Do epidurals cause higher intrapartum temperatures in parturients and neonates? A Belgian experience

B. Baheri, H. Coppejans, E. Joukes, M. Vercauteren

Abstract

In a prospective study including 200 parturients, maternal and neonatal temperatures were registered and changes were evaluated in relationship with epidural treatment, duration of labor or parity.

Epidural analgesia was more often requested by nulliparous parturients, prolonged the duration of labor by approximately 1 hour and also resulted in more need for oxytocin.

Parturients receiving epidural analgesia had a higher body temperature at full cervical dilation as compared to their non-epidural counterparts. In the epidural group 31.1% of women had temperatures > 37.5°C versus only 8.9% in the non-epidural group (p < 0.001). However, epidurally-induced fever was not significantly correlated with parity (p = 0.3) and duration of labor (p = 0.8) although. Similarly, neonates of epidurally treated mothers also had higher body temperatures. This fever does not cause a problem in a vast majority of mothers and neonates with respect to early outcome parameters.

More studies are needed to develop a reasonable concept of mechanism for this phenomenon, whether it should be considered to be fever or hyperthermia and how it might be prevented.

However, there is no reason to dissuade neuraxial analgesia based in the present results while pain-free mothers may cooperate better and may be more satisfied. Alternative analgesic methods such as opioid patient controlled analgesia may also affect neonatal outcome.

Key words: analgesia, epidural, fever, hyperthermia, labor, maternal, neonatal

Introduction

The epidural technique is one of the methods for relieving pain in laboring women. One of the controversial complications of epidural analgesia is the effect on mother and baby’s body temperature. An association between the use of epidural analgesia during labor and an elevation in maternal temperature was first noted by Fusi et al. [1] reporting that the vaginal temperatures of 18 parturients receiving epidural analgesia increased by 1°C during 7 hours compared to women receiving intramuscular analgesia. They concluded that the increase in temperature was not clinically important but their report raised concern regarding the effects of epidural anaesthesia on possible maternal temperature and detrimental fetal effects. Other subsequent reports confirmed this conclusion [2, 3].

Further debate about fever and epidural analgesia was prompted by the reports by Lieberman et al. [4, 5]. Elevated temperatures in mothers and newborns where an epidural had been used resulted in investigation for sepsis and treatment with antibiotics. In addition, they found higher temperatures with labors exceeding 18 hours as compared to labors lasting < 6 hours, while a correlation was found between the occurrence of fever and the risk of instrumental delivery and cesarean section. Despite the limitations of that study the authors stated that women requesting epidurals must be aware of these complications.

In the present prospective study we wanted to evaluate if fever may also be a problem for parturients in a European country where labor durations rarely
exceed 6 hours and where small dose epidurals is common practice.

Methods

Study Population

We conducted a prospective, non-randomized, observational study of women with (EA group) and without (NEA group) epidurals to determine if there is any association between peripheral temperature and epidural use. Following institutional ethical approval and written informed consent two hundred healthy or low-risk term parturients (ASA classification 1 or 2) with singleton vertex presentation and in spontaneous labor were selected to take part in this study.

In Belgium the epidural rate during labor analgesia approximates 70%. To obtain an equal number of participants in both groups, each epidurally treated parturient was followed by the first non-epidural patient, after which a subsequent epidural could be included provided that labor analgesia was not converted into cesarean section anaesthesia. This signified that many epidurally treated patients could not be included unless first a subsequent non-epidural gave consent. It also allowed to compare equal numbers per group as otherwise more than twice as many epidurals would have taken part in the study.

Excluded were women with any possible pre-existing infection, chorioamnionitis, rupture of membranes > 12 h, use of antibiotics, patients presenting with fever, twin pregnancies, those receiving analgesia less than 6 hours prior to enrollment.

None of the patients in control group received any other pain medication. Oxytocic induction or augmentation was administered upon the obstetrician’s discretion.

Analgesic methods

The epidural analgesia technique, material and medications were all the same in group, including only median approach epidural catheterization (no combined spinal-epidural analgesia), using loss of resistance to saline technique in lumbar levels of L2-L4. All the analgesic solutions, containing a mixture of 0.16% ropivacaine and sufentanil 0.8 µg/ml, were prepared in advance by the hospital pharmacist in 125 ml bags, kept in standard temperature conditions.

