Initially, selective bone marrow depression was thought to be the responsible mechanism [5], but, after phenytoin-dependent antiplatelet antibodies were demonstrated, an immune-mediated destructive process was deemed more likely [4]. It has been postulated that the epoxide metabolite of phenytoin covalently binds to platelet walls, inducing antiplatelet antibodies against the hapten created, leading to destruction of circulating platelets [6]. The necessary metabolism of phenytoin to phenytoin epoxide, platelet binding and subsequent immune response would account for the delay in onset of thrombocytopaenia. Low concentrations of epoxide hydrolase, the enzyme responsible for the breakdown of phenytoin epoxide, would potentially predispose patients to phenytoin-induced thrombocytopaenia, on top of those unknown factors that contribute to idiosyncratic reactions. Interestingly, it has been demonstrated that dexamethasone can induce certain hepatic cytochrome p450 enzymes, but inhibits epoxide hydrolase production, conceivably resulting in an increased concentration of phenytoin epoxide [7]. Other agents that potentially increase the concentration of phenytoin epoxide, and have therefore been implicated as a contributory factor in phenytoin-induced thrombocytopaenia, include histamine-2-receptor antagonists [6]. The treatment of phenytoin-induced thrombocytopaenia is discontinuation of phenytoin and, if the patient has associated life-threatening haemorrhage, platelet transfusion. Giving $1\,g\,kg^{-1}$ of intravenous immunoglobulin has been associated with a rapid increase in the platelet count, and should be considered [3].

Although an uncommon complication of treatment, this case highlights that phenytoin-induced thrombocytopaenia can be potentially fatal in neurosurgical patients if undetected before surgery. We recommend that a repeat platelet count be performed on all patients that are started on phenytoin before surgery, especially if it has been prescribed in combination with dexamethasone.

G. Thorning, K. Raghavan
Department of Anaesthesia
Critical Care and Pain Management
King's College Hospital
London, UK

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Anaesthetic management and perioperative monitoring of a patient with narcolepsy

doi: 10.1017/S0265021507000841

EDITOR:
Narcolepsy, also known as Gélineau syndrome, is a chronic sleep disorder characterized by excessive sleepiness during the day, sleep paralysis, hypnagogic hallucinations and cataplexy (sudden loss of muscle tone). Common features are uncontrollable attacks of deep sleep and disturbed nocturnal sleep. We report the anaesthetic management for laparoscopic cholecystectomy of a patient with a long history of narcolepsy.

A 50-yr-old woman (92 kg, 172 cm) suffering from narcolepsy was scheduled for laparoscopic cholecystectomy under general anaesthesia. Narcolepsy was diagnosed 20 years ago, after evaluation in

Correspondence to: C. Staikou, Department of Anaesthesia, Aretaieio Hospital, Medical School, University of Athens, 76 Vassilissis. Sophias Ave., 11528, Athens, Greece. E-mail: c_staikou@yahoo.gr; Tel: +30210 6218819; Fax: +30210 6218493

Accepted for publication 12 May 2007 EJA 4513
First published online 9 July 2007

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https://doi.org/10.1017/S0265021507000841 Published online by Cambridge University Press

a sleep disorder centre. The daytime sleep attacks had a duration of 2–3 h and were characterized by uncomfortable sensation in the extremities, excessive sleepiness and sleep paralysis. She reported one attack about every 4 days. The patient was not receiving any medication for narcolepsy. She had received a general anaesthetic for a hysterectomy 13 years ago.

Preoperatively, a psychiatric evaluation confirmed no disturbance and the physical examination was unremarkable. A baseline EEG was recorded 24 h preoperatively, while the patient was sitting relaxed in a chair with her eyes closed. The EEG was normal, showing an alpha rhythm with peak frequency at 9 Hz. The patient was calm and very co-operative. She did not receive any premedication the night before surgery.

Before induction of anaesthesia, apart from routine monitoring (electrocardiography, heart rate, non-invasive blood pressure, S_PO_2), a BIS^{TM} sensor was attached to the patient's forehead for connection to a BIS XP monitor (Aspect Medical Systems Inc., Newton, MA, USA). Also, an adult sensor (Somasensor®; Somanetics Corporation, Troy, MI, USA) connected to an INVOS 4100 cerebral oximeter (Somanetics Corporation, Troy, MI, USA) was attached to the skin over the right frontal area.

Anaesthesia was induced with thiopental 450 mg and cisatracurium 17 mg intravenously (i.v.). The patient received 3 $\mu g\,kg^{-1}$ of fentanyl for intraoperative analgesia. Anaesthesia was maintained with sevoflurane in a nitrous oxide : oxygen mixture (F_iO_2 : 0.4). Inhalational agent concentration was titrated according to bispectral index (BIS) values. At the end of the procedure, paracetamol 1200 mg and diclofenac 75 mg were administered intramuscularly for postoperative analgesia.

BIS and regional cerebral oxygenation ($rRSO_2$) baseline values were recorded before induction of anaesthesia (BIS 98 and $rRSO_2$ 70%) and every 5 min thereafter. End-tidal sevoflurane concentration was titrated between 0.23% and 1.8% according to BIS. BIS values fluctuated between 40 and 60 and $rRSO_2$ values between 68% and 76%. An EEG was recorded 24 h postoperatively and was normal without significant changes compared with the preoperative EEG. The postoperative course was uncomplicated and the patient was discharged on the third postoperative day. During her stay in the hospital, there was not any postanaesthetic change in the frequency and characteristics of her narcoleptic episodes.

