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Reply to the letter to the Editor

Respuesta a la carta al Editor

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The SES-Hospital Universitario de Caldas takes care of approximately 210 deliveries per month, with an overall cesarean section rate of 32 %, of which 72 % were conducted with, or had an epidural catheter, as an extension of the analgesia delivered during labor and were therefore excluded from the trial. This may address some of the concerns expressed by Sotelo (1). It is important to consider the observational character of the study discussed; in the discussion paragraph, mention is made of a potential selection bias, based on the convenience sampling and the non-randomized approach which are typical of the design used (2).

According to the regulatory framework, the INVIMA 2019M-0010014-R1 registry of hydromorphone, valid until February 2021, includes the intrathecal administration of the drug, while the currently valid INVIMA 2020M-0010453R1 registry applicable for morphine chlorhydrate injection, only includes the subcutaneous administration; however, traditionally it has been administered intravenously, epidural and intrathecal in the country, and this is a clear example of the compassionate use of the medication.

Now then, with the regards to the safety of neuraxial opiates during pregnancy, there are numerous articles since 1988 describing their use in anesthesia and postoperative analgesia following cesarean section (3). It is common knowledge that neuraxial analgesia techniques with opioids may result in improved Apgar scores and arterial blood gases readings from the umbilical cord blood, as compared with systemic opioid analgesia (4). Notwithstanding the rapid systemic absorption of the intrathecal administration of opioids, the dose used is very low, therefore there is less likelihood of any adverse effects on the fetus or the neonate (4).

Reynolds et al. conducted a systematic review comparing epidural analgesia versus local anesthetic agent plus systemic opioids, including 12 clinical trials and a total population of 2,102 females. The researchers indicated that replacing systemic opioids by moderate doses of neuraxial opioids, not only resulted in superior analgesia for labor, but had a favorable effect on neonatal outcomes (5).

Recently there has been a growing number of articles published on the use of hydromorphone in the obstetric population. Sherp et al. (6) in a randomized clinical trial with 138 patients, published in June 2020, found no differences in the analgesia obtained with hydromorphone vs. morphine 24 hours after surgery. Also in 2020, Terhi Puhto et al., studied the maternal pharmacokinetics and the neonatal exposure after a single dose of epidural hydromorphone (1.5-0.5 mg), higher than the intrathecal dose, with no events reported in the newborn babies (7).

Whilst hydromorphone has a low protein binding level -19 % - (4) and a F/M ratio > 1 (6), indicating a high placental transfer and a pKa of 8.1 (4), which in the lower fetal pH versus the maternal pH, could result in ion entrapment (8), there are other conditions such as its low non-ionized fraction and its low lipid solubility, that prevent its accumulation in maternal and placental tissues. Moreover, the single intrathecal doses of hydromorphone used are so small, and the time of exposure to reach stable concentrations and fetal transfer is so short, that the absolute fetal concentrations may be lower than those associated with significant neonatal side effects (4). This explains the absence of negative clinical outcomes such as

the reduction of the Apgar score or delayed breastfeeding, in newborn babies from mothers receiving neuraxial hydromorphone.

Certainly, further studies are needed, with better designs and larger samples; however, with the evidence available so far, the use of intrathecal hydromorphone for anesthesia and postoperative analgesia in cesarean section is a safe and effective option.

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