Prolonged myoclonus and meningism following propofol

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The purpose of this report is to describe a new complication of propofol administration. A previously fit patient underwent intravenous anaesthesia with propofol for removal of dental wires. Postoperatively he developed myoclonic jerking of his limbs. On regaining consciousness he complained of an occipital headache, neck stiffness and photophobia, and was found to have nuchal rigidity on examination. These clinical features resolved over the following week. Subsequent investigations failed to explain the aetiology of the symptoms of meningeal irritation, which suggests that propofol was the causative agent. While prolonged myoclonus has been previously described with propofol administration, this is the first report of meningism occurring with its use.

Cette observation décrit une nouvelle complication causée par l'administration de propofol. Un patient jusque là bien portant reçoit une anesthésie intraveineuse pour l'ablation de broches dentaires. Après l'intervention, il présente des secousses myocloniques aux membres supérieurs. A la période de réveil, il se plaint de céphalée occipitale, de raideur du cou et de photophobie. A l'examen physique, on note une raideur de la nuque. Ces signes cliniques disparaissent au cours de la semaine suivante. L'investigation clinique ne parvient pas à expliquer l'étiologie de ces symptômes d'irritation méningée, ce qui porte à croire que le propofol serait l'agent causal. Alors que des myoclonies prolongées ont déjà été rapportées avec l'administration du propofol, c'est la première fois que le méningisme est associé à son utilisation.

Key words

ANAESTHESICS, INTRAVENOUS: propofol;
COMPLICATIONS: myoclonus, meningism.

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Propofol was introduced into clinical practice in 1986, and since then has been given to over 16 million patients worldwide (data provided by Zeneca formerly ICI Pharma). The incidence of adverse effects has been low and confined mainly to excitatory neurological manifestations. Increased use, however, has unveiled a broadening spectrum of such phenomena, and here we describe the first case of meningism occurring in association with propofol administration.

Case report

A 15-yr-old boy, weighing 52 kg, presented for removal of dental wires under general anaesthesia. These had been inserted five weeks previously for fixation of a fractured mandible, and on that occasion anaesthesia ($O_2:N_2O$: iso-flurane following induction with thiopentone) had been uneventful. The patient had no previous medical history, and had not sustained a head injury or loss of consciousness when fracturing his mandible. There was no history of epilepsy, drug abuse or recent infections.

The patient presented as a day case and was unpremedicated. On arrival in theatre intravenous access was established and 50 µg of fentanyl were given. Monitoring consisted of non-invasive blood pressure measurement, ECG, and pulse oximetry. After pre-oxygenation, anaesthesia was induced with propofol 175 mg, and this was not accompanied by excitatory phenomena or pain on injection. The dental wires were quickly removed (one minute), and no further anaesthetic agents were administered. On resumption of spontaneous ventilation the patient was brought to the recovery room where five minutes after induction of anaesthesia he developed generalised myoclonic jerking. These spasmodic contractions were asynchronous in nature, involved the muscles of his arms, trunk and legs, and were exacerbated by attempts to rouse him. He remained unresponsive and was noted to have a marked disconjugate gaze and pupillary dilatation. This state persisted for 35 min and during this time temperature, blood pressure, heart rate, arterial blood gas, and blood glucose measurements were within normal limits. Then the patient regained consciousness but there was no improvement in the myoclonus. Diazepam, 5 mg iv, was administered with minimal effect on the myoclonic jerking.

The patient began to complain of a severe occipital headache which was not effected by posture, and photophobia. On examination he was found to have marked neck stiffness which did not involve the musculature of his shoulder or back, and there was no associated extension of his extremities. A neurological opinion was sought and a CT scan of brain and a lumbar puncture (LP) were performed, both of which were found to be normal. Subsequent cultures and viral studies of CSF fluid were also negative.

