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### Case report

## Dexmedetomidine as adjunct for analgesia in labor: a report of two cases

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#### ABSTRACT

At present, remifentanyl is the first choice in obstetrical patients who are candidates for intravenous analgesia during labor, although in some cases, the use of this opioid does not provide adequate pain control. This article summarizes two cases where dexmedetomidine was used successfully as an analgesic adjunct to intravenous remifentanyl during labor.

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#### Dexmedetomidina como coadyuvante analgésico para el trabajo de parto. Reporte de dos casos

#### RESUMEN

Actualmente el remifentanil es el medicamento de elección en las pacientes candidatas para analgesia intravenosa durante el trabajo de parto; sin embargo, en algunas parturientas no se consigue un adecuado control del dolor con el uso de este opioide. El presente artículo resume dos casos donde la dexmedetomidina se utiliza como coadyuvante en la analgesia intravenosa con remifentanil, con buenos resultados.

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## Case 1

Thirty-three year-old patient, gravida 1, with a history of right hemiparesis due to a thrombotic stroke, and antiphospholipid syndrome. During the third trimester her paresis increased and she developed severe lumbosacral pain that radiated to her lower limbs, but with no findings of radicular disease. The magnetic resonance imaging of the lumbosacral spine revealed a hemangioma at the level of the vertebral body L2, with no evidence of active bleeding. She was admitted to the Obstetrics Department in active labor, complaining of severe pain (8/10 on the visual analog scale). A remifentanyl infusion was initiated for analgesia, titrated up to 0.1 µg-1Kg-1min-1 under basic maternal monitoring and continuous fetal heart rate monitoring, oxygen supplementation through a nasal cannula, and gastric prophylaxis. The patient subsequently reported mild pain, but three hours later she again reported severe pain with uterine activity, together with constant moderate pelvic pain. There was no pain improvement with the remifentanyl infusion, titrated at that point to 0.2 µg-1Kg-1min-1 and, moreover, the patient became tachycardic and diaphoretic.

After achieving no improvement when two bolus doses of remifentanyl 0.05 µg-1Kg-1min-1 were added, it was decided to start with one bolus dose of dexmedetomidine 0.4 µg-1Kg-1 given over 30 minutes, followed by an infusion at a rate of 0.4 µg-1Kg-1h-1. After 20 minutes, the patient reported relief of her pelvic pain and the pain caused by uterine activity, with remission of her sympathetic response. Throughout the following 10 minutes she reported complete pain relief during contractions. She remained alert, hemodynamically stable, with an SaO<sub>2</sub> greater than 94%, and no side effects.

Approximately 1 hour after initiating dexmedetomidine, the patient was prepared for the expulsion phase. The two analgesic infusions were maintained and a single dose of 15 mg intravenous Ketamine was given for instrumented birth. Tolerance to the procedure was excellent and no other intervention was required.

The baby's Apgar scores were 8 and 10 at 1 and 10 minutes, respectively. During analgesic infusions, the fetal heart rate ranged between 156 and 121 beats per minute (b.p.m.). No worrisome signs were seen on the fetal tracings at any time. The baby continued to show good neonatal adaptation over the next 24 hours postpartum.

In the immediate postpartum period, the patient developed uterine atony that was resolved with bimanual uterine massage, a single dose of carbetocin 100 µg i.m., and misoprostol 1000 µg i.r. Twelve hours into the postpartum period, the mother reported not having felt pain during the expulsion phase and excellent satisfaction with the analgesic method.

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## Case 2

A 31 year-old patient, gravida 2, was admitted to the labor room in severe pain (10/10 on the visual analog scale - VAS) at 40 weeks of gestation and in active oxytocin-induced labor

with a 4 cm dilatation. During the pre-anesthetic assessment, multiple petechiae were observed on both arms. The patient reported a history of petechia and hematoma formation, either spontaneously or under minimal stimulus, as well as a positive family history of this finding. Consequently, it is decided to offer the use of intravenous analgesia with remifentanyl.

A continuous remifentanyl infusion was initiated with titration up to 0.1 µg-1Kg-1min-1 under basic maternal monitoring and continuous fetal heart rate monitoring, oxygen supplementation through a nasal cannula, and gastric prophylaxis. The VAS score during the first hour of infusion was 0/10, with a respiratory rate ranging between 3 and 20 per minute, pulse oximetry measurements greater than 96%, heart rate between 68-72 b.p.m, and fetal heart rate between 118-130 b.p.m. The patient reported slight dizziness without nausea as a side effect.