Narcolepsy is an under-diagnosed neurologic disorder characterized by derangement of sleep–wakefulness cycle. The incidence of the syndrome internationally is estimated to be 0.02–0.16% [1]. A genetic contribution via human leukocyte antigens DR2 and DQwl is possible. The alleles DQB_1*0602 and DQA_1*0102 have been strongly associated with the syndrome [2].

The disabling symptoms of the syndrome have a dramatic impact on patients' lifestyle and can lead to social isolation and depression. The pharmacological treatment is symptomatic and may be supplemented by behavioural strategies and psychological support. Central nervous system (CNS) stimulants (dextroamphetamine, methylamphetamine, methylphenidate, pemoline and modafinil) and antidepressants (tricyclics and selective serotonin reuptake inhibitors) have been used in narcolepsy [3]. CNS stimulants are useful in reducing sleepiness, while antidepressants are effective in controlling cataplexy.

Due to the rarity of the syndrome, guidelines for the anaesthetic management of patients with narcolepsy have not been established. Our patient was not receiving any treatment. However, interactions of drugs to treat narcolepsy and anaesthetics are very likely. Amphetamines produce decreased sympathetic response to hypotension due to depletion of CNS catecholamine stores. Haemodynamic instability may occur intra- and postoperatively. Despite these possible complications, preoperative discontinuation of medication is under question. Burrow and colleagues [4] suggest that pharmacological therapy for narcolepsy should be continued perioperatively, since they found no increased risk for anaesthetic complications related to the narcolepsy medication. However, it all depends on the type of drugs used for narcolepsy treatment.

Prolonged recovery after general anaesthesia, postoperative hypersomnia and apnoeic episodes due to possible increased sensitivity to anaesthetic drugs may occur. On the other hand, regional anaesthesia may be an alternative choice. Unfortunately, narcoleptic fits have been reported during spinal anaesthesia and such an undesirable complication cannot be underestimated [5].

Oversedation can be prevented perhaps by avoiding benzodiazepines and using agents other than opioids for postoperative pain control [6]. We avoided premedication and postoperative opioids. We also avoided the ultrashort-acting opioid remifentanil, which is associated with acute tolerance development and postoperative secondary hyperalgesia [7,8]. Tolerance development to the opioid receptors may decrease the efficacy of other opioids, which our patient might need postoperatively. Paracetamol and non-steroidal anti-inflammatory drugs offered adequate postoperative analgesia to the patient without sedative effects.

Propofol has been used uneventfully in anaesthetic management of narcoleptic patients [6]. Total

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https://doi.org/10.1017/S0265021507000841 Published online by Cambridge University Press

i.v. anaesthesia with short-acting agents such as propofol and remifentanil has been reported to be successfully used in a patient with narcolepsy who underwent cardiac surgery [6]. The authors of that report considered that perioperative monitoring of the patient's hypnotic state would have added valuable information, but this kind of monitor was not available in their department [6].

There are limited data about inhalational anaesthesia in narcoleptic patients while there are no reports of using BIS and brain oximetry as adjuncts to the anaesthetic management of patients with narcolepsy. There is one case report in Spanish of using inhalational anaesthesia in Gélineau syndrome and the authors reported postoperative complications due to anaesthesia [9].

We used sevoflurane to maintain general anaesthesia. Although we do not know the impact of narcolepsy on BIS monitoring, we used BIS values to titrate the volatile anaesthetic agent, hoping to decrease our patient's anaesthetic requirements. We maintained BIS values between 40 and 60 in order to avoid either awareness or prolonged recovery. The surgical procedure lasted 95 min. After discontinuation of general anaesthesia, the BIS values increased from 62 to 97 over a period of 14 min. The patient recovered and was extubated safely. There were no postoperative undesirable events related to general anaesthesia.

Brain oximetry was also used for continuous monitoring of the regional cerebral oxygen saturation. We observed no significant changes in the intraoperative $rRSO_2$ values as well as in the postoperative EEG when compared to the preoperative $rRSO_2$ values and EEG.

For the management of this narcoleptic patient, we avoided preoperative benzodiazepines, kept opioid analgesics to a minimum and used inhalational anaesthesia with sevoflurane. The anaesthetic technique was uneventful. Since non-invasive brain monitoring is harmless and might provide some information, we used BIS and cerebral oximetry despite the lack of evidence-based data of this monitoring in narcolepsy.

C. Staikou, A. Tsaroucha, A. Fassoulaki
Department of Anaesthesia
Aretaieio Hospital
Medical School
University of Athens
Athens, Greece

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Intravenous phenytoin and percutaneous arterial cannulation: the purple-glove syndrome

doi: 10.1017/S0265021507001007

EDITOR:
Phenytoin is commonly associated with various adverse effects; rare ones include drug-induced lupus, purple-glove syndrome (PGS), pigmentary alterations, IgA bullous dermatosis and generalized cutaneous eruptions [1]. We here report a case of distal limb ischaemia following severe soft tissue injury (PGS) on intravenous (i.v.) administration of phenytoin in the same limb having arterial cannulation.

A 38-yr-old male (82 kg), with a medical history significant for hypertension and epilepsy, presented

Correspondence to: Yatindra Kumar Batra, Department of Anaesthesia and Intensive Care, Post-graduate Institute of Medical Education & Research, Chandigarh 160012, India. E-mail: ykbatra@glide.net.in; Tel: +91 172 2715545; Fax: +91 172 2744401

Accepted for publication 18 May 2007 EJA 4150
First published online 21 July 2007

https://doi.org/10.1017/S0265021507000841 Published online by Cambridge University Press