Status Epilepticus Following Intrathecal Administration of Bupivacaine: A Case Report

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Abstract
Spinal anesthesia is common practice and rarely causes complications. Although extended experience is present, seldom side effects of this technique and the administration of intrathecal local anesthetics and/or opioids can occur. We present a case in which a 76-year old woman undergoing total hip arthroplasty received a low dose of intrathecal bupivacaine and sufentanil. One hour after administration, she developed myoclonic seizures of the lower extremities followed by generalized tonic-clonic seizures and status epilepticus. We conclude that status epilepticus is a rare and possible lethal side effect of intrathecal bupivacaine. Symptoms may be misleading, highlighting the importance of early recognition and adequate management.

Keywords
intrathecal, bupivacaine, spinal anesthesia, status epilepticus, generalized tonic-clonic seizures

Introduction
Spinal anesthesia is routine practice for surgery of the lower abdomen, the pelvis or the lower extremities. Adverse systemic effects of local anesthetics (LA) include local anesthetic systemic toxicity (LAST) and allergic reactions. In contrast, LA can also cause direct toxic effects to muscle tissue, leading to myocytes destruction. LAST occurs when plasma concentrations of LA reaches toxic levels. This may result from direct intravascular injection or after significant systemic absorption depending on the site, concentration and amount of LA.

Systemic effects can be further subdivided into central nervous system (CNS) toxicity and cardiovascular systemic toxicity. CNS toxicity occurs when LA crosses the blood brain barrier. The potential for CNS toxicity correlates with the potency of LA. Potent lipid-soluble agents such as bupivacaine can cause CNS toxicity at lower doses than less potent agents. Toxicity leads to CNS excitation followed by CNS inhibition with potential respiratory depression and even death. When systemic concentrations reaches higher levels, LA can also cause cardiovascular system toxicity with dysrhythmias and low systemic vascular resistance. Generalized tonic-clonic seizures after intrathecal administration of bupivacaine however is very rare. We hereby present a case of status epilepticus in a woman after intrathecal administration of a low dose of bupivacaine.

Case Report
A 76-year-old woman underwent a total hip arthroplasty with spinal anesthesia. She had a medical history of a total hysterectomy and supraventricular tachycardia for which she had undergone an ablation and received flecainide and bisoprolol. Preoperative assessment was normal. There was no history of drug abuse or epilepsy. No premedication was used. Surgical antibiotic prophylaxis with cefazolin was given. Spinal anesthesia was performed on the level of L4-L5. The skin was disinfected with chlorhexidine and locally anesthetized with 3 ml lidocaine 2%. After obtaining cerebrospinal fluid, 3ml hyperbaric bupivacaine 0.5% and 0.5 ml sufentanil 5 µg/ml was administered and a good block was achieved. Dexamethasone 10 mg and tranexamic acid 1000 mg were given intravenously in line with our orthopedic protocol. Paracetamol 1000 mg and ibuprofen 600 mg were also administered. The operation was uneventful and the surgeons did not locally infiltrate the hip with anesthetics. One hour...
after the intrathecal administration of bupivacaine the patient developed abdominal pain. Five minutes later she developed myoclonic seizures of the lower extremities followed by myoclonic seizures of the upper extremities without losing consciousness. Another five minutes later she developed generalized tonic-clonic seizures and status epilepticus. Midazolam 5 mg, levetiracetam 1 g and magnesium sulfate 1 g did not stop the status epilepticus. The patient was sedated with propofol, intubated and transported to the intensive care unit where sodiumvalproate loading dose was given, followed by a continuous infusion. An EEG was obtained and confirmed epileptic activity. CT scan and MRI of the brain showed no intracranial abnormalities. Analysis of spinal fluid was normal. The next day, a control EEG showed burst suppression after which sedation was decreased. Clonic symptoms, however, reoccurred and, in agreement with the neurologists, full sedation was administered for 72 hours. Thereafter, control EEG showed a non-epileptiform disturbed trace and sedation was stopped. Only 6 days after stopping the sedation there was a gradual recovery of consciousness with a successful extubation attempt. Eighteen days after the insult the woman was discharged from the intensive care unit. The woman fully recovered and there were no residual neurological symptoms at discharge.

