Case Report

Prolonged myotonia and dystonia after general anaesthesia in a patient taking gabapentin

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This is the report of a 55-yr-old female who developed severe myotonia and dystonia after general anaesthesia. Before starting on gabapentin therapy for a neuropathic pain condition, she had undergone numerous uneventful general anaesthetics. Since receiving treatment with gabapentin, she has experienced severe movement disorders on emergence from each subsequent general anaesthetic. The events were unrelated to the choice of anaesthetic or anti-emetic. The most recent event that required a protracted stay in hospital after a day-case surgery is presented in detail, and the possible mechanisms to explain the interaction are discussed.

Keywords: anaesthesia, general; analgesics, gabapentin; complications, dystonia; complications, movement disorders; complications, myoclonus

Accepted for publication: April 4, 2007

Mild transient movement disorders associated with induction and emergence from anaesthesia are a common occurrence. These are very often attributable to the use of propofol or certain anti-emetics. Severe and persistent myotonia and dystonia after emergence from anaesthesia is very rare in a patient without a prior diagnosis of movement disorder. Movement disorders are recognized side-effects of gabapentin therapy, but occur only rarely. General anaesthesia has never previously been reported to exacerbate this side-effect of gabapentin.

Case report

A 55-yr-old female (160 cm, 60 kg) underwent elective removal of metalwork from the right first metatarsal bone in the day-surgery unit. She had a past medical history of chronic right shoulder pain. This was attributed to a previous rotator cuff tear, subsequent repair, and post-operative infection requiring several washout procedures. She had been taking paracetamol 1 g as required, codeine phosphate 50 mg as required, and gabapentin 600 mg three times per day. She did not smoke or drink alcohol. The other significant history she reported was an ‘allergy’ to propofol. Before taking long-term analgesics (since May 2005), she had undergone at least five general anaesthetics using a variety of inhalation and i.v. techniques for minor orthopaedic procedures. All these anaesthetics had been uneventful and recovery had been swift and uncomplicated. However, since starting on the analgesics, in July 2005 she underwent a total i.v. general anaesthetic for Scarf and Akin osteotomies, and developed a severe movement disorder on emergence from anaesthesia. The anaesthetic lasted for 90 min, during which she received alfentanil 0.5 mg, fentanyl 0.1 mg, dexamethasone 8 mg in addition to propofol. This movement disorder was myoclonic in nature, involving mainly her upper limbs, she was conscious throughout the episode. The episode persisted for 3 h and was not relieved by benztropine 2 mg. She was discharged without further symptoms after an overnight stay for observation.

In June 2006, she underwent general anaesthesia for varicose vein surgery. Anaesthesia was induced with propofol 150 mg and fentanyl 50 mg, and was maintained with isoflurane 0.9–1.4%, oxygen, and air. On emergence from anaesthesia, she again developed a severe myoclonic movement disorder involving all limbs, which persisted for several hours, and was not relieved by midazolam administered in boluses of 1 mg. She remained conscious throughout the episode. A neurological opinion was obtained; however she was not symptomatic during the subsequent assessment. She was kept in overnight for observation, but was discharged symptom free the next day. Upon discharge, she was advised that the movement disorder episodes were related to propofol, a medic alert bracelet recommended, and appropriate documentation made in the medical notes to this effect.

The most recent presentation was in December 2006. At the pre-anaesthetic consultation, the notes were reviewed and a plan for gaseous induction and
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Discussion

In 1994, gabapentin was originally approved by the US Food and Drugs Administration as an adjuvant medicine in the treatment of partial seizures. In 2002, approval was granted for gabapentin to be used in the treatment of post-herpetic neuralgia and other neuropathic pain conditions. Gabapentin (1-aminomethyl-cyclohexanecarboxylic acid) is structurally similar to the neurotransmitter gamma-aminobutyric acid (GABA). Its mechanism of action is not completely understood, and it is not clear whether it acts upon GABA receptors. A number of binding sites have been identified for gabapentin, including the \( \alpha_5 \delta \) subunit of voltage-dependent calcium channels in the central nervous system (CNS). It is via this binding site that gabapentin is thought to mediate its analgesic activity.

This is the first reported case of a movement disorder developing as a result of interaction between general anaesthesia and gabapentin. In this case, the patient had previously undergone numerous general anaesthetics before the treatment with gabapentin without any complication. However, after starting the treatment with gabapentin each subsequent general anaesthetic resulted in progressively severe movement disorders. The onset of the movement disorder appeared to be independent of anaesthetic technique. During the most recent episode, the movement disorder manifested despite avoiding the known precipitants such as anti-emetics or propofol, which was resistant to anticholinergic treatment and benzodiazepine therapy, and it lasted for 5 days.

Acute dystonia after general anaesthesia has been previously reported, although these cases have been attributed to the extrapyramidal effects of certain anti-emetics and to the movement disturbances associated with propofol anaesthesia. There have also been several case reports of patients undergoing treatment with gabapentin for essential tremor and for partial seizures who have subsequently developed movement disorders. Pfizer reports in the advisory literature for gabapentin that the drug can cause dystonia infrequently (0.1–1%) and localized myoclonus rarely (<0.1%).

It is not immediately clear how gabapentin and general anaesthesia could have interacted in this case to cause the movement disorders. One possible mechanism could be that gabapentin was somehow displaced from its binding site by general anaesthesia, resulting in a sudden elevation of free drug in the plasma. Serial samples of plasma obtained on the day of the episode and subsequent days do not support this hypothesis. The initial plasma concentration was 2.2 mg litre\(^{-1}\) (reference range 2–20 mg litre\(^{-1}\)) and the concentration rapidly decreased to undetectable over the following days.

Another possible mechanism is that of a direct interaction between the general anaesthetic and gabapentin at the cellular level. It has been established that gabapentin has multiple transmembrane binding sites within the CNS, including various ion channels such as the \( \alpha_5 \delta \) subunit of the voltage-gated calcium channel. It is also accepted that the final common mechanism of general anaesthesia is to somehow disrupt the normal function of ion channels within the CNS. This calcium channel is found throughout the CNS including the basal ganglia. The binding of...
gabapentin to the $\alpha_2\delta$ subunit results in reduced monoamine release\textsuperscript{11} which could reduce dopamine release at this site. A disruption in the balance of dopaminergic and cholinergic transmission at the basal ganglia could induce movement abnormalities.

Recently, there has been renewed interest in the activity of gabapentin at the GABA$_B$ receptor complex.\textsuperscript{8} Given the fact that the GABA receptor is implicated in the mechanism of action of general anaesthetics, this might present the possibility of an alternative site for direct interaction.

An alternative explanation for these events would be that of attention-seeking behaviour. However, our patient did not show such behaviour on other occasions. Also, she was directly observed by a number of doctors over the period of her stay, including a consultant neurologist, none of whom questioned the veracity of her symptoms.

There would appear to be a risk of severe prolonged movement disorder associated with general anaesthesia in patients taking gabapentin, particularly those individuals who report a history of previous minor movement disturbances related to gabapentin use. Where possible in such cases, it may be advisable to use alternative techniques to achieve anaesthesia. It is clear that we do not fully understand the mechanism of action of numerous drugs used in routine practise. This case serves to highlight the need for continued research in this field.

References

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