

# Labor analgesia and its impact on the maternal and perinatal outcomes

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## SUMMARY

**OBJECTIVE:** This study aimed to assess adverse maternal and perinatal outcomes in parturients undergoing labor analgesia.

**METHODS:** This was a retrospective cohort study in parturients who underwent labor analgesia. Parturients were categorized into three groups: Group 1 (n=83)—analgesia performed with cervical dilatation  $\leq 4.0$  cm; Group 2 (n=82)—analgesia performed with cervical dilatation between 5.0 and 8.0 cm; and Group 3 (n=83)—analgesia performed with cervical dilatation  $\geq 9.0$  cm.

**RESULTS:** Analgesia in parturients with cervical dilatation  $\geq 9.0$  cm showed a higher prevalence and a 3.86-fold increase (OR 3.86; 95%CI 1.50–9.87;  $p=0.009$ ) in the risk of forceps delivery. Analgesia in parturients with cervical dilatation  $\leq 4.0$  cm showed a higher prevalence and a 3.31-fold increase (OR 3.31; 95%CI 1.62–6.77;  $p=0.0016$ ) in the risk of cesarean section. Analgesia in parturients with cervical dilatation  $\geq 9.0$  cm was associated with a higher prevalence of fetal bradycardia (20.7%), a need for neonatal oxygen therapy (6.1%), and a need for admission to a neonatal intensive care unit (4.9%). Analgesia in parturients with cervical dilatation  $\leq 4$  cm was associated with a higher prevalence of Apgar score  $< 7$  at 1st minute (44.6%).

**CONCLUSION:** Performing labor analgesia in parturients with cervical dilatation  $\leq 4.0$  or  $\geq 9.0$  cm was associated with a higher prevalence of adverse maternal and perinatal outcomes.

**KEYWORDS:** Delivery room. Analgesia. Perinatal mortality.

## INTRODUCTION

One of the main concerns among parturients regarding vaginal delivery is the pain experienced during labor. Labor pain is a complex phenomenon influenced by anatomical and physiological characteristics along with psychosocial and cultural factors. Regarding pain intensity, the scores of labor pain are comparable with those of other clinical conditions, such as non-terminal cancer, acute myocardial infarction, renal colic, and burns. There are biochemical and neurophysiological evidences that maternal pain during labor results in deleterious consequences for the parturient and fetus<sup>1</sup>.

Epidural analgesia is the most frequently used treatment modality during labor. Effective labor analgesia controls maternal pain and anxiety, benefiting the maternal-fetal binomial with effective pain relief using low anesthetic doses, without significant motor block. Moreover, there is a possibility of analgesic complementation through a catheter<sup>2</sup>. However, some undesired effects are still associated with this technique. The risks include arterial hypotension, prolonged labor, labor instrumentation, the need for oxytocin, and adverse fetal outcomes<sup>3</sup>.

In general, epidural analgesia at an early stage of labor in patients with a cervical dilatation of  $< 4.0$  cm could be associated with higher rates of cesarean sections, which would relatively contraindicate this procedure during this period. However, a systematic review showed that there was no difference in the rate of cesarean sections between parturients who underwent epidural analgesia in the early active phase and those who underwent analgesia in the late active phase of the first stage of labor. The study also showed that the appropriate time for analgesia depends on maternal demand<sup>4</sup>.

Pain relief during labor has received considerable attention, which is aimed at maternal well-being, reducing the stress caused by pain, and reducing its consequences for the fetus. However, there are controversies regarding the possibility that analgesia interferes with the progress of labor and fetal vitality. This study aimed to evaluate adverse maternal and perinatal outcomes in parturients undergoing labor analgesia.

## METHODS

This was a retrospective cohort study conducted at the Mário Palmério University Hospital in Uberaba, State of Minas Gerais,

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Brazil, through an active search using the SOUL MV system (MV Informática Nordeste Ltda., Recife, Brazil) in the electronic medical records of parturients who underwent analgesia during labor between August 2014 and October 2021. This study was approved by the Research Ethics Committee of the University of Uberaba (CAAE N°. 52405921.6.0000.5145).

