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CASE REPORT / OLGU SUNUMU

Status epilepticus induced by intrathecal bupivacaine use: A case report

İntratekal bupivakain kullanımına bağlı status epileptikus: Olgu sunumu

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ABSTRACT

Local anesthetics are commonly used as analgesics and anesthetics. Local anesthetics from the amide group may lead to symptoms of the central nervous system (CNS) such as depression, seizures or altered mental state, while they may lead to arrhythmia in the cardiovascular system (CVS). The causes of the neurologic complications observed with spinal local anesthetics are the administration of high doses, rapid entry into the systemic circulation, erroneous administration through the IV route, or the diffusion of the drug towards the cephalic region. Bupivacaine is among the most commonly used local anesthetics from the amide group. However rare, neurological injury after administered bupivacaine can be distressing to patients and their families. In our patient, we have administered bupivacaine through the intrathecal route. Thus, we would like to present a case where status epilepticus in the form of generalised tonic-clonic seizures (GTC) has developed subsequent to the intrathecal administration of bupivacaine. *J Clin Exp Invest 2014; 5 (1): 108-111*

Key words: Local anesthetics, status epilepticus, bupivacaine

ÖZET

Lokal anestezikler anestezik ve postoperatif analjezik olarak sıkça kullanılmaktadırlar. Bupivakain en sık kullanılan amid grubu lokal anestezik maddelerden biridir. Amid grubu lokal anesteziklerin santral sinir sistem(SSS)'de depresyon, nöbet ve bilinç değişikliğine neden olurken kardiyovaskuler sistem (KVS)'de aritmilere yol açmaktadır. Spinal lokal anesteziklerin nörolojik komplikasyonların nedenleri ilacın yüksek dozda verilmesi, hızla sistemik dolaşıma geçmesi, yanlışlıkla İV verilmesi ya da ilacın sefale doğru yayılmasıdır. Bizim olgumuzda intratekal bupivakain kullanıldı. İntratekal bupivakain kullanımına bağlı jeneralize myoklonik nöbet bildirilmişitir. Ancak araştırmalarımıza göre intratekal bupivakain kullanıma bağlı Jeneralize tonik klonik (JTK) tarzda status epileptikus olgusu bildirilmemiştir. Olgumuz intratekal bupivakain kullanım sonrası gelişen JTK tarzda status epileptikus vakası olması nedeni ile sunuldu.

Anahtar kelimeler: Lokal anestezikler, status epileptikus, bupivakain

INTRODUCTION

Local anesthetics are commonly used as analgesics and anesthetics. Bupivacaine is among the most commonly used local anesthetics from the amide group. Bupivacaine is considered to be more toxic than levobupivacaine or ropivacaine, which are also from the amide group[1]. Anesthetics from the amide group affect both the central nervous system (CNS) and the cardiovascular system (CVS) and may cause serious complications [2]. Generalised tonic-clonic seizures (GTCS), myoclonus and sudden death have been reported subsequent to the epidural administration, use for plexus block, and erroneous intravenous (IV) administration of local anesthetics.

In our patient, we have administered bupivacaine through the intrathecal route. Although generalised myoclonic seizures have been reported in relation with the intrathecal administration of bupivacaine [3], according to our literature research, no status epilepticus in the form of GTC has yet been reported in association with the intrathecal use of bupivacaine. Thus, we would like to present a case where status epilepticus in the form of GTC has developed subsequent to the intrathecal administration of bupivacaine.

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CASE REPORT

In a 23-year old male patient who presented with a history of varicoceles, surgery under spinal anesthesia was planned. The preoperative hemogram, biochemistry (glucose, creatinine, sodium, potassium, calcium, urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), electrocardiography (ECG), and chest X-ray were within normal limits. The systemic and neurologic exams of the patient were normal. The patient and family history included no evidence of epilepsy or any other chronic diseases. The spinal anesthesia was performed under routine monitorization and through the insertion of a spinal catheter into the vertebral space. The aspirated cerebro-spinal fluid (CSF) was observed to be clear and without any trace of blood. Bupivacaine 12.5mg (marcaine heavy) was administered into the vertebral space in the appropriate dose and duration. Soon after the infusion of the medication, the patient complained about pain and contractions in the perineal region. The neurological examination of the patient carried out 10-15 minutes later revealed that he was mildly confused and stereotypic and involuntary myoclonic movements were occurring in his legs. In order to resolve the contractions in the perineal region and to achieve full anesthesia, 15 ml of 1% plirocaine (citanest) was injected into the incision area. Although the contractions and the pain were relieved, since the patient was still slightly confused, he was administered 1mg/kg of propofol in order to achieve full anesthesia and to start the surgery. The operation was completed successfully. As the patient regained consciousness, just before he was fully awake, he had a generalised tonic-clonic (GTC) epileptic seizure that continued for 2-3 minutes. The seizure was stopped through the administration of 10mg of intravenous (IV) diazepam (diazem). However, about 6-8 minutes later, the GTC seizure restarted. Another 10mg dose of (IV) diazepam was injected; but as the seizure continued, the patient was given a 20mg/kg loading dose of valproate followed by a dose of 3mg/kg/min for 10 minutes. When the seizure still did not recede, the patient was administered 1mg/kg of propofol. He was intubated and the infusion of propofol continued at a dose of 1mg/kg/h. After 8 hours without seizures, the propofol dose was tapered and discontinued, and the patient was extubated. He was prescribed a maintenance dose of valproate and was followed up for one month in terms of seizures and through electroencephalography (EEG). Since no seizure activity in the EEG or any clinical seizure was observed, the medication was discontinued. The patient was followed up for five months without medication and no seizures occurred during this period.