Over the following two hours the remifentanyl infusion was titrated progressively up to 0.2 µg-1Kg-1min-1 in order to maintain the pain score below 4/10, with no variation in maternal vital signs or fetal heart rate, but when the cervical dilatation was in 7 cm, the pain became severe again. The patient developed tachycardia and diaphoresis.

Two bolus doses of 0.05 µg-1Kg-1min-1 of remifentanyl were given, but there was no improvement. After the bolus administration there was evidence of bradypnea and a fall in the oxygen saturation to 92%-93%, although there was adequate response to verbal stimulation. It was decided to start dexmedetomidine with a bolus dose of 0.4 µg-1Kg-1, given over 30 minutes, followed by an infusion at 0.6 µg-1Kg-1h-1.

Within 10 minutes, the patient reported improvement of her pain and the diaphoresis resolved. Her pain remained under control until the time of transfer to the delivery room, with the patient alert, hemodynamically stable, with good ventilatory pattern, and pulse oximetry readings higher than 94%. The fetal heart rate remained between 115-127 b.p.m, and there were no disquieting findings on the fetal tracings. The infusions were maintained during the expulsion phase, with reported moderate pain.

The baby's Apgar score was 9 and 10 at one and five minutes, respectively, with no problems of neonatal adaptation early on or within the next 24 hours. When questioned two hours into the postpartum period, the patient reported satisfaction with the analgesic technique.

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## Discussion

Due to its pharmacokinetic and pharmacodynamic characteristics, remifentanyl is currently the drug of choice for patients who are candidates for intravenous analgesia during labor. At Clínica Universitaria Bolivariana, continuous infusions are preferred as patient-controlled analgesia (PCA) pumps are not available. Using this technique, adequate pain relief is achieved, without serious side effects, in most pregnant women in labor. However, sometimes this goal is not achieved and drug combinations are required, although recommendations are still lacking in this regard.

This report describes two patients who received intravenous analgesia with remifentanyl. The two of them required rapidly

increasing titrations in order to achieve pain scores under 4/10, and they both developed severe pain during the advanced active phase of labor despite high infusion doses.

Ultimately, the quality of analgesia improved in both patients following a continuous infusion of dexmedetomidine leading to sympatholysis and superficial sedation that enabled an adequate interaction with their environment, with no evident clinical side effects that might have impaired their hemodynamic condition or the fetal status. Moreover, they both reported satisfaction with the analgesic technique. A disadvantage of dexmedetomidine when compared to remifentanyl is the longer latency period before achieving complete analgesic effect (with a time range in both cases of 20-30 minutes).

Dexmedetomidine produces sedation, analgesia and sympatholysis due to its effects on  $\alpha_2$ -agonist receptors on the locus coeruleus and the spinal cord.<sup>1,2</sup> In combination with opioids, it produces a synergistic effect that results in lower analgesic requirements and less adverse events such as nausea and vomiting, without increasing the incidence of respiratory depression.<sup>3</sup>

Studies in humans and animals show that dexmedetomidine has high placental retention (0.77 maternal/fetal index; DS 0.06)<sup>4</sup> and increases the frequency and amplitude of uterine contractions directly and in a dose-dependent fashion,<sup>5,6</sup> suggesting advantages for use as an analgesic adjunct during labor.

Palanisamy et al.<sup>7</sup> reported the successful use of continuous-infusion dexmedetomidine as analgesic adjunct in intravenous PCA with fentanyl for labor in a patient with occult spina bifida.

Abu-Halaweh et al.<sup>8</sup> reported a case of an obese diabetic patient with severe eclampsia who rejected spinal analgesia for labor, and received only dexmedetomidine, achieving mild pain scores and superficial sedation during the infusion, with no other side effects. The patient eventually underwent C-section under general anesthesia due to late persistent decelerations. Other authors describe the use of dexmedetomidine in pregnant women for non-obstetric surgery<sup>9</sup> and for C-section.<sup>10</sup>

Acute exposure to dexmedetomidine has not shown to be teratogenic in rats,<sup>11</sup> and the potential neuroprotective properties of this drug are being studied in brain injury of prematurity.<sup>12</sup> However, further research is required in order to determine maternal and fetal safety in humans, and to make recommendations about its use. For the time being, the few studies and case reports suggest that this drug might have an adequate profile as an adjunct in analgesia for labor when other options have failed, although this is still an off-label application. For this reason, patients need to be thoroughly informed about the potential side effects before receiving this drug.

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## Competing Interests

None declared.

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