The parturients were categorized into three groups: Group 1—analgesia performed with cervical dilatation  $\leq 4.0$  cm; Group 2—analgesia performed with cervical dilatation between 5.0 and 8.0 cm; and Group 3—analgesia performed with cervical dilatation  $\geq 9.0$  cm. The inclusion criteria were as follows: primigravidas of single fetuses who underwent epidural analgesia at a gestational age of  $\geq 37$  weeks; those admitted during the active phase of the first stage of labor; and those with no fetal malformations, chromosomal disorders, or Doppler changes in the umbilical artery, middle cerebral artery, or ductus venosus.

The decision of the parturient was respected for the indication of labor analgesia. Contraindications included refusal, infection or tumors at the puncture site, coagulation disorders, changes in consciousness, sepsis, known allergies to the administered drugs, and hemodynamic instability. In the absence of contraindications, once the diagnosis of labor was confirmed, analgesia was performed by a resident physician and supervised by an anesthesiologist experienced in labor. In this hospital, epidural analgesia was performed by administering 0.2% ropivacaine and 50  $\mu$ g of fentanyl in a total volume of 10 mL.

The variables analyzed in this study were age, body mass index (BMI), hypotension, nausea, vomiting, pruritus, respiratory depression, cervical dilatation at the time of analgesia, use of oxytocin, the need for labor instrumentation, the presence of fetal bradycardia after analgesia, birth weight, Apgar score at 1st and 5th minutes, the need for neonatal oxygen therapy, and the need for admission to a neonatal intensive care unit (ICU).

The GPower 3.1 software (Heinrich-Heine-Universität, Düsseldorf, Germany) was used to calculate the sample size. According to the analysis, the study required a sample size of 248 patients who underwent analgesia during labor. The sample size analysis was based on a  $w$  effect of 0.25,  $\alpha$  error probability of 0.05, and a power ( $1-\beta$  error probability) of 0.95, with two degrees of freedom.

Data were transferred to an Excel 2019 spreadsheet (Microsoft Corp., Redmond, WA, USA) and analyzed using SPSS version 20.0 (IBM Corporation, Armonk, NY, USA) and Prism version 7.0 (GraphPad Software, San Diego, CA, USA). Quantitative variables were analyzed using a normality test (D'Agostino-Pearson), and those with a normal distribution were presented as means and standard deviations. Variables with a non-normal distribution were presented as medians and minimum and maximum values. Categorical variables were described based on absolute and percentage frequencies and are represented as tables. To study the difference between categorical variables and their proportions, the Chi-square test was used. Analysis of variance (ANOVA) was used for normally distributed variables to study the difference between continuous variables. The Kruskal-Wallis test was used for non-normally distributed variables. Dunn's post hoc test was used for pairwise comparison. The significance level for all tests was set at  $\alpha < 0.05$ .

## RESULTS

Overall, 247 parturients undergoing labor analgesia were evaluated and were categorized into three groups: Group 1 (n=83), Group 2 (n=82), and Group 3 (n=82), as described above. The characteristics of the study population are summarized in Table 1.

The different degrees of cervical dilatation were negatively correlated ( $r=-0.78$ ) with the time to delivery (Figure 1) and showed a linear relationship. The model's coefficient of determination ( $R^2=0.71$ ) indicated that 71.0% of the variation in

**Table 1.** Characteristics of the study population.

|                           | Group 1 (n=83)                 | Group 2 (n=82)   | Group 3 (n=82)   | p-value              |
|---------------------------|--------------------------------|------------------|------------------|----------------------|
| Age (years)               | 18.0 (16.0–27.0) <sup>AB</sup> | 22.0 (20.7–26.0) | 25.0 (21.0–30.0) | <0.0001 <sup>†</sup> |
| BMI (kg/m <sup>2</sup> )  | 32.3 (28.6–33.9)               | 30.8 (28.6–32.4) | 30.9 (29.0–32.9) | 0.05 <sup>†</sup>    |
| Gestational age (weeks)   | 40.1 (39.0–40.5)               | 39.3 (38.1–40.2) | 39.6 (37.7–40.7) | 0.05 <sup>†</sup>    |
| Birth weight (g)          | 3180.0 (474)                   | 3207 (439)       | 3139 (543)       | 0.605 <sup>f</sup>   |
| Apgar score at 1st minute | 8 (6–8) <sup>AB</sup>          | 8 (8–8)          | 8 (8–8)          | 0.0004 <sup>†</sup>  |
| Apgar score at 5th minute | 9 (9–9)                        | 9 (9–9)          | 9 (9–9)          | >0.9999 <sup>†</sup> |

