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Retrograde amnesia after intravenous sedation and general anaesthesia in a dental hospital

G. Aulakh *, B. Shokouhi, K. Beneng

Oral Surgery Department, Guy's Hospital, Great Maze Pond, London, SE1 9RT, United Kingdom

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Abstract

Midazolam, a benzodiazepine, is commonly used for intravenous sedation for dental procedures and, together with other benzodiazepines, can cause anterograde amnesia. Retrograde amnesia, however, is rare. It is defined as a loss of access to memory of events that occurred, or information that was learned, before the injury or event that caused the amnesia. We know of no reports of this occurring after the intravenous use of midazolam alone and few after general anaesthesia. We present two cases of retrograde amnesia: one after intravenous sedation and one after general anaesthesia.

Keywords: intravenous sedation; general anaesthesia; retrograde amnesia; cognitive dysfunction

Introduction

Midazolam, a benzodiazepine that is used commonly for intravenous sedation in dentistry, causes few side effects and is water-soluble with a rapid onset. Flumazenil is an effective reversal agent. Benzodiazepines act on the gamma aminobutyric acid-A (GABA-A) receptor as a positive allosteric modulator.[1] GABA is the most common neurotransmitter in the central nervous system, and it acts to reduce the excitability of neurons, producing a calming effect on the brain.[2]

Midazolam, among other benzodiazepines, has a known anterograde amnesic effect[3] that limits the recollection of events after it is given. It impairs the acquisition of new information in episodic memory and disrupts the transfer of information from short to long-term memory but has no deleterious effects on the retention or retrieval of information that was previously stored.[4] This effect has been well documented after being given intravenously,[5] intramuscularly,[6] or orally.[7]

Retrograde amnesia is the inability to recollect information that was gained before the onset of memory loss.[8] In its purest form it occurs after injury to the areas of the brain responsible for declarative or episodic memory, or both, though this is rare.[9] Head injuries therefore are accepted causes[10] because of coup and contrecoup injuries that result in cerebral oedema and axonal lesions.[11] Another cause is hypoxia,[12] which can result from drowning, myocardial infarction, or cerebrovascular accident. Dundee and Pandit[13] reported retrograde amnesia in a patient after pethidine 100 mg, hyoscine 0.4 mg, and diazepam 10 mg was given intravenously, but the effect was attributed to a degree of hypoxia that had been caused by profound respiratory depression.

Retrograde amnesia is not, however, an accepted side-effect of benzodiazepines. The few reported cases[11,14] that we know of occurred after general anaesthesia and did not involve midazolam alone.

In their investigation of the amnesic effect of midazolam in children, Twersky et al found that retrograde memory

* Corresponding author. Tel.: +44 020 7188 4397.
E-mail addresses: gsaulakh90@gmail.com, g.aulakh@nhs.net (G. Aulakh), bizhan.shokouhi@gstt.nhs.uk (B. Shokouhi), kiran.beneng@kcl.ac.uk (K. Beneng).

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was not affected, but anterograde memory was weakened.[3] Other authors have also shown that higher doses of sedative drugs increase the duration and degree of anterograde amnesia,[4,15,16] but Hupp and Becker found that its extent and duration did not seem to be affected by the dose of midazolam given.[17]

We present two cases of profound retrograde amnesia, one after midazolam alone and one after a general anaesthetic.

Case 1

A 31-year-old woman attended Guy's Dental Hospital for extractions of upper and lower left third molars under intravenous sedation alone. She was accompanied by her cousin who was present for the second consent process, and left only when sedation had started. The patient had attended for initial consultation four weeks earlier. Her medical history was unremarkable (American Society of Anesthesiologists (ASA) grade I), and she had never had intravenous sedation and had no contraindications to midazolam. There was no history of depression or mental illness in her family, she did not smoke or drink alcohol, and had not used narcotics. Routine preoperative monitoring showed that blood pressure was 113/75 mmHg, heart rate 74 bpm, and oxygen saturation 100%.