Following a negative test dose after epidural catheter placement, patients assumed a supine position with left uterine displacement (LUD) or sitting upright position.

An epidural bolus was allowed to a maximum of 15 ml of the mixture. Then a patient-controlled epidural analgesia (PCEA) pump device was installed at a basal continuous rate of 4 ml/h along with demand doses of 4 ml/h and a lock-out interval of 15 min. No other analgesic drugs were administered in both groups. All epidural catheters were removed directly after delivery.

Data Collection

The maternal axillary body temperature was measured and monitored in both study groups at admittance, time of complete cervical dilation and post-delivery. All data were collected on a registration sheet and a special computer program (Partogram).

In both groups vital parameters, including non-invasive systolic and diastolic blood pressure, heart rate, peripheral body temperature and fetal heart rate (FHR) were registered peripartially in a relative controlled temperature environment, based on patient’s request. Decreases in systolic blood pressure 20% less than baseline or hypotensive symptoms were treated with IV lactated ringers and ephedrine.

In order to compare the labor-time correctly, we considered the labor duration in epidural group as the time interval between starting the epidural analgesia and the baby’s birth. By knowing the mean cervical dilation at the moment of placing the epidural catheter i.e. 4 cm, which was determined after the termination of the study, we were finally able to calculate the labor times in non-epidural group by measuring the interval from a 4 cm dilation moment until the delivery.

The other registered characteristics of patients were maternal age, parity, the temperature of the neonate, oxytocin induction/augmentation, rupture of membranes (spontaneous before hospital admission, spontaneous in the labor ward or artificially broken).

Statistical methodology and data analysis

All de patients’ data were encoded in the Statistical Package for the Social Sciences (SPSS) 12th version for Windows. The data were analyzed with 95% reliability (CI 95%), frequency tables, odds ratios (OR’s), Pearson’s correlation coefficients, Student’s t-test and multiple logistic regression.

The patient’s characteristics and parameters were contributed as continuous and categorical variables. The mean (standard deviation) is displayed for continue parameters. The percentage of each group is shown for categorical parameters.

Normally distributed continuous parameters are compared between the epidural and non-epidural groups with an unpaired t-test.

For non-normally distributed continuous parameters and non-parametric data we used the Mann-Whitney test. Categorical parameters are compared with the Chi-square or Fisher exact test (when numbers were low).

A logistic regression model is used to simultaneously study the effects of the combination of parameters at the temperature (of mother or neonate). The chance for a temperature above 37.5°C is studied by using
the logistic regression. A p-value of < 0.05 was considered to be significant.

Results

The study was conducted between January 2011 and December 2011. During this period 900 deliveries were performed in our tertiary care center. With 220 C-sections, of the remaining 680 parturients, 470 received an epidural of whom somewhat more than 100 could enter the epidural arm of the study. Some of them needed to be discarded during the initial phase in case of a secondary cesarean section. When terminating the study period, 200 patients had been included. One hundred eighty were fulfilling the criteria statistical comparison as 20 patients (10 in each group) needed to be excluded due to incomplete data or protocol violation. We finally obtained two groups of 90 parturients each with and without epidural analgesia which were comparable with respect to patients’ characteristics (Table 1).

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>NEA</th>
<th>EA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of parturients</td>
<td>90</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Parturients’ age (yr)</td>
<td>29.63 (4.68)</td>
<td>29.06 (5.34)</td>
<td>0.4414</td>
</tr>
<tr>
<td>Parity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>nulliparous</td>
<td>23.33%</td>
<td>52.22%</td>
<td>0.0001</td>
</tr>
<tr>
<td>multiparous</td>
<td>76.67%</td>
<td>47.78%</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean (SD) or number of patients (percentage); EA = epidural analgesia group, NEA = non-epidural analgesia group

The mean age of the study population was 29.6 years for the NEA and 29.0 for the EA group. No statistically significant differences were found in membrane rupture history or maternal temperature at admittance.

As the first epidural injection was given at a mean cervical dilation of 4.08 (1.38) cm (Fig. 1) this was considered in the NEA group to be the starting point to calculate time intervals.