**Discussion**

Bupivacaine is a frequently used LA from the amide group and is associated with more complications compared to the other amide LA such as levobupivacaine and ropivacaine. Serious complications with LA have been described after inadvertent intravenous administration or after important systemic absorption. Side effects include central nervous system excitation followed by depression and cardiovascular symptoms with reduced systemic vascular resistance and dysrhythmias. The risk of CNS toxicity is directly correlated with the potency of LA. Local anesthetics may cause myoclonus and generalized tonic-clonic seizures after epidural administration, plexus block, or erroneous intravenous administration. Severe neurological complications after intrathecal administration of LA however are very rare (0.4/10000 Moen et al). Thereby, our knowledge about neurotoxicity of local anesthetics is limited and we have little experience with the presenting symptoms and the appropriate treatment.

If neurologic complications after intrathecal administration of LA do occur, this mostly results from high doses with systemic absorption or from cephalic diffusion of the drug. In our case the exact mechanism is unknown. Although cerebrospinal fluid was aspirated, inadvertent intravascular injection of bupivacaine is possible. Furthermore, bupivacaine leads to an increase of blood flow to the spinal cord due to vasodilation with increased systemic absorption. Generalized tonic-clonic seizures have also been reported after inadvertent intravenous injection and following intrathecal administration of bupivacaine for cesarean section. Similar to our case, Akil et al reported a case in 2014 in which a 23-year-old man received intrathecal bupivacaine for a varicocele repair after which he developed myoclonic movements of the legs followed by generalized tonic-clonic seizures. They also concluded that intrathecal administration of bupivacaine was responsible for the status epilepticus. We added a table which provides the clinical details of the references and compared them to our case. (Table 1)

Other causes should be excluded before concluding that intrathecal bupivacaine is responsible for the neurological symptoms. Therefore, we performed a CT scan of the brain and a lumbar puncture, both of which showed no abnormalities. It is also possible that the epilepsy was caused by drugs like tranexamic acid or antibiotics such as cephalosporins but considering the timing of symptoms and the resistance to initial therapy, this seems less plausible. We believe that the

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**Table 1. Clinical Details of the References and Our Case.**

| Article | Age  | Gender | Medical history | Type of surgery | Type of anesthesia | Toxicity |
|---------|------|--------|----------------|-----------------|-------------------|----------|
| Generalized tonic-clonic seizure following spinal anesthesia for Cesarean section with bupivacaine - A case report | 27 years | Female | Hepatitis B carrier | Emergency cesarean section | Spinal anesthesia: 8 mg hyperbaric bupivacaine | Generalized tonic-clonic seizures |
| Generalized Tonic-clonic Seizures Following Spinal Anesthesia Using Bupivacaine for Cesarean Section: A Case Report | 19 years | Female | No medical history | Emergency cesarean section with indication of meconium-stained liquor | Spinal anesthesia: 11 mg hyperbaric bupivacaine | Generalized tonic-clonic seizures |
| Status epilepticus induced by intrathecal bupivacaine use: A case report | 23 years | Male | Varicoceles | Varicocelectomy | Spinal anesthesia: 12.5 mg bupivacaine | Generalized tonic-clonic seizures |
| Status epilepticus following intrathecal administration of Bupivacaine—a case report | 76 years | Female | Total hysterectomy and supraventricular tachycardia | Total hip arthroplasty | Spinal anesthesia: 15 mg hyperbaric bupivacaine and 2.5 µg sufentanil | Generalized tonic-clonic seizures and status epilepticus |
intrathecal administration of bupivacaine was responsible for the generalized tonic-clonic seizures and status epilepticus.

Conclusion
Intrathecal use of hyperbaric bupivacaine is common and considered to be safe, although this case highlights a very rare but important side effect, that is, status epilepticus. Documenting uncommon side effects may help us to try to understand the underlying pathophysiology and inform colleagues, in order to recognize and treat promptly.

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Ethics Approval
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Informed Consent
Informed consent for patient information to be published in this article was not obtained because the ethics committee did not consider it necessary given that this case report is completely anonymous.

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