Midazolam 1 mg/ml was introduced with an initial bolus of 2 mg over 30 seconds and the sedative effect assessed over the next 90 seconds. After this, 1 mg increments were given every 30 seconds to a total volume of 4 mg. Adequate sedation was measured by ptosis and slurred speech. Intraoperatively there were no surgical or sedative complications, and an Ellis sedation score of 1 was achieved. Observations remained stable throughout the procedure and oxygen saturation remained above 94%.

The escort greeted the patient and sat with her when she arrived in recovery. After a short time the escort raised concerns with the recovery nurse that the patient did not recognise her. The patient was unable to recall where she was or what year it was, and did not recognise pictures of her children and husband. She spoke about a university assignment she was doing, though her escort mentioned that this had been completed about six years earlier. Observations taken in recovery were within normal ranges and the patient had full sensory and motor function. Flumazenil had not been given. She was closely monitored, and one and a half hours later she suddenly became aware of where she was and was able to recognise her escort. There were no further signs of retrograde amnesia and she was discharged home. Follow up showed no long-term effects.

Case 2

A 27-year-old woman attended Guy's Dental Hospital for the planned removal of all four third molars under general anaesthesia. She was fit and well and took no medication. She had no known allergies, no previous history of a general anaesthetic or intravenous sedation, and did not smoke, take recreational drugs, or drink alcohol. Her mother accompanied her as the responsible adult to escort her home.

The patient was treated in the day-case operating theatre and the anaesthetic (fentanyl 50 μg with propofol 180 mg as an anaesthetic induction agent) was delivered by a consultant anaesthetist. Anaesthesia was maintained with 8% sevoflurane with an oxygen saturation of 100% and no episodes of desaturation. The operation was uneventful and took 45 minutes from the induction of anaesthesia until discharge to first-stage recovery.

Her initial recovery was uneventful and there was a normal return of spontaneous respiration. She was given an infusion of Hartmann's solution 500 ml, ondansetron 4 mg, paracetamol 1 g, and diclofenac 75 mg intravenously. Her pulse rate was 73 bpm, respiratory rate 15 breaths/minute, blood pressure 122/77 mmHg, and oxygen saturation 100%.

She regained full consciousness, but was unable to remember why she was in hospital. She thought that she was 15 years old and that her birthday was the following day. She was also unable to recognise her mother and thought that her father was coming to collect her. She was closely monitored and no additional medication was prescribed. Her state of memory remained consistent for about one hour, after which it suddenly and completely returned together with all her cognitive functions. She recognised her mother, knew her age, and knew that she had just had a dental operation. After being monitored for a further 30 minutes she was discharged.

Discussion

Retrograde amnesia after intravenous sedation with midazolam alone or a general anaesthetic is poorly understood. Possible explanations could include the side effects and interactions of the drugs, hypoxia, mental state, family history of mental illness, and use of narcotics. As midazolam was the sole sedative drug used in Case 1 and was not prescribed for induction of general anaesthesia in Case 2, we conclude that the drug was not the causative factor. However, a case of retrograde amnesia after general anaesthesia (fentanyl 150 μg, midazolam 2 mg, thiopental 375 mg, and vecuronium 8 mg intravenously, maintained with 65% nitrous oxide, 34% oxygen, and 1% isoflurane) was immediately reversed after flumazenil was given.[14]

Flumazenil, a benzodiazepine receptor antagonist developed by Hoffmann-La Roche in the 1980s,[18] has been shown to reverse both the amnesic[19] and sedative[20] effects of midazolam. A multicentre study found that flumazenil reversed midazolam-induced sedation more effectively than anterograde amnesia, with only 60% of patients recovering partial memory.[21] Koht and Moss reported improvements in short and long-term memory loss within one minute of flumazenil being given, but the expected anterograde amnesic effect of midazolam was, however, unaffected.[14] In another case,

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