Not unexpectedly the epidural group contained more nulliparous women (52% vs 23%, p < 0.001) (Table 1). Among the control (NEA) group, 20 parturients (22%) were not actively in labor but needed oxytocin for induction or augmentation of labor, whereas in EA group the rate of need for oxytocin was significantly higher (n = 34, 37.8%, p = 0.034) (Table 2).

Table 2. The maternal mean body temperature at different times, the incidence of maternal postpartum fever, the duration of labor and need for oxytocin

<table>
<thead>
<tr>
<th></th>
<th>NEA</th>
<th>EA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers of parturients</td>
<td>90</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>T °C at admission (SD)</td>
<td>36.65 (0.42)</td>
<td>36.71 (0.36)</td>
<td>0.3259</td>
</tr>
<tr>
<td>T °C full dilatation (SD)</td>
<td>36.81 (0.48)</td>
<td>37.20 (0.51)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>T difference (full dilatation-admission)</td>
<td>0.16 (0.49)</td>
<td>0.49 (0.54)</td>
<td>0.0006</td>
</tr>
<tr>
<td>T °C mother postpartum (SD)</td>
<td>36.81 (0.37)</td>
<td>37.07 (0.40)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>T °C at full cervical dilatation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 37.5°C</td>
<td>91.11%</td>
<td>68.89%</td>
<td></td>
</tr>
<tr>
<td>≥ 37.5°C</td>
<td>8.89%</td>
<td>31.11%</td>
<td></td>
</tr>
<tr>
<td>Duration of labor (h, min)</td>
<td>4h16' (1h31')</td>
<td>5h07' (2h19')</td>
<td>0.0036</td>
</tr>
<tr>
<td>Oxytocin:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>–</td>
<td>77.78%</td>
<td>62.22%</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>22.22%</td>
<td>37.78%</td>
<td>0.0345</td>
</tr>
<tr>
<td>Rupture of membranes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- spontaneous at home</td>
<td>25.56%</td>
<td>26.66%</td>
<td>0.7449</td>
</tr>
<tr>
<td>- spontaneous at hospital</td>
<td>32.22%</td>
<td>30.00%</td>
<td>0.7594</td>
</tr>
<tr>
<td>- artificially broken</td>
<td>42.22%</td>
<td>43.33%</td>
<td>0.8832</td>
</tr>
</tbody>
</table>

Fig. 1. The average cervical dilatation at the start time of epidural analgesia in the 90 patients of EA group.
The mean body temperature on admission was 36.65°C in NEA group and 36.71°C in EA group whereas at the time of complete cervix dilation it was 36.81°C in NEA group versus 37.20°C in EA group respectively (Table 2). There was a significantly higher maternal body temperature at the time of full cervical opening in EA group compared with NEA group (p < 0.0001) while the increase in temperature was significantly more pronounced in the EA group (0.49 vs 0.16°C, p = 0.0006).

The maternal mean temperature in postpartum period was 37.07°C in EA whereas no change was registered in control group (p < 0.0001).

Eight parturients in NEA group (9%) had body temperature equal or above 37.5°C at the time of complete cervical dilatation versus 28 patients (31%) in EA group (p < 0.001).

The average length of labor in EA group i.e. from the epidural loading dose to delivery, was calculated to be 5 h 07 min versus 4 h 16 min in NEA group (difference of 51 minutes, p = 0.0036). These prolonged labor durations were noticed in both nulli- and multiparous parturients (Fig. 2). When splitting the patients according to their duration of labor (< 4 h, 4-7 h, > 7 h) a difference in temperature is seen between epidural and control group while significantly more epidurally treated mothers had labor durations > 7 h than in the control group (21 vs 2, p < 0.001) (Fig. 3).

After adjustment for duration of labor, parity, temperature on admittance and epidural administration, we calculated only a significant correlation between epidural anaesthesia and maternal temperature > 37.5°C during full dilatation OR 3.97, p = 0.002). There was no correlation with the duration of labor (p = 0.8) nor with parity (p = 0.3). Although the temperature differences seem to be larger with labor duration > 7 h, no straightforward conclusions are possible as the control group contained only 2 subjects.

With respect to the neonates, the mean body temperature immediately following delivery was 36.94°C in EA group versus 36.56°C in NEA group (difference of 0.38°C, p < 0.0001) (Table 3).

