amnesia, and 44% had partial amnesia.

Operator D: A total of seven patients were included in the audit. Immediately postoperatively only 14% had full amnesia, and 76% had partial amnesia.

Operator E: A total of 20 patients were included in the audit. Immediately postoperatively only 9% had full amnesia, and 55% had partial amnesia.

Operator F: A total of four patients were included in this audit. Immediately postoperatively 50% had full amnesia, and 25% had partial amnesia.

theatre staff involved in collecting data prior to the commencement of this audit. The sedationists carried out their usual method of administering and titrating midazolam. All sedationists agreed that they continued incremental titration of the midazolam until clinically the patient was mildly to moderately sedated, enough to allow them to tolerate the procedure free from anxiety and in a comfortable manner.

The aim of the questionnaires was to assess anterograde amnesia with both objective and subjective measurements. The objective measure of sedation was investigated by asking the patient to remember the name of a fruit (pineapple) during the peak sedation time. The subjective measure was the patients' recollection of the procedure. Literature has shown that the peak sedation effect of midazolam is between five and 10 minutes after the final incremental dose.[7,8] As a result of this, the first time point for asking the patient to remember the name of the fruit was during this timeframe (at 10 minutes). This word was not mentioned to the patient again. Once the procedure was completed the patient was asked to answer the immediate postoperative questions (**Appendix 1**). The time interval varied depending on the length of the procedures but the patient was still sedated at this time. At the review appointment (generally one week postoperatively) the patient was asked to answer the same questions (**Appendix 2**).

Results

A total of 104 patients who underwent IV sedation with midazolam in the DDUH and the National Centre for Coagulation Disorders in St James's Hospital between January and March 2015 were included in this audit. This involved six sedationists who were each assigned a letter (A, B, C, etc.). All sedationists

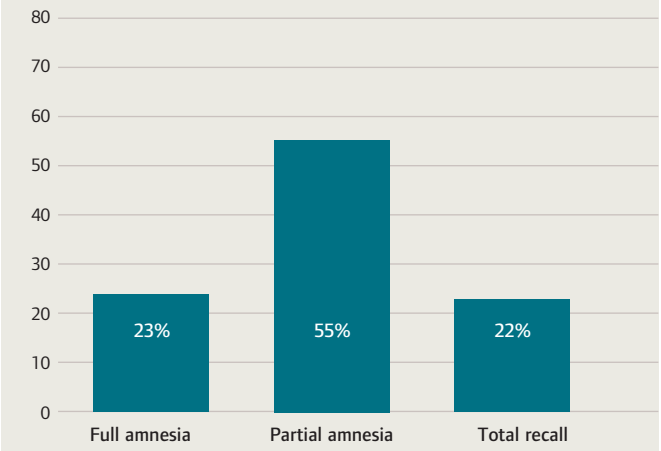

FIGURE 2: Immediate results – percentages based on all patients sedated.

Full amnesia:	23% (24 patients)
Partial amnesia:	55% (57 patients)
Total experiencing amnesia:	78% (81 patients)
Full recall:	22% (23 patients)

titrated midazolam until they were satisfied that adequate and safe sedation had been achieved for each patient. The dose varied from 2-7.5mg of midazolam with a large inter-individual response. There did not appear to be a linear correlation between the dose administered and the degree of amnesia experienced; however, as this was an audit rather than research, this was not investigated for other associations. Some patients had incremental midazolam titrated during the procedure, while others did not.

For the purpose of this audit, patients who did not recall the procedure or the name of the fruit were classified as having total amnesia. Those that could recall either the procedure or the name of the fruit, but not both, were classified as having partial amnesia. The benchmark was that 90% of patients should have some degree of amnesia, partial or total.[8] The results show that all patients had greater amnesia when they had completely recovered from sedation. The percentage of full amnesia improved significantly after recovery. **Figure 1** shows the immediate postoperative questionnaire results. The results shown in **Figure 2** were achieved immediately postoperatively as a percentage of the total number of patients involved in the audit. Results at the review appointment are illustrated in **Figure 3**, and those in **Figure 4** were achieved at the review appointment as a percentage of the total number of patients involved in the audit.

