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Editorial Comment

Should We Use Dexmedetomidine for Sedation in Parturients Undergoing Caesarean Section Under Spinal Anaesthesia?

Andrea Cortegiani, Giuseppe Accurso, Cesare Gregoretti

Department of Biopathology and Medical Biotechnology (DIBIMED), Section of Anesthesia Analgesia Intensive Care and Emergency. Policlinico Paolo Giaccone. University of Palermo, Italy

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With the increasing advanced maternal age, the rate of caesarean sections has been increasing year by year, particularly in some Asian countries such as China (1). Regional anaesthesia is usually preferred for caesarean section because it can keep patients in a painless and awake state during the whole process. In addition, regional anaesthesia allows the mother to participate in the birth process, thereby avoiding anaesthetic drugs from entering the maternal blood circulation and decreasing the adverse effects and risks of general anaesthesia (2). However, parturients after foetal extraction may be reluctant to remain awake in an uncomfortable position potentially interfering with the end of surgical procedure (usually surgery ends within 20–30 min after the delivery) (3). For this reason, there is a need for improving confort of parturients during the caesarean delivery using drugs characterized by minimal haemodynamic and respiratory effects. Several agents such as midazolam, ketamine, propofol, remifentanil and dexmedetomidine have been used with this aim (4-6). Some recent placebo-controlled studies suggested that α-2 adrenergic agonists have both analgesic and sedative properties when used as adjuvants in regional anaesthesia (7). Dexmedetomidine is a α-2 receptor agonist, which is able to produce sedation and analgesia without the unwanted vascular effects due to the activation of α-1 receptors (7, 8).

For many years, anaesthesiologists have used dexmedetomidine with caution in parturients because of possible uteroplacental transfer, which may cause undesirable effects in the baby. However, recent findings show that because dexmedetomidine has a high placental retention (0.77 maternal/foetal index) and is highly lipophilic, it does not get transferred to the baby (9).

Some case reports found that dexmedetomidine has no harmful effects during caesarean delivery (10-13). Many cases describe the successful use of dexmedetomidine in parturients when regional anaesthesia was contraindicated or refused. Moreover, it has been used as an adjunct to labour epidural if pain relief was not satisfactory, without any adverse foetal outcomes with the recommended doses (9).

In the current edition of the *Journal*, Wang et al. (14) showed that to achieve adequate sedation, ED50 and ED95 of the loading dexmedetomidine dose were 0.82 and 0.96 μg kg^{-1}, respectively, for caesarean section under spinal anaesthesia.

It was recently revealed that a 0.6-μg kg^{-1} loading dexmedetomidine dose via intravenous pumping within 10 min before caesarean section and an intraoperative maintenance dose of 0.2 μg kg^{-1} h^{-1} until the end of the delivery could achieve good haemodynamic stability and satisfied sedation at 30 min after administration in 200 patients undergoing spinal–epidural anaesthesia (15). Although the study by Jiang et al. (16) randomly assessed different fixed doses of dexmedetomidine (0.2 μg kg^{-1}, 0.4 μg kg^{-1} and 0.6 μg kg^{-1}), to date, no studies have systematically investigated the effective loading dose for inducing adequate sedation in parturients undergoing caesarean section under spinal anaesthesia. The study by Wang et al. (15) is the first that used a Dixon up-and-down method (16) to calculate ED50 and ED95 of dexmedetomidine loading dose in a parturient undergoing spinal anaesthesia for caesarean section. The starting loading dose for the first parturient was 1.0 μg kg^{-1}. According to Dixon up-and-down methodology, the loading dose of the subsequent enrolled parturient was increased or decreased (step size of 0.1 μg kg^{-1}) according to sedation level achieved in the previous parturient. After the loading dose, all parturients received a dexmedetomidine maintenance dose at a rate of 0.3 μg kg^{-1} h^{-1}. The sedation target (assessed at

Address for Correspondence: Andrea Cortegiani E-mail: cortegiania@gmail.com

5 minutes after loading dose) was a Ramsey sedation score of 3 or 4, which means a drowsy or asleep patient but still able to follow commands. Of note, surgeons, parturients and outcome assessors were blind to the loading dose of dexmedetomidine. No oversedation (Ramsey score equal to 5) was detected, and no significant differences were found in ephedrine use, atropine use and adverse effects between the success and fail groups (patients who did not reach an adequate sedation).

The result of this study is consistent with that of a recent literature (15), which indicate that an appropriate loading dexmedetomidine dose of 1 μg kg^{-1} for spinal anaesthesia and a consequently low maintenance infusion (0.3 mcg kg^{-1} h^{-1}) should result in adequate sedation with minimal haemodynamic instability and without delayed recovery.

However, the study has several limitations that were not very well addressed in the limitation section. 1) Subarachnoid block may alter the dose required for loading and maintenance of adequate sedation without a cardiovascular effect in pregnant women. Thus, doses should be theoretically titrated according to the individual patient's need. Moreover, haemodynamic data were not recorded, so there are no data regarding the cardiovascular effects of the drug. 2) The result of this study is applicable only to pregnant women who have given pharmacokinetic and pharmacodynamic characteristics (e.g. fat-free mass, serum albumin level, plasma albumin level, alanine aminotransferase activity and increased cardiac output) (17). Moreover, analgesia and sedation in parturients are influenced by serum corticotrophin and beta-endorphin levels that have a peak after foetal extraction (18). 3) It may also be argued that the selected time point of outcome assessment (5 minutes after the loading dose) might have been too early to detect the complete effect of the dexmedetomidine dose. The reason for this is the higher volume of the distribution of parturients and the potentially longer onset of sedation (17).

The possible difference between the sedation level and vital signs of participants in the two groups (success and fail groups) should be analysed in future controlled trials.

In conclusions, beyond the fact of whether or not to use dexmedetomidine, future studies should address the real need for sedation after patients undergoing spinal or combine epidural–spinal anaesthesia deliver the baby. Because parturients undergoing caesarean section are anxious and nervous until delivery, most of them calm down after hearing the first cry or getting together with the baby while surgery continues. Thus, do we need to come back to old times? If yes, dexmedetomidine, once known for its contraindication (14, 18), appears to be one of the best choices.

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