However, we did not find a significant difference between two groups in terms of newborn’s body temperature ≥ 37.5°C. In the EA group 5 neonates (5.6%) had temperatures equal or above 37.5°C versus one (1.1%) in the NEA group (p = 0.211). There was no correlation between epidural analgesia and labor duration with neonatal hyperthermia ≥ 37.5°C.

Discussion

The present study shows that EA is associated with maternal hyperthermia which is statistically significant but probably not clinically important. It also revealed that there were significant differences between the epidural and the control group with respect to parity, length of labor and need for labor induction.
The association between epidural analgesia and labor hyperthermia is subject of much debate. Labor itself may be associated with fever in the absence of any infection. The contractions of the uterus and subsequently the uterine blood vessels lead to very small increase in temperature which can accumulate over hours of labor and cause the body temperature to increase. As a consequence prolonged labor may further facilitate this increase due to more uterine contractions. The counteraction in normal conditions is sweating and panting.

Despite significant research, the precise mechanism of epidural-associated fever remains poorly understood [6].

Multiple mechanisms have been suggested to explain maternal fever development related to epidural labor analgesia. Vallejo et al. found that fever was only to be explained by the presence of (subclinical) chorioamnionitis and not by the epidural per se [7]. Also other studies contested that epidurals were a risk for intrapartum temperature increases [8]. This would be too easy to explain all studies that have found temperature increases with epidurals and less in the control groups although the latter was explained then by the antipyretic effects of systemic rather than epidural opioids [1, 9]. Most explanations are related to altered temperature regulation, longer and dysfunctional labors with epidurals especially in nulliparous women also requiring more oxytocin and vaginal examinations [10]. Still others found that intermittent analgesia caused less hyperthermia than continuous techniques as practices nowadays [11]. Most recently even higher BMI values (also due to longer lasting labors?) were found to be correlated with the development of maternal hyperthermia with epidural analgesia [8]. All of this only demonstrates that there are still many gaps in finding the exact mechanism. Altered thermoregulatory transmission from the periphery to the hypothalamus may be a possible mechanism for the increase in temperature seen during epidural analgesia.

Epidural analgesia may interfere with normal temperature regulation by different hypothetical mechanisms, i.e. blockage of the sympathetic nerve branches that innervates sweat glands in large part of the body affected by epidural analgesia, vasoconstriction of the blood vessels in areas unaffected by the block and less sweating and hyperventilation (also facilitating heat dissipation) due to better pain relief as compared to less effective analgesic methods. On the other hand, fluid loading (as still performed in many departments in case of epidural analgesia) with relatively cold intravenous fluids and vascular dilatation due to the sympathetic block caused by the neuraxial block may prevent fever development although this may also be counterproductive as may result in shivering and overproduction of heath.

Also the discrepant findings between intravenous versus neuraxial opioids is still unclear. Deleting opioids in the epidural mixture may not prevent fever although it does not occur when opioids are given intravenously. An explanation may consist of larger local anaesthetic requirements if deleting the opioid within the mixture, thus possibly prolonging labor duration, a risk factor for fever development.

However, most recent research has focused on placental inflammation and cytokine release [12]. With respect to possible inflammation, the level of interleukin-6 (IL-6), a pro-inflammatory cytokine, is increased in women receiving epidural analgesia [13, 14]. A longer duration of epidural infusion is associated with higher levels of IL-6, whereas this elevation is not seen in prolonged labors without epidural. In addition, the role of the transient receptor potential vanilloid I (TRPV1 II Capsaicin receptor I Vanilloid receptor) in epidural-induced hyperthermia is recently reviewed by Kozlov [15].

The vanilloid receptor (VR-l/TRPV1) is a receptor, found on the free nerve endings of both C and Aδ fibers. TRPV1 regulates vasomotor tone and metabolic heat production. Blockage of this receptor elicits hyperthermia in humans [16]. Local anaesthetics work as agonist/antagonist on these TPRV1 receptors. Antagonist action may cause hyperthermia through modifying thermoregulation. Agonist action may cause hyperthermia by release of IL-6 and other inflammatory agents. Studies have found that the use of dexamethasone may alleviate these increases in body temperature which may support the impact of inflammation rather than infection [17].