A total of 78% of patients included in the audit had some degree of anterograde amnesia. This fell short of the 90% benchmark. The sample size for operator F was not adequate for their results to be a true representation of the level of sedation achieved. Because of this, these results have been discredited.

Discussion

The control of pain and anxiety is an integral part of dentistry. As it is necessary to have a co-operative patient for an oral surgery procedure to be safely carried out,[6] the adjunctive use of IV sedation is routinely prescribed. Using IV midazolam to sedate patients is commonly employed as a safe and effective method to reduce anxiety prior to dental treatment.[16]

Sedation has been shown to reduce postoperative recall, which is important in patients with anxiety or dental phobia.[3,6] Many studies have shown that

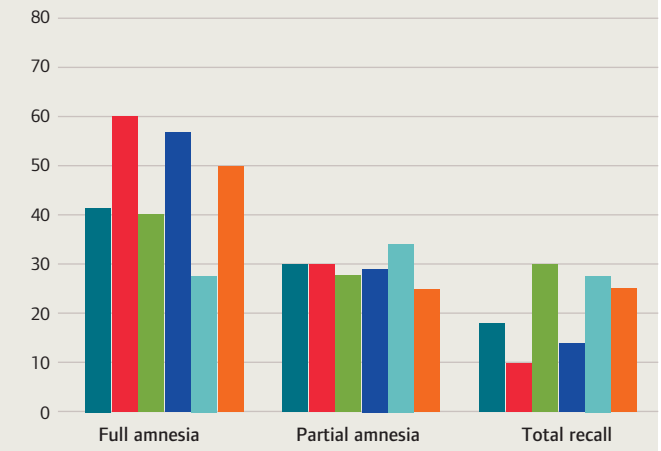

FIGURE 3: Review appointment questionnaire results.

Operator A: A total of 28 patients were included in the audit. Full amnesia increased from 14% to 41%. A total of 71% of Operator A's patients had some degree of amnesia. This fell below the benchmark by 19%.

Operator B: A total of 20 patients were included in the audit. Full amnesia increased from 25% to 60%. A total of 90% of Operator B's patients had some degree of amnesia. This met the benchmark of 90%.

Operator C: A total of 25 patients were included in the audit. Full amnesia increased from 24% to 40%. A total of 68% of Operator C's patients had some degree of amnesia. This fell below the benchmark by 22%.

Operator D: A total of seven patients were included in the audit. Full amnesia increased from 14% to 57%. A total of 86% of Operator D's patients had some degree of amnesia. This fell below the benchmark by only 4%.

Operator E: A total of 20 patients were included in the audit. Full amnesia increased from 9% to 28%. A total of 63% of Operator E's patients had some degree of amnesia. This fell below the benchmark by 27%.

Operator F: A total of four patients were included in this audit. There was no change in the degree of amnesia with 50% having full amnesia. A total of 75% of Operator F's patients had some degree of amnesia. This fell below the benchmark by 15%.

sedation with IV midazolam has the most potent amnesic effects in comparison to all other benzodiazepines.[3,10] Amnesia is essential to optimise patient comfort, especially when undergoing IV sedation due to dental anxiety,[6,16] and anterograde amnesia is proven to improve patient satisfaction postoperatively.[5]

While anterograde amnesia can be related to dose of midazolam administered, a challenge that we are faced with is the continuum of sedation from mild to deep, and it is not always possible to predict how an individual patient will respond.[2] Because of this, an accurate method of monitoring and evaluating the level of sedation is important.[2]

There are a number of confounding factors, which have not been accounted for here, and which may have influenced the results. The peak sedation level is measured subjectively by each sedationist carrying out the procedure, which has its limitations. In addition, the patient-operator relationship, length of procedure, and type and difficulty of the procedure being carried out can also influence the patient experience and amnesic effect. The skill of the clinician carrying out the surgical procedure may also have an impact. These can influence the patient perception of a procedure and the subjective recollection of the event. While inclusion criteria were set, the study had a wide age range. It is well known that the pharmacokinetics of midazolam renders elderly