Two hours postoperatively the myoclonic movements had decreased in frequency, and the occipital headache, photophobia and neck stiffness had decreased in intensity. The patient was returned to the ward where he was kept for observation. Here his headache which remained unchanged in character, improved slightly in response to nonsteroidal anti-inflammatory agents, and gradually resolved over the next seven days. While the resolution of his neck stiffness followed a similar pattern his photophobia had resolved by the third postoperative day. The myoclonic jerking decreased in frequency but also persisted for one week. At a follow-up visit two weeks postoperatively he was completely asymptomatic.

Discussion

A wide range of neurological excitatory events (37 from 1987–1992) following induction of anaesthesia with propofol has been reported,¹ including myoclonus,² opisthotonus,³ and grand-mal seizures.⁴ In this instance we have described a case of persistent myoclonic jerking associated with symptoms of meningeal irritation following propofol administration.

There can be no doubt that in this case the myoclonus was induced by propofol. Aside from a small dose of fentanyl, propofol was the only drug used. While grand-mal seizures have been reported in association with fentanyl,⁵ there have been no reports of dystonic reactions associated with its use. Not only has this phenomenon been well described in association with propofol, but there have also been case reports of these movements persisting for a number of days postoperatively.^{6,7} There is much debate as to whether these neuroexcitatory phenomena, which contradict the convincing evidence of propofol's anticonvulsant activity,⁸ are due to true cortical seizure activity or are due to a subcortical (i.e., midbrain and brainstem) excitatory-inhibitory centre imbalance.⁹ This latter theory is supported by the fact that propofol is thought to have more subcortical potency than other anaesthetic agents,^{10,11} and this effect on subcortical centres may persist at subhypnotic doses.

Associated signs and symptoms of meningeal irritation have not been previously reported with the use of propofol, and it is not easy to explain the possible patho-

physiology of the meningeal symptoms in this patient. Their presence in association with a normal CT scan and CSF studies would tend to rule out concurrent infective or neoplastic process. While there are other possible causes for symptoms of meningeal irritation in the presence of normal radiological and CSF studies, their close association with the myoclonus both in intensity and duration would suggest a common aetiological factor. A form of propofol-induced opisthotonus may explain the finding of neck stiffness. This was not, however, associated with any degree of extension of the extremities, nor would it explain fully the patient's headache and photophobia. It is possible that the symptoms of headache and photophobia may have been exacerbated by performing the diagnostic LP. This is not supported by the fact that at no time was the headache related to posture, and that both these symptoms preceded the LP. Meningism has been previously described as part of a central anticholinergic reaction to a scopolamine premedication¹². As propofol has been shown to have a uniformly depressant effect on the central nervous system it is possible that at subhypnotic doses, inhibition of vagal nuclei may have produced some anticholinergic activity which caused symptoms of meningeal irritation. The marked disconjugate gaze and pupillary dilatation which were present would also suggest abnormal activity at a subcortical level. The accumulating evidence of propofol's specific antiemetic action at subhypnotic doses¹³ indicates a possible action at dopaminergic¹⁴ and cholinergic sites. Appadu *et al.*¹⁵ have recently shown that propofol does not bind strongly to dopamine D₂ receptors which further supports a possible role for an anticholinergic component to propofol's antiemetic action.

In conclusion it has to be admitted that a conclusive explanation of these neurological manifestations in association with propofol has yet to be found. We can, however, take some comfort in the knowledge that they do appear to resolve completely with time. Ries *et al.*¹⁶ postulated that neuroexcitatory events associated with propofol may have a common mechanism, namely an enduring refractoriness of inhibitory pathways in the brainstem. It may be particularly relevant to this case, that an anticholinesterase agent (physostigmine) proved successful in reversing the opisthotonus in one instance.¹⁷ In the event of encountering these phenomena, it has been recommended that therapy be aimed at potentiating the inhibitory neurotransmitters glycine and γ -aminobutyric acid (GABA) using benzodiazepines, physostigmine, and chlormethiazole.¹⁶

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