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CLINICAL REPORT

Successful epidural analgesia for a vaso-occlusive crisis of sickle cell disease during pregnancy: a case report

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Abstract We describe a 19-year-old Cameroonian primigravid young woman with sickle cell disease who was admitted to a local hospital in Cameroon where the first author performed his internship gynecology and obstetrics. She presented at 28 weeks of gestation with severe pain in her left leg caused by a vaso-occlusive crisis. As recommended, high doses of intravenous morphine were administered, but without significant pain relief. She received a single bolus injection of 5 mg morphine, followed by a continuous infusion of 0.05 mg/kg/h during 48 h. Lumbar epidural blockade with bupivacaine combined with sufentanil successfully alleviated her severe peripheral ischemic pain induced by a vaso-occlusive crisis caused by sickle cell disease. Until now, only one case report and no clinical trials have been published concerning the use of epidural analgesia for treatment of a vaso-occlusive crisis of sickle cell anemia in a pregnant woman who is not in labor.

Keywords Anesthesia · Obstetric · Pregnancy · Sickle cell disease · Epidural analgesia

Introduction

Sickle cell disease (SCD) is one of the most common inherited disorders and is associated with anemia and intermittent severe pain crises. These crises are caused by sickling of erythrocytes and subsequent occluding of end arterioles, leading to chronic hemolysis and microinfarction of diverse tissues [1]. In 1991, the Cooperative Study of Sickle Cell Disease (CSSCD) defined a sickle cell crisis as "pain related to SCD in the extremities, back, abdomen, chest or head lasting at least 2 h and leading to a clinic visit or hospitalization" [2].

Vaso-occlusive sickle cell crises tend to appear more frequently during pregnancy as a consequence of the increased metabolic demands, hypercoagulable state, and vascular stasis [3] and are associated with increased maternal and fetal morbidity and mortality [4]. As many as 55.8 % of such women will suffer from at least one painful event during their gestation [5].

No evidence-based guideline exists for the management of SCD-associated acute pain episodes. The current treatment is essentially supportive and conservative: fluid replacement therapy, packed red cell transfusion, analgesic drugs (both nonsteroidal antiinflammatory drugs and opioids), steroids, and oxygen therapy [6]. Until now, there was only one report [7] of pain caused by sickle cell crisis in a pregnant woman who was treated with epidural block. No clinical trials have been published concerning the use of epidural analgesia for treatment of a vaso-occlusive crisis of sickle cell anemia in a pregnant woman who is not in labor.

Case report

A 19-year-old Cameroonian primigravid woman at 28 weeks of gestation was referred to our attention 2 days after she was admitted to the hospital because of acute and severe joint pains localized in her left leg. She recognized

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these sharp and penetrating pains from previous sickle crises and mentioned having had multiple episodes during pregnancy ("but not as bad as this"), but she had always managed them at home with traditional medicines. In the past 2 years before conception she was treated with oral hydroxyurea 1,500 mg/day, which significantly reduced the incidence of her painful crises. Because hydroxyurea is known to be teratogenic and embryotoxic, her gynecologist advised her to stop this drug as she wished to become pregnant. The physical examination was unremarkable. A peripheral blood smear demonstrated significant sickling of red blood cells. Laboratory values revealed a hemoglobin concentration of 7.9 g/dl and a white blood cell count of 21,000 $\times$ 10^6/l, with a shift to the left. Diagnosis of a vaso-occlusive sickle cell crisis was made.

Our patient had been admitted 2 days earlier and was treated with oxygen via a nasal cannula and intravenous fluids. Intravenous morphine was administered without significant pain relief. She received a single bolus injection of 5 mg morphine, followed by a continuous infusion of 0.05 mg/kg/h during 48 h. Her body weight was 61 kg, so the cumulative dose of morphine was 151.4 mg. Patient-controlled analgesia systems (PCA) were not available in the hospital.

We searched the medical literature and, based on the reports of Finer et al. [8] and Danzer et al. [9], in which vaso-occlusive crises during labor were terminated secondary to the sympathectomy produced by epidurally administered bupivacaine and opioids and the case report published by Winder et al. [7], we decided to treat her with lumbar epidural blockade with bupivacaine combined with sufentanil. Our patient did not take any anticoagulants. As epidural analgesia infusion pumps were not available, we opted for giving the analgesia in boluses.

With the patient in the sitting position, an epidural catheter was placed at the L3–L4 interspace using a midline approach. Having confirmed a negative aspiration test for blood or cerebrospinal fluid, 3 ml 0.5 % bupivacaine with epinephrine 5 μg/ml was injected as a test dose. The patient was observed for any increase in heart rate that would indicate intravascular injection of epinephrine, and she was questioned about tinnitus, dizziness, or metallic taste in the mouth. As the response was negative, 8 ml 0.25 % bupivacaine with 1 ml sufentanil 5 μg/ml was injected after 5 min. An analgesic level to the eighth thoracic dermatome level was obtained, and this anesthetic level was confirmed throughout the treatment course. Within 10–15 min, the patient reported complete resolution of her pain symptoms. After 1 h, she received hourly a bolus of 5 ml 0.25 % bupivacaine with 1 ml sufentanil 5 μg/ml via the epidural catheter. The catheter was fixed to the skin, and the patient was returned to the left lateral position.

She received six boluses, i.e., a total of 33 ml 0.25 % bupivacaine and 6 ml sufentanil 5 μg/ml. She continued to be pain free from the first bolus and exhibited no respiratory depression, hypotension, nausea, headache, vomiting, or urinary retention. As she was still pain free the following morning, we removed the epidural catheter, and she was transferred to the ward. After a 1-day observation period, she was discharged.

Regrettably, we have no information about the remainder of her pregnancy and the delivery, as she gave birth elsewhere.

Discussion

Although several articles recommend a prophylactic dose of low molecular weight heparins (LMWHs) throughout pregnancy and post partum [10], our patient did not take any anticoagulants. Aspirin, standard heparin, and warfarin have been used in clinical trials for the treatment of acute painful crises, without conclusive results [10]. Only tinzaparin is justified in the treatment of acute painful crisis [10]. An epidural block, however, is relatively contraindicated for anticoagulated patients because of an increased risk of spinal hematoma [11].

Morphine is a vasoconstrictor of the placental vasculature [12], and SCD is associated with severe placental damage [13]; therefore, this combination could be deleterious for the fetus. Moreover, some studies suggest that opioids might trigger neuronal apoptosis in the fetus [14, 15]. However, opioids administration, both orally and parenterally, is recommended as a treatment of choice for an acute episode of vaso-occlusive pain that requires hospitalization [6, 10], but it is often unsatisfactory [16]. Furthermore, pregnant women are excluded from all clinical trials studying opiate or non-opiate analgesics for treating painful sickle cell crises [17].

Because the intravenous analgesics did not provide sufficient pain relief, we chose the epidural analgesia, based on the case reports of Finer et al. [8] and Winder et al. [7].

Finer et al. [8] proposed two different mechanisms by which epidural analgesia can provide pain relief in patients with SCD suffering from a vaso-occlusive crisis: sickling of red blood cells and subsequent vaso-occlusion with resulting tissue ischemia and inflammation is the basis for much SCD-related pain. Because epidural local anesthetics produce sympatholysis and vasodilatation, it might have minimized sludging by enhanced blood flow through the affected part of the body and terminated the crisis in this case. Even if the vaso-occlusive phenomenon did not improve in our patient, epidural bupivacaine and sufentanil might have reduced the pain by their pain-relieving effect.

When practitioners consider the strategies for pain management for the pregnant female, they should carefully take into account the adverse events (AEs) induced by the interventions. In this case, AEs of epidural bupivacaine and sufentanil on the fetus were the major concerns. Maternal hypotension resulting from local anesthetic-induced sympathetic block may reduce placental perfusion. A decrease in perfusion pressure will result in decreased fetal oxygenation, which is manifested by deterioration in the fetal heart rate pattern (e.g., bradycardia, repetitive late decelerations). However, in the absence of hypotension, epidural local anesthetics have minimal effect on uterine or fetal umbilical vasculature as assessed by Doppler velocimetry [18].

As already stated, some animal studies suggest that morphine (and consequently perhaps also opioids) might induce neuronal apoptosis [14, 15]. Nevertheless, epidural fentanyl and sufentanil have a faster onset of action and lower concentration in the fetal circulation than morphine because of their high lipid solubility. Therefore, they have, for the most part, supplanted morphine for epidural labor analgesia. Moreover, sufentanil has a reduced neonatal opioid exposure compared to fentanyl, which is an advantage compared to fentanyl [19]. The cumulative effect of opioids delivered as part of continuous epidural infusions is another concern, as this may result in a potentially significant total opioid dose over time. However, neurobehavioral assessment of neonates of mothers who received prolonged epidural infusions of sufentanil has not shown perceptible changes using the Neurologic and Adaptive Capacity Score (NACS) [19].

Very few case reports have been published in which epidural analgesia is used to manage patients suffering from a vaso-occlusive crisis of sickle cell anemia. The use of epidural analgesia for this purpose seems a promising technique in patients not responding to intravenous opioids. Collaborative and multicenter prospective, randomized, and double-blind international studies would be of great help in finding the best management options to relieve intolerable pain caused by vaso-occlusive crises of SCD.

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