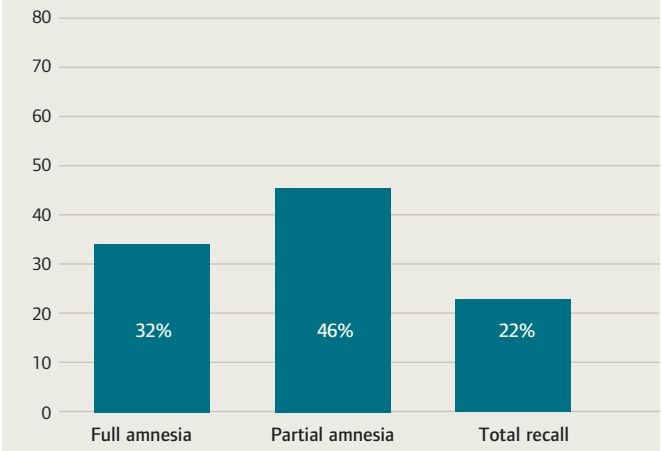

FIGURE 4: Review results – percentages based on all patients sedated.

Full amnesia:	32% (33 patients)
Partial amnesia:	46% (48 patients)
Total experiencing amnesia:	78% (81 patients)
Full recall:	22% (23 patients)

patients more sensitive to its effects,[17] and so further investigation should control for this variable. As this was an audit, further research is recommended to investigate the influences these factors may have.

It was observed that a percentage of patients who were optimally sedated (i.e., did not recall the word) did remember the end of the procedure. This correlated with an oral surgery procedure lasting longer than 50 minutes where the IV midazolam dose was not topped up once the procedure had commenced. This illustrates the short-lived effects of midazolam and the importance of further titration in longer procedures.

In this sample of patients, 22% remembered the word and the surgical procedure. Interestingly, all patients who could recall the word immediately postoperatively could also recall it at the subsequent review. This demonstrates that this cohort did not have the effect of anterograde amnesia. There was no correlation to BMI, dose administered or use of concurrent medications in this group; however, further research in a larger sample and investigation for confounding factors is required to try to establish a reason for this.

While immediately postoperatively many patients reported knowledge of receiving the local anaesthetic and the surgical procedure, the majority of these patients did not recall any part of the procedure at the follow-up review, thus supporting the successful anterograde amnesic effects of midazolam.

It is clear that objective measures are more reliable than subjective analysis for testing a patient's amnesia as many factors can contribute to subjective recall of the procedure. These include the length of the procedure, the type and difficulty of the procedure, and previous dental experience. The results found that recollection of the word 'pineapple' was consistent between immediately postoperatively and at the review, whereas recall of the procedure increased one week later. Whether this is a true account of the procedure or had external influences could not be accounted for in this study.

While 78% of patients in this sample had anterograde amnesia, we cannot explain why 22% of patients had recollection. This audit has comparable results to a similar study of patients undergoing oral surgery procedures following IV sedation with midazolam, where it was observed that the anterograde amnesic effect was unreliable, especially in lower doses.[18] However, the sample size in

that study was low, with only four subjects. Further research with a larger sample needs to be carried out in order to inform and improve future practice. A study carried out over a longer period and with several objective measures being recorded, as well as accounting for confounding factors between operators and patient, would provide more information and thus improve patient care.

Recommendations

At the end of this audit the following recommendations can be made:

1. The benchmark for future audits and research is that 80% of patients will experience anterograde amnesia.
2. Sedationists should ensure that they are maintaining an adequate level of sedation throughout the procedure by closely monitoring the patient's level of sedation and incrementally titrating midazolam as required, especially for procedures of long duration.
3. A larger-scale study should be undertaken to get a full representation of patients undergoing sedation and examine the degree of recollection and likely cause of this.

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CPD questions

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CPD

1. What is the most commonly used drug for IV sedation in dentistry?

- ○ A: Propofol
- ○ B: Midazolam
- ○ C: Clonidine
- ○ D: Lorazepam

2. IV sedation is routinely used for oral surgery procedures for:

- ○ A: Children
- ○ B: Adults
- ○ C: Both

3. What family of drug does midazolam come from?

- ○ A: Non-steroidal anti-inflammatories
- ○ B: Opioids
- ○ C: Benzodiazepines
- ○ D: SSRIs

4. IV sedation provides:

- ○ A: Anxiolytic effect
- ○ B: Partial amnesia
- ○ C: Analgesia
- ○ D: All of the above