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 thrombocytopenia. Low concentrations of epoxide hydrolase, the enzyme responsible for the breakdown of phenytoin epoxide, would potentially predispose patients to phenytoin-induced thrombocytopenia, 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, conservatively 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 thrombocytopenia, include histamine-2-receptor antagonists [6]. The treatment of phenytoin-induced thrombocytopenia 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 thrombocytopenia 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.

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**References**


**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...
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, \( S_{\text{PO}_2} \)), a BIST\(^\text{TM} \) 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 (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 (\( \text{FiO}_2:0.4 \)). 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 \((r\text{RSO}_2)\) baseline values were recorded before induction of anaesthesia (BIS 98 and \( r\text{RSO}_2 70\% \)) 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 \( r\text{RSO}_2 \) 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 DQw1 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 hypoxomnia 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].
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-year-old male (82 kg), with a medical history of epilepsy and hypertension, presented with distal limb ischaemia following severe soft tissue injury (PGS) on intravenous (i.v.) administration of phenytoin in the same limb having arterial cannulation.