Whatever the underlying mechanisms, epidural analgesia is causatively associated with maternal body temperature enhancement. Our findings, that epidural analgesia prolongs the duration of labor, either the first or second stage, and requires more oxytocin, has been confirmed by a recent Cochrane Database analysis [18].

In our study this fever prompted no change in clinical outcome of mother and baby. Maximum maternal temperature rose to 39.2°C in only 1 of 90 women who received epidural analgesia. Although other study found that temperature increases were moderate, not affecting neonatal outcome nor requiring further work-up, maternal and neonatal fever may have more consequences than previously thought. Studies have found a significant linear trend between the occurrence of maternal fever > 38.5°C and the risk of hypotonia, assisted ventilation, low Apgar scores and neonatal brain injury evidenced by cerebral palsy, early seizures, encephalopathy and learning deficit at later ages [19, 20]. The decision to perform additional testing in the newborn was left to the discretion and physical
examinations at birth and on the subsequent day of the attending neonatologist.

There are some points that make this study different from other trials comparing laboring women to epidural versus control. All the characteristics of participants, labor management protocol and epidural regimen were the same in all parturients while the control group did not receive any substance to treat labor pain. Secondly, multiple cervical examinations can lead to maternal discomfort and possibly raise the risk of infection or hyperthermia. In our patient population (an academic hospital setting), the frequency of cervical examination was by means of a computer program (Partogram), so we could exactly define the cervical dilatation at any moment of labor course.

There are also some limitations to this study. Our study could not estimate the other possible confounding variables, for example changed temperature regulation due to less sweating, genetical susceptibility, room temperature and humidity. Although these two last are individual factors which depend on patients demand and comfort, they can affect the individual’s body temperature. Secondly, we measured only peripheral (axillary) body temperature, which can be falsely lower than real core temperature. Third, there may have been an inevitable selection bias as the epidural prolonged the duration of labor either because of the epidural effect itself or the predominance of nulliparous women in epidural group. It would have been better to conduct the study only in nulliparous patients. Finally, to confirm that temperature elevations in epidural group were due to the epidural and not a probably existing underlying infection, it had been better to perform a histopathological examination of all placentas’ after birth.

Conclusion

Epidural analgesia prolongs the duration of labor by approximately 1 hour and may necessitate more oxytocic substances. Some laboring women develop fever, which is significantly more common among those who have received an epidural. However, the development of epidural-induced fever does not significantly depend on parity and duration of labor. This fever does not cause a non-well being feeling in the parturient nor a problem in a vast majority of neonates. More studies are needed to develop a reasonable concept of the underlying mechanism for this phenomenon and whether it should be considered to be fever or hyperthermia. There is no reason to dissuade neuraxial analgesia based upon the present results.

Conflict of interest

Nothing to declare

References

Produce analgezie peridurală la naștere creșterea temperaturii intrapartum la parturiente și nou-născuți? O experiență belgiană

Rezumat

Într-un studiu prospectiv care a inclus 200 de parturiente, s-a înregistrat temperatura maternă și a nou-născuților, iar modificările apărute au fost evaluate în relație cu tratamentul peridural, durata travaliului și paritatea sarcinii.

Analgezia peridurală a fost mai frecvent solicitată de către nulipare, a prelungit durata travaliului cu aproximativ o oră și a determinat un necesar mai ridicat de oxitocină.

Parturientele care au primit analgezie peridurală au avut o temperatură corporală mai ridicată la dilatație cervicală maximă în comparație cu cele la care nu s-a utilizat acest mod de analgezie. În grupul cu analgezie peridurală, 31,1% din femei au înregistrat temperaturi > 37,5°C față de numai 8,9% în grupul fără peridurală (p < 0,001). Cu toate acestea, febra induză de analgezie peridurală nu a fost corelată semnificativ cu paritatea (p = 0,3) și nici cu durata travaliului (p = 0,8). În mod similar, nou-născuții mamelor care au beneficiat de analgezie peridurală au prezentat o temperatură corporală mai ridicată. Această febră nu a determinat la marea majoritate a mamelor și nou-născuților nici un fel de probleme privind evoluția imediată postpartum.

Sunt necesare studii suplimentare pentru a dezvolta un concept rezonabil privind mecanