Are there any strategies to improve neonatal outcomes associated with epidural analgesia in labor?

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Abstract. Background and aim of the work: This study was aimed at evaluating the relationship between epidural analgesia and perinatal outcomes and at verifying the advisability of procedural changes in assistance to labor. Subjects and methods: From January to December 2012, we conducted a retrospective case-control study on 1,963 laboring pregnant women admitted to the Parma University Hospital. We considered two groups: Group 1 received epidural analgesia and Group 2 received no analgesia. Women with elective caesarean sections, multiple pregnancies or deliveries at <34 weeks were excluded. We recorded maternal data (age, type of delivery, obstetric procedures, premature rupture of membranes, screenings for Group-B Streptococcus) and neonatal data (birth weight, gestational age, 1- and 5-minute Apgar scores, diagnosis at discharge). Results: Of the 1,963 laboring women, 287 requested analgesia and 1,676 did not. We found no significant differences between the two groups in the rates of cesarean section, clavicle fracture, and 1-minute Apgar score between 4 and 7. By contrast, we observed a higher rate of instrumental deliveries (p<0.01), fetal occiput posterior position (p<0.05), neonatal cephalohematoma (p=0.01) in Group 1 than in Group 2. In Group 1 we also found a higher number of newborns with 1-minute Apgar score of 3 or less (p=0.016). In addition, a significantly higher number of women in Group 1 had fever during labor (p=0.003, odds ratio 5.01). Conclusions: Our results suggest that strategies should be activated to overcome or limit the side-effects of analgesia in labor through prospective and multidisciplinary studies. (www.actabiomedica.it)

Key words: epidural analgesia, labor; newborn, body temperature, breastfeeding; delivery

Introduction

Evidence-based medicine considers epidural analgesia the most effective form of analgesia in labor and its use is rapidly spreading also in Italy. Knowing and evaluating the impact of epidural analgesia in labor on delivery and neonatal outcome is the starting point for improving delivery assistance procedures and controlling possible side-effects.

The use of epidural analgesia has been associated with dystocia and an increased need for instrumental delivery, because patients receiving epiduals have a longer second stage of labor and show an increased incidence of fetal head malposition (3), particularly the occiput posterior position. Its use has also been associated with an increased need for oxytocin administration during labor, because of reduced uterine motility (4). A subject of greater debate is the effect of analgesia on the cesarean section rate, which appears increased according to some authors (5).

By decreasing maternal stress, epidural analgesia improves blood oxygenation and uteroplacental circulation, possibly having a positive impact on the fetus (6), although most studies in the literature report basically unchanged Apgar scores. On the other hand, analgesia can have side-effects that may affect the ba-
by, such as those resulting from maternal hypotension during analgesia induction or maternal hyperthermia in labor. Hypotension is a major side-effect that can have severe consequences on the fetus, but is uncommon nowadays and can be prevented with appropriate devices. Hyperthermia and its potential negative effects on neonatal outcome have not yet been thoroughly investigated but are arousing more and more interest in the scientific community. Long-term effects of analgesia on neonatal outcome are still unknown.

The purpose of this study was to define the impact of epidural analgesia on delivery and on neonatal well-being in our hospital throughout 2012.

Subjects and Methods

We conducted a retrospective study on 2,549 deliveries that took place at the Parma University Hospital throughout 2012, with a total of 2,593 babies being born. We included in the study 1,963 laboring women; 287 (14.6%) of them received epidural analgesia (Group 1), while the remaining 1,676 (85.4%) received no analgesia (Group 2). A total of 630 newborns were excluded from the study: 588 born by elective cesarean section or emergency section before onset of labor or with early labor signs, 11 from multiple pregnancies, and 20 delivered at <34 weeks.

In all of the 1,963 patients included in the study, we evaluated the following variables.

Mothers: age; ethnic group; parity; way of delivery (vaginal, instrumental or cesarean section); type of cesarean section (planned, urgent or emergency) and its indications; episiotomy; vaginal/perineal tears and their degree; maternal disorders before and during pregnancy; maternal complications such as post-partum hemorrhage or fever ≥38°C during labor.

Newborns: birth weight; gestational age; 1- and 5-minute Apgar scores; neonatal resuscitation; possible neonatal disorders immediately after birth or during the hospital stay; diagnosis at discharge.

Data were retrieved from nursery and neonatal intensive care unit (NICU) medical records, delivery and operating room records, and from ob-gyn maternal case histories.

The therapeutic protocol consisted of local anesthetics (levobupivacaine, ropivacaine) in combination with opiates, administered as epidural top-up.

Data were tabulated for analysis, then entered into a computerized data analysis program (IBM-Statistical Package for Social Science [SPSS], version 20.0). Categorical variables were reported as rates and compared using the chi-square test. Continuous variables were compared by Student’s t-test.

Results

Of 1,963 laboring women, 287 (14.5%) requested epidural analgesia (Group 1), while the remaining 1,676 (85.5%) did not (Group 2).

Parturients and deliveries

Epidemiology

In Group 1, 255 women (88.9%) were from Italy, nine (3.1%) from South America, 10 (3.5%) from Eastern Europe, five (1.7%) from Africa and Maghreb, four (1.4%) from Asia and the Middle East, and four from EU countries.

The mean age of mothers was 33.8±4.45 years in Group 1 and 31.1±5.38 years in Group 2 (p<0.01). Those receiving epidural analgesia were in the 18-44 age range: 42 (14.6%) were aged 18 to 29 years and 245 (85.4%) were aged 30 to 44 years.

Nulliparous women were 200 (69.7%) in Group 1 and 897 (53.5%) in Group 2 (p<0.01).

Cesarean sections and instrumental deliveries

Fifty laboring women out of 287 with epidural analgesia (17.7%) and 225 (13.2%) out of 1,676 without analgesia needed an urgent cesarean section. The difference between the two groups was not entirely statistically significant (p=0.0546, odds ratio [OR] 1.39).

Over the period considered, operative deliveries in the 1,963 laboring women were 172 (8.6%): 53 (18.5%) in Group 1 and 119 (7.1%) in Group 2. The difference between the two groups was extremely significant (p<0.01, OR 2.9). Of the women who needed an instrumental delivery, two out of 53 (3.8%) in
Group 1 and four out of 119 (3.4%) in Group 2 finally underwent a cesarean section (3.4%) (p=0.8).

We found two fetal occiput posterior positions in Group 1 (0.7%) and two cases in Group 2 (0.1%), p<0.045 and OR 5.9.

The rate of episiotomy and vaginal/perineal (V/P) tears is shown in Table 1.

**Newborns**

**Gestational age**

Gestational age ranged from 34+5 to 41+5 weeks in Group 1 and from 34 to 41+5 weeks in Group 2. The characteristics of the two groups are shown in table 2.

**Birth weight**

Birth weight data are shown in table 3.

### Table 1. Rates of episiotomy, vaginal/perineal (V/P) tears and other tears in Group 1 and Group 2

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episiotomy</td>
<td>135 (47%)</td>
<td>550 (32.8%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>1st-degree V/P tear</td>
<td>26 (9.0%)</td>
<td>177 (10.6%)</td>
<td>0.4</td>
</tr>
<tr>
<td>2nd- or 3rd-degree V/P tear</td>
<td>42 (14.6%)</td>
<td>371 (22.1%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Colporrhaphy</td>
<td>6 (2.1%)</td>
<td>17 (1%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Trachelorraphy and suture of the posterior commissure</td>
<td>41 (14.3%)</td>
<td>358 (21.4%)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

### Table 2. Gestational ages in group 1 and 2

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Group 1 (n=287)</th>
<th>Group 2 (n=1676)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>34-37 wks</td>
<td>3 (1%)</td>
<td>81 (4.8%)</td>
<td>0.003</td>
</tr>
<tr>
<td>37-41 wks</td>
<td>220 (75.6%)</td>
<td>1335 (79.6%)</td>
<td>0.2</td>
</tr>
<tr>
<td>&gt;41 wks</td>
<td>64 (22.3%)</td>
<td>260 (15.5%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

### Table 3. Birth weight in Group 1 and Group 2

<table>
<thead>
<tr>
<th>Birth weight (g)</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2500</td>
<td>7 (2.4%)</td>
<td>67 (4%)</td>
<td>0.2</td>
</tr>
<tr>
<td>2500-4000</td>
<td>262 (91.3%)</td>
<td>1494 (89.1%)</td>
<td>0.3</td>
</tr>
<tr>
<td>&gt;4000</td>
<td>18 (6.3%)</td>
<td>114 (6.8%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Average weight</td>
<td>3375.5±393</td>
<td>3332.5±464.1</td>
<td>0.096</td>
</tr>
</tbody>
</table>

**Birth trauma**

As regards birth traumas, occipital cephalohematoma occurred in 117 cases, including 26 in Group 1 (9.05%) and 91 in Group 2 (5.4%) (p=0.01), while clavicle fracture occurred in four cases in Group 1 (1.39%) and 27 cases in Group 2 (1.1%) (p=0.8).

In detail, considering only babies born by instrumental delivery, we found 16 newborns with cephalohematoma in Group 1 (30.2%) and 25 in Group 2 (21%) (p=0.1).

**Apgar Scores**

The data collected are shown in Table 4.

Among the nine newborns with 1-min Apgar score of ≤3 in Group 1, six had a 5-min Apgar score of ≥7. Of the 17 in Group 2, 10 had a 5-min Apgar score of ≤7 and seven of <7, including four with a 5-min Apgar score of 3.

**Maternal hyperthermia and neonatal outcome**

Eleven laboring women out of 1,987 had a fever (body temperature ≥38°C); among them, five (1.7%) received epidural analgesia (max. temperature, 38.2°C) and six (0.35%) did not (p=0.003, OR 4.93).

In Group 1, all maternal temperatures increased after the induction of epidural analgesia, including two cases showing a temperature elevation after only 30 minutes. Four women out of five had premature rupture of membranes (PROM) occurring more than 12 hours before (more than 18 hours before in two of them). All of them had negative urine cultures, but two had vaginal swabs testing positive for Group-B streptococcus (GBS). However, all these women received

### Table 4. 1-minute Apgar scores in Group 1 and Group 2

<table>
<thead>
<tr>
<th>1-minute Apgar score</th>
<th>Group 1 (n=287)</th>
<th>Group 2 (n=1676)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3</td>
<td>9 (3.1%)</td>
<td>17 (1.1%)</td>
<td>0.0056</td>
</tr>
<tr>
<td>4-7</td>
<td>8 (2.8%)</td>
<td>32 (1.9%)</td>
<td>0.3</td>
</tr>
<tr>
<td>≥7</td>
<td>270 (94.1%)</td>
<td>1626 (97%)</td>
<td>0.0113</td>
</tr>
</tbody>
</table>

### Table 4. 1-minute Apgar scores (excluding 172 instrumental deliveries)

<table>
<thead>
<tr>
<th>1-minute Apgar score</th>
<th>Group 1 (n=234)</th>
<th>Group 2 (n=1557)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3</td>
<td>3 (1.3%)</td>
<td>15 (1%)</td>
<td>0.6</td>
</tr>
<tr>
<td>4-7</td>
<td>4 (1.7%)</td>
<td>26 (1.66%)</td>
<td>0.8</td>
</tr>
<tr>
<td>≥7</td>
<td>227 (97%)</td>
<td>1516 (97.3%)</td>
<td>0.7</td>
</tr>
</tbody>
</table>
complete intrapartum antibiotic prophylaxis. In the only woman who hadn't PROM, urine culture and the vaginal swab were both negative; she received one dose of ampicillin. Of the five babies born from hyperthermic women, one was admitted to NICU because of tachypnea associated with transient hypotonia, received antibiotic therapy and was discharged in the second day of life with a diagnosis of transient tachypnea. The other four newborns showed a normal adaptation to extrauterine life and were discharged in the second day of life. In all cases, neonatal blood culture, polymerase chain reaction (PCR) and blood count were normal and no diagnosis of infection was made.

Of the babies born from hyperthermic mothers in Group 2, four were admitted to NICU and received antibiotic therapy because polypnea was also present in addition to maternal hyperthermia; however, only one of them was discharged with a diagnosis of infection because of elevated PCR levels, GBS-positive maternal vaginal swab, and amnionitis.

Overall, considering all the newborns included in the study, we did not find any significant difference (p=0.28) in the number of babies who received antibiotic therapy between the two groups (1.7% in Group 1 vs 2.9% in Group 2).

Breastfeeding and formula milk

Data concerning the type of lactation are shown in Table 5.

Discussion

The scientific community considers epidural analgesia the most safe and effective method of relieving labor pain. An increasing number of women request it, even if in Italy it is not as widely used as in other European countries yet. This treatment option is a conquer for women and allows them, especially primiparas, to approach delivery in a less apprehensive way, possibly reducing the rate of elective cesarean sections on maternal request.

Data on parturients and deliveries

Epidemiology

Considering that until November 2012 epidural analgesia in our hospital was provided mainly by self-employed professionals, we believe that ours is a selected sample, mostly consisting of middle/upper-class women with supervised and mainly low-risk pregnancies. The mothers' ethnic diversity demonstrates that epidural analgesia is beginning to be chosen beyond cultural differences, provided that women are adequately informed and that they have equal access to it. The average age of mothers who chose analgesia in Group 1 was older than the average age of women who didn't in Group 2, in spite of the higher rate of nulliparous women (69.7% vs 53.5%, \( p<0.01 \)). Indeed, most of them were 30-44 years old (85.4%), with a mean age of 33.8 vs 31.1 for Group 2. Group 1 was probably composed of well-educated and well-informed women with a high social, economic and cultural level, who were giving birth, often for the first time, at an older age than women in Group 2.

Cesarean sections and instrumental deliveries

The impact of epidural analgesia on caesarean sections is one of the most debated issues: we found a difference between the two groups (17.7% in Group 1 vs 13.2% in Group 2), but it wasn't entirely statistically significant (p= 0.054, OR 1.397), providing no conclusive answers to the question.

Another issue is the impact on operative deliveries (vacuum or forceps). Some authors did not find any positive correlation between operative deliveries and analgesia, but most of the studies published recently in the literature consistently show an increasing recourse to vacuum extraction during epidural analgesia. In fact, its use has been associated to a prolonged second stage of labor and to an increased incidence of fetal head malposition (11), particularly occiput posterior rotation. These conditions are among the most common indications to instrumental delivery (12), as is
confirmed by our results, which show a larger number of instrumental deliveries in Group 1 (p<0.01, OR=2.69). However, we cannot exclude that some of these women might have requested epidural analgesia because of severe pain caused by a dystocic labor that required instrumental delivery.

The literature associates epidural analgesia to an increased recourse to episiotomy and to a reduction of 2nd-, 3rd- and 4th-degree V/P tears (13). In our sample, episiotomy was significantly more frequently performed in Group 1 (p<0.01). This was probably due to the increased number of instrumental deliveries, because using vacuum extractor often makes episiotomy necessary to facilitate instrument placement. Furthermore, any excessive dose of local anesthetic during the second stage of labor may reduce the perineal pressure sensation and the push reflex, increasing the recourse to Kristeller maneuver and consequently the rate of episiotomy. This, in turn, might explain the decreased rates of 2nd-degree V/P tears, external vulvar sutures, trachelorraphy and suture of the posterior commissure of the vulva in Group 1 (p=0.004).

Newborns

Epidemiology

As a result of the fact that in our hospital epidural analgesia was provided mainly by self-employed professionals until November 2012, the women in our sample were generally from a high socio-cultural background, with repercussions on fetal characteristics in terms of gestational age, as it is known that a medium-low socio-economic status is a risk factor for preterm births. This might explain the low rate of preterm births in Group 1 compared with Group 2 (p=0.01). Birth weight rates were similar in the two groups. We believe that the larger number of post-term newborns in Group 1 (p=0.04) may be related to the higher percentage of nulliparous and the older age of Group 1 women.

Apgar scores

We observed significant differences between the two groups: in Group 2 (no analgesia), 1-min Apgar scores ≥7 were increased (p=0.0056) while 1- min Apgar scores ≤3 were decreased (p=0.01) compared with Group 1. Apart from this difference, if we exclude babies delivered instrumentally, the scores in the two groups were comparable. It is difficult to determine whether Apgar scores were influenced more by analgesia or by the type of delivery (10). We suppose that analgesia may have indirectly affected 1-min Apgar scores through its impact on the instrumental delivery rate.

Birth traumas

The rate of cephalohematoma appeared significantly higher in Group 1 (9.0% vs 5.4%, p=0.01), probably due to the larger number of instrumental deliveries. On the other hand, the rate of clavicle fracture, usually linked to shoulder dystocia, did not differ in the two groups (1.39 % in Group 1 vs 1.0% in Group 2, p=0.8).

Maternal intrapartum hyperthermia and neonatal outcome

A side-effect of epidural analgesia is maternal hyperthermia during labor: the temperature elevation starts right after the beginning of the procedure and is related to labor length. The risk is higher in nulliparous women, who have a longer duration of labor: studies have shown that almost a third of them have a temperature elevation during labor (14-16). The most credible hypothesis is that epidurals cause this side-effect in a small number of predisposed women and, through a mechanism that is not yet well known, induce an inflammatory state without maternal and/or fetal infection (15). Maternal hyperthermia during labor may affect neonatal health and studies have reported a two-to six-fold increase in the risk of adverse neonatal outcomes, such as hypotonia, assisted ventilation, 1-min and 5-min Apgar scores <7, early-onset neonatal seizures, in full-term newborns exposed to maternal temperature exceeding 38°C. The proportion of adverse outcomes increased with the degree of the epidural-related maternal temperature elevation (17). In our sample, the hyperthermia risk was increased five-fold in Group 1 women, in agreement with literature reports. Among the newborns from hyperthermic mothers in Group 1, only one was admitted to NICU but was discharged already in the second day of life with a diagnosis of transient tachypnea. However, in this baby the cause of symptoms could not be con-
clusively established and we cannot exclude a possible relation with maternal hyperthermia during labor. It has been assumed that the elevation of maternal body temperature may lead to an increased rate of neonatal sepsis evaluation and neonatal antibiotic treatment. In our study, however, we did not find any significant difference in antibiotic therapy over the two groups (1.7% vs 2.9%, p=0.3). In our opinion, it would be worthwhile to perform a proper analysis of the thermal curve during labor together with a correct and careful evaluation of infectious risk factors to optimize both obstetric and neonatal management.

Breastfeeding at discharge

Breastfeeding rates were comparable in the two groups, in agreement with the most recent literature studies that have not found any differences in short-term breastfeeding rates between groups with or without epidural analgesia (20). It is possible that good pain control may have a positive effect, helping mothers to take care of their babies right after delivery and facilitating early mother-baby contact and the start of breastfeeding. As regards the duration of breastfeeding, opinions differ in the literature: some authors reported that women choosing epidural analgesia were more likely to stop breastfeeding their infants and to have difficulties breastfeeding in the few days after birth (21), possibly due to a weakened suction reflex caused by opioids. However, other authors pointed to other factors that could influence results, such as socio-economic status, cultural factors, or mother-baby contact. Owing to our study methodology, we were not able to draw any final conclusions about the duration of breastfeeding.

Conclusions

Our results agree with previous studies and suggest that strategies should be activated to overcome or limit the side-effects of analgesia in labor through a prospective and multidisciplinary approach involving anesthesiologists, obstetricians and neonatologists. Every one of the professionals involved would have a role to play: anesthesiologists by optimizing the timing of drug administration; obstetricians by monitoring maternal body temperature, indicating the most appropriate positions during labor and determining when is the best time for the woman to start pushing in order to facilitate spontaneous delivery (24); neonatologists by reviewing the neonatal anti-infection protocol and evaluating all obstetrical and neonatal data in light of the epidural analgesia being performed, so as to later include such data in the neonatal records.

In conclusion, although epidural analgesia can be considered a safe procedure for mother and neonate, there is still room for improvement. Existing evidence suggests that it may alter the dynamics of labor and maternal temperature regulation, but these issues should be investigated with appropriately designed, prospective, and multidisciplinary studies.

References


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