Group 1: analgesia performed in patients with cervical dilatation  $\leq 4.0$  cm; Group 2: analgesia performed in patients with cervical dilatation between 5.0 and 8.0 cm; Group 3: analgesia performed in patients with cervical dilatation  $\geq 9.0$  cm. BMI: body mass index; Kruskal-Wallis <sup>†</sup>median (interquartile range); ANOVA <sup>f</sup>mean (standard deviation); <sup>A</sup>Group 1 vs. Group 2; <sup>B</sup>Group 1 vs. Group 3.

the time to delivery was linearly related to cervical dilatation at the time of analgesia, and the remaining 29.0% of the variation results from other factors that are not considered in the model. Increase in this dilatation by 1.0 cm at the time of labor analgesia reduced the time to delivery by 0.94 h.

A statistically significant association was observed between the need to use oxytocin and the use of analgesia in parturients with smaller cervical dilatation ( $p < 0.001$ ). Parturients who underwent analgesia with cervical dilatation  $\leq 4.0$  cm had a higher prevalence of the need to use oxytocin than those who underwent analgesia with cervical dilatation between 5.0 and 8.0 cm (89.2 vs. 59.8%,  $p < 0.0001$ ) and  $\geq 9.0$  cm (89.2 vs. 52.4%,  $p < 0.0001$ ). Parturients who used oxytocin presented a 2.6 times (OR 2.67; 95%CI 1.31–5.57;  $p = 0.0125$ ) greater probability of progressing to vaginal delivery than to cesarean section.

A significant association was observed between cervical dilatation at the time of analgesia and the need for instrumentation during delivery ( $p = 0.010$ ). Parturients who underwent analgesia with cervical dilatation  $\geq 9.0$  cm had a higher prevalence of forceps delivery than those with cervical dilatation  $\leq 4.0$  cm (14.6 vs. 2.4%,  $p = 0.005$ ). Patients with cervical dilatation of  $\geq 9.0$  cm showed a 3.86-fold increase (OR 3.86; 95%CI 1.50–9.87;  $p = 0.009$ ) in the risk of forceps delivery. Alternatively, parturients with cervical dilatation  $\leq 4.0$  cm showed a reduction of 79.0% (OR 0.21; 95%CI 0.04–0.89;  $p = 0.040$ ) in the risk of forceps delivery.

Parturients who underwent analgesia with cervical dilatation  $\leq 4.0$  cm had a higher prevalence of cesarean sections than those with cervical dilatation between 5.0 and 8.0 cm (24.1 vs. 11.0%,  $p = 0.039$ ) and  $\geq 9.0$  cm (24.1 vs. 6.1%,  $p = 0.0019$ ). Parturients with cervical dilatation of  $\leq 4.0$  cm showed a 3.31-fold increase

(OR 3.31; 95%CI 1.62–6.77;  $p = 0.0016$ ) in the probability of progression to cesarean section. Alternatively, parturients with dilation between 5.0 and 8.0 cm and  $\geq 9.0$  cm showed reductions of 74.0% (OR 0.26; 95%CI 0.12–0.56;  $p = 0.0003$ ) and 29.0% (OR 0.29; 95%CI 0.12–0.78;  $p = 0.010$ ), respectively, in the probability of progression to cesarean section.

There were no cases of arterial hypotension, nausea, vomiting, pruritus, or respiratory depression in the three groups. Analgesia in parturients with cervical dilatation  $\geq 9.0$  cm was associated with a higher prevalence of fetal bradycardia (20.7, 9.6, and 8.5% for Groups 1, 2, and 3, respectively). The neonates of Group 3 had a higher prevalence of the need for neonatal oxygen therapy (6.1, 0.0, and 0.0% for Groups 3, 1, and 2, respectively) and the need for neonatal ICU admission (4.9, 0.0, and 0.0% for Groups 3, 1, and 2, respectively) than the neonates of the other groups. Labor analgesia in parturients with cervical dilatation  $\leq 4.0$  cm was associated with a higher prevalence of Apgar score  $< 7$  at the 1st minute (44.6, 17.1, and 22.0% for Groups 1, 2, and 3, respectively) than in the parturients of the other groups (Table 2).

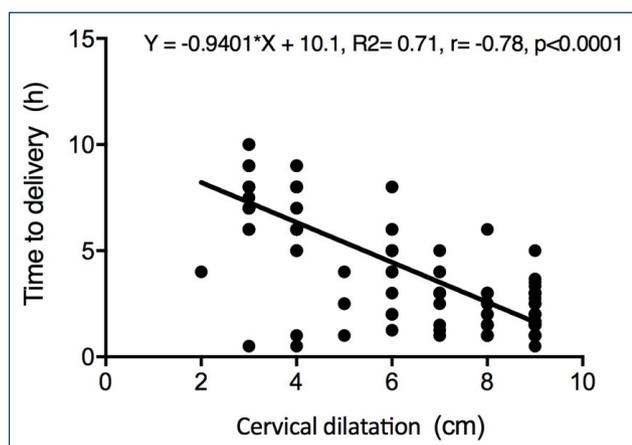
## DISCUSSION

In the USA, 61% of women who had a single-fetus vaginal delivery underwent epidural analgesia in 2008<sup>5</sup>. According to the American College of Obstetricians and Gynecologists, in the absence of a medical contraindication for analgesia, a request from the mother is a sufficient medical indication for pain relief during labor. A woman who requests epidural analgesia during labor should be allowed to undergo this procedure irrespective of her health insurance status<sup>6</sup>.

Epidural analgesia involves the use of low doses of local anesthetics along with opioids. Initial indications were based on maternal chronic diseases that could decompensate during the second stage of labor due to sympathetic stimulation caused by the pain and Valsalva efforts. Currently, these indications have expanded to include several high-risk conditions of the fetus as well as preeclampsia<sup>7</sup>.

However, epidural analgesia poses several risks to the mother and fetus. These risks include respiratory depression in the newborn associated with the use of fentanyl, which reaches the maternal circulation and crosses the placenta<sup>8</sup>. Other complications of epidural analgesia include intrapartum maternal fever and sepsis in the newborn<sup>9</sup>.

In a systematic review of five randomized clinical trials comprising 879 parturients undergoing epidural anesthesia, the standing and reclining positions were compared during the second stage of labor, and no statistical difference was observed between the groups in terms of operative delivery rates (cesarean



**Figure 1.** Correlation between the degree of cervical dilatation at the time of analgesia and the time to delivery (Spearman's correlation test,  $p < 0.05$ ).

**Table 2.** Side effects and adverse maternal and perinatal outcomes.

|                                  | Group 1 (n=83) | Group 2 (n=82) | Group 3 (n=82) | p-value <sup>s</sup> |
|----------------------------------|----------------|----------------|----------------|----------------------|
| Arterial hypotension             | 0% (0/83)      | 0% (0/82)      | 0% (0/82)      | *                    |
| Nausea                           | 0% (0/83)      | 0% (0/82)      | 0% (0/82)      | *                    |
| Vomiting                         | 0% (0/83)      | 0% (0/82)      | 0% (0/82)      | *                    |
| Pruritus                         | 0% (0/83)      | 0% (0/82)      | 0% (0/82)      | *                    |
| Respiratory depression           | 0% (0/83)      | 0% (0/82)      | 0% (0/82)      | *                    |
| Fetal bradycardia                | 9.6% (8/83)    | 8.5% (7/82)    | 20.7% (17/82)  | 0.036                |
| Apgar score <7 at 1st minute     | 44.6% (37/83)  | 17.1% (14/82)  | 22.0% (18/82)  | <0.001               |
| Need for neonatal oxygen therapy | 0% (0/83)      | 0% (0/82)      | 6.1% (5/82)    | 0.016                |
| Need for neonatal ICU            | 0% (0/83)      | 0% (0/82)      | 4.9% (4/82)    | 0.017                |

Group 1: analgesia performed in patients with cervical dilatation  $\leq 4.0$  cm; Group 2: analgesia performed in patients with cervical dilatation between 5.0 and 8.0 cm; Group 3: analgesia performed in patients with cervical dilatation  $\geq 9.0$  cm. ICU: intensive care unit; Chi-square <sup>s</sup>percentage (n/N);  $p < 0.05$ . \*It was not possible to calculate the p-value due to the absence of at least three cases in each group.

section or instrumental)<sup>10</sup>. In the present study, the association between patients' positions during labor and the type of delivery was not assessed. It is known that epidural analgesia affects labor progression and is associated with higher rates of vacuum- and forceps-assisted delivery<sup>11</sup>. Additionally, epidural analgesia leads to difficulty in standing and walking, and this has been shown to reduce the duration of the first stage of labor as well as the rates of cesarean sections<sup>12</sup>.

In the present study, epidural analgesia in patients with a cervical dilatation of  $\geq 9.0$  cm was associated with adverse perinatal outcomes, such as fetal bradycardia, the need for neonatal oxygen therapy, and the need for neonatal ICU admission. Alternatively, epidural analgesia in patients with a cervical dilatation  $\leq 4.0$  cm was associated with a higher prevalence of Apgar score of <7 at the 1st minute. Shiro et al.<sup>13</sup> evaluated 138 parturients who received epidural analgesia and categorized them into two groups according to cervical dilatation ( $\leq 3.0$  cm and  $\geq 4.0$  cm). In nulliparous women, no differences were noted in perinatal outcomes, except for a longer duration of the first stage in the  $\leq 3.0$  cm group. Similarly, in multiparous women, no differences were observed in perinatal outcomes, except for a higher proportion of Apgar scores of <7 at the 1st minute in the  $\leq 3.0$  cm group, which is in agreement with the results of the present study. Kumar et al.<sup>8</sup> evaluated neonates at an age of  $\geq 34$  weeks who developed respiratory distress within the first 24 h and required oxygen therapy at  $\geq 2$  h and/or positive-pressure ventilation in a neonatal ICU. They observed a significant association between epidural analgesia and respiratory distress in newborns (OR 1.75; 95%CI 1.03–2.99;  $p = 0.04$ ). However, discontinuation of epidural analgesia did not reduce adverse perinatal outcomes, such as lower rates of instrumental births, as demonstrated in a systematic review of five studies comprising 462 women<sup>14</sup>.

In the present study, parturients who underwent epidural analgesia with a cervical dilatation of  $\leq 4.0$  cm had a higher prevalence of the need for oxytocin than those in the other two groups. Additionally, parturients who were administered oxytocin presented a 2.6 times (OR 2.67; 95%CI 1.31–5.57;  $p = 0.0125$ ) higher probability of progressing to vaginal delivery. In a previous study, Shmueli et al.<sup>15</sup> evaluated 15,500 deliveries of full-term singletons and observed that the use of oxytocin was associated with a longer duration of the second stage of labor in nulliparous women, regardless of whether they underwent epidural analgesia. A systematic review of two studies comprising 319 parturients demonstrated that the use of oxytocin in women who underwent epidural analgesia did not reduce the rates of cesarean sections or instrumental deliveries. Furthermore, it did not reduce the adverse perinatal outcomes, such as Apgar scores of <7 at the 1st minute, admission to a neonatal ICU, uterine hyperstimulation, or postpartum hemorrhage<sup>16</sup>.

## CONCLUSION

In summary, performing labor analgesia in parturients with cervical dilatation of  $\leq 4.0$  cm or  $\geq 9.0$  cm was associated with a higher prevalence of adverse maternal and perinatal outcomes.

## AUTHORS' CONTRIBUTIONS

**ABP:** Conceptualization, Formal Analysis, Methodology, Supervision, Visualization. **GDG:** Data curation, Visualization, Writing – original draft. **GAM:** Data curation, Visualization. **MCP:** Investigation, Project administration, Visualization. **EAJ:** Validation, Visualization, Writing – original draft, Writing – review & editing.

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