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CLINICAL INFORMATION

Ropivacaine withdrawal syndrome: a case report

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KEYWORDS
Cancer pain;
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Abstract
Introduction and objectives: Ropivacaine is a long-acting local anesthetic that causes prolonged anesthesia and is beneficial for a wide variety of surgeries. Systemic toxicity has been reported after usage of high dose ropivacaine or inadvertent intravascular administration. We report a case of ropivacaine withdrawal, which to our knowledge has not been previously described in the literature.
Case report: The patient presented to our department with uncontrolled belt-like upper-abdominal pain, self-rated as a 9/10 on the numeric rating scale. We decided to use continuous epidural analgesia with ropivacaine through a multi-port epidural catheter. Pain was well controlled for one month without significant adverse effects. However, ropivacaine unexpectedly ran out and two hours later the patient developed agitation, generalized tremor, tachycardia, and tachypnea. These symptoms resolved 30 minutes after reinitiating epidural ropivacaine.
Discussion: Our hypothesis of ropivacaine withdrawal was related to the timing of symptoms in relation to drug administration over two episodes. The possible mechanism of the observed withdrawal syndrome is upregulation of voltage-gated sodium channels after prolonged inhibition, resulting in increase in sodium influx and genetic variation.

PALAVRAS-CHAVE
Dor oncológica;
Ropivacaína;
Abstinência

Síndrome de abstinência de ropivacaína: relato de caso

Resumo
Justificativa e objetivos: A ropivacaína é um anestésico local de ação prolongada indicado em uma ampla variedade de cirurgias. Toxicidade sistêmica tem sido relatada após o uso de dose alta de ropivacaína ou administração intravascular inadvertida. Relatamos um caso de crise de abstinência de ropivacaína que, até onde sabemos, não foi descrita anteriormente na literatura.

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Relato do caso: O paciente procurou nosso departamento com dor não controlada abdominal do tipo em cinta, avaliada pelo paciente como sendo 9/10 no escala de avaliação numérica. Decidimos usar analgesia peridural contínua com ropivacaína através de cateter peridural multiperfurado. A dor foi bem controlada por um mês sem efeitos adversos significativos. No entanto, a ropivacaína inesperadamente se esgotou e, duas horas depois, o paciente desenvolveu agitação, tremor generalizado, taquicardia e taquipneia. Esses sintomas regrediram completamente 30 minutos após o reinício da ropivacaína por via peridural.
Discussão: Nossa hipótese de abstinência de ropivacaína foi relacionada à cronologia dos sintomas em relação à administração da droga ao longo de dois episódios. O possível mecanismo da síndrome de abstinência observada é a regulação positiva dos canais de sódio dependentes de voltagem após inibição prolongada, resultando em aumento do influxo de sódio e variação genética.

Introduction

Local anesthetics reversibly inhibit nerve impulse conduction, by reducing the permeability of sodium ions.[1,2] Ropivacaine is a long-acting local anesthetic that causes prolonged anesthesia and is beneficial for a wide variety of surgeries.[3] It has multiple clinical applications through different routes of administration. It can be administered epidurally,[4] intrathecally[5] and also be used for peripheral nerve block.[6] Ropivacaine is less lipid-soluble than bupivacaine and has a lower risk of the central nervous system and cardiac toxicity than bupivacaine in human studies.[7] However, systemic toxicity has been reported after usage of high dose ropivacaine or inadvertent intravascular administration.[8] We report a case of ropivacaine withdrawal, which to our knowledge has not been previously described in the literature.

Case presentation

A 60 year-old man with metastatic colon cancer was admitted to the department of pain management with uncontrolled severe abdominal pain. The patient was diagnosed with adenocarcinoma of the splenic flexure of the colon (T4NXM1) one year earlier, and stenting of the colon was performed at that time. He previously underwent a laparoscopic left-sided hemicolectomy and had received multiple courses of chemotherapy.

On presentation, he had uncontrolled belt-like upper-abdominal pain, self-rated as a 9/10 on the Numeric Rating Scale (NRS) and stated that he had experienced pain for at least 5 months. After evaluation, we suspected that the pain was most likely caused by distention of the hepatic capsule due to metastatic overgrowth in the liver. For our initial pain management plan, we prescribed 1500 mg.day^{-1} of oral paracetamol and 150 mg.day^{-1} of oral tramadol and gradually increased the dose to 300 mg.day^{-1} over a 3 month period. This regimen achieved good pain control and the patient self-rated his pain as 2–3/10 on the NRS. Six months after the initial presentation to our pain clinic, his pain increased due to cancer progression and was self-rated as 7/10 on the NRS. Fentanyl 25 mcg.hr^{-1} patches were prescribed but were discontinued because the patient developed severe nausea, vomiting and constipation.

After the evaluation of available options, we decided to use continuous epidural analgesia with ropivacaine. A multiport epidural catheter was inserted under fluoroscopic guidance at the level of T7; it was advanced to T3 and secured. All other analgesics, including opioids, were discontinued. The patient was discharged home with the epidural catheter. The pain was well controlled using ropivacaine 0.2% solution infused at a rate of 2 mL.h^{-1} for one month without significant adverse drug reactions. One month later, Ropivacaine unexpectedly ran out because the pump was not refilled on time (the patient did not come to the clinic to refill it), and two hours later he developed agitation, generalized tremor, tachycardia and tachypnea. He also reported that the pain worsened and was rated as 5/10 on the NRS during this episode). These symptoms resolved 30 minutes after the reinitiation of epidural ropivacaine. The patient requested a change to his pain management modality to avoid repeating this negative experience, so we performed a test block followed by radiofrequency ablation of the splanchnic nerves. We discontinued the epidural ropivacaine and the previous symptoms of ropivacaine withdrawal (agitation and generalized tremor, tachycardia, tachypnea; however, there was no rebound pain) recurred about two hours later. We re-started epidural ropivacaine and the symptoms resolved after 30 minutes. After these two episodes in which there was a clear temporal relationship between stopping ropivacaine and onset of adverse symptoms, we gradually weaned the patient off ropivacaine by reducing the infusion rate from 2 mL.h^{-1} to 0.2 mL.h^{-1} over a one week period, and then discontinued ropivacaine. This procedure was well tolerated by the patient.

Discussion

Our hypothesis of ropivacaine withdrawal was related to the timing of the symptoms in relation to the drug administration over two episodes. We failed to find any

other compelling alternative explanation for the events. We used a Naranjo Causality Scale for causality assessment which indicated that it was a probable Adverse Drug Reaction (ADR). Our patient scored 7/13 on the Naranjo Causality Scale, in which >9 = definite ADR; 5–8 = probable ADR; 1–4 = possible ADR; 0 = doubtful ADR). Several different diagnoses were taken into account: benzodiazepine withdrawal, autonomic dysreflexia, neuroleptic malignant syndrome, serotonin syndrome, malignant hyperthermia, infection/sepsis, intracranial bleeding, hypoglycemia, Cushing's triad, electrolyte imbalance, status epilepticus, and toxic, metabolic and immune-mediated disorders. However, none of these were probable. A possible mechanism of the observed withdrawal syndrome is upregulation of voltage-gated sodium channels after prolonged inhibition, resulting in an increase in sodium influx. Genetic variation is known to affect the function of sodium channels, and while we did not perform genetic analysis, this may explain the observed reactions in this patient.

Informed consent

We received informed consent from the patient.

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Conflicts of interest

The authors declare no conflicts of interest.

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