The patient's blood test during the seizure was as follows: WBC: 13.000 K/UL; creatinine: 1.6mg/dl; creatine kinase: >4000U/L. Other biochemical values were within normal limits. No cells were detected in the cerebro-spinal fluid and the protein glucose was normal. The contrast cranial magnetic resonance imaging (MRI), and the MRI venography and arteriography were also normal. The EEG taken within the first 24 hours showed a slow wave activity originating from the bilateral frontal areas. The follow up EEGs were normal.

DISCUSSION

Our knowledge about the neurotoxicity of spinal local anesthetics, which are being used in humans for 100 years, is either based on personal experience or a few small-scale studies. There is no large-scale neurotoxicity study on spinal local anesthetics [4]. In a study by Moen et al., the frequency of severe neurological complications with spinal local anesthetics has been found to be approximately 0.4/10000 [5]. Although this ratio does not constitute a high individual risk, it should not be overlooked that these medications may lead to severe neurological complications. Such a severe neurological complication that occurs subsequent to spinal local anesthesia causes great stress for the patient and his/her family. Bupivacaine is one of the most frequently used spinal local anesthetics from the amide group. Local anesthetics from the amide group may lead to symptoms of the CNS such as depression, seizures or altered mental state, while they may lead to arrhythmia in the CVS [6]. The relatively new levobupivacaine and ropivacaine have also been reported to induce GTC type of seizures when used for plexus blockage or epidural anesthesia [7, 8]. In our case, the altered mental state was observed a very short while after the administration of bupivacaine into the vertebral space, followed by myoclonus in the legs and stereotypical involuntary movements. Plirocaine was injected into the incision site of the patient. In the wake of the surgery, status epilepticus in the form of a generalised tonic-clonic seizure developed. Considering the timing and form of the event, it can be inferred that the local anesthetic was responsible for the epileptic seizure. The causes of the neurologic complications observed with spinal local anesthetics are the administration of high doses, rapid entry into the systemic circulation, erroneous administration through the IV route, or the diffusion of the drug towards the cephalic region [2]. In our patient, the rapid entry of bupivacaine into

the systemic circulation or a diffusion towards the cephalic region seem to be plausible explanations for the status epilepticus in the form of generalised tonic-clonic seizures.

Case reports involving the loss of consciousness, aphasia and automatism induced by the intrathecal administration of combined spinal anesthetics that include fentanyl–bupivacaine or sunfentanyl-bupivacaine have been published. Loss of consciousness and aphasia that developed subsequent to the intrathecal administration of sunfentanyl-bupivacaine in an article by Franeto and Fisher were found to be associated with opioids [9]. However, a later article by Barbara M. reported of a case where the altered mental state and focal seizures with automatism observed subsequent to the administration of fentanyl-bupivacaine could not be stopped in spite of the twice I.V. administration of a total dose of 160 µg naloxone, and thus the altered mental state and focal seizures with automatism were associated with bupivacaine [10]. In another study conducted on two volunteers, complications of the CNS including a transient loss of consciousness, muscle twitches, confusion, dysarthria and tinnitus developed after the I.V. infusion of bupivacaine [11]. These reports show us that bupivacaine may cause epileptic seizures as well as various neurological complications.

Since our patient was in a confused state and had stereotypic and myoclonic movements in his legs until he was sedated with propofol, the position of his head was changing rapidly. These position changes may have caused the drug to diffuse to the cephalic region. The probability of the drugs to diffuse into the cephalic region has also been mentioned in a study and it has been recommended to elevate the head to a 10° angle in order to reduce the diffusion [12].In our patient, the stereotypical and myoclonic movements in the legs followed by the GTC seizure that occurred soon after the infusion of the bupivacaine into the vertebral space may point out that the drug may have spread towards the cephalic region and caused a GTC type of status epilepticus.

Bupivacaine has been reported to cause myoclonus in the legs when used as a spinal anesthetic [3]. It is already known that, when injected into the vertebral space, local anesthetics may cause subacute spinal neuritis or myoclonus that occurs due to the irritation of the inhibitor neurons in the motor neurons. In a study conducted in animals, it has been demonstrated that the small moderate thorn-like complexes in the amygdaloid nucleus, brought about by local anesthetics from the amide group depending on the dose, may lead to generalised clonic seizures [13]. Our patient has also experienced spasms in the perineal region, myoclonic twitches/jerks and stereotypical movements in the legs just before the seizure started. Later, 15 ml of 1% plirocaine, which is

also a local anesthetic from the amide group, was injected to the incision site. We are of the opinion that the bupivacaine injected into the vertebral space irritated the inhibitor neurons in the motor neurons and the plirocaine injected into the incision site entered the circulation and suppressed the cerebral cortex. Thus, the synergic effect of bupivacaine and plirocaine has led to the status epilepticus.

In our patient, it is also possible that the bupivacaine may have entered the blood circulation to cause the GTC seizure. Although CSF has been aspirated from the vertebral space and it was confirmed that the injection was made into the vertebral space and not intravenously, it is also known that bupivacaine leads to vasodilatation when administered through the spinal route and thus increases the blood flow to the spinal cord [14]. Therefore, we believe that bupivacaine increased the blood flow to the spinal cord and thus entered the circulation. There are also case reports where bupivacaine has led to GTC seizures when accidentally injected through the I.V. route [15]

In conclusion, we would like to present this case where the intrathecal administration of bupivacaine led to a status epilepticus. In cases of status epilepticus resistant to classical antiepileptics, toxic causes must be investigated. Especially frequently used drugs affecting the central nervous system must be taken into consideration. It must also be kept in regard that a frequently used local anesthetic such as bupivacaine may lead to a status epilepticus when administered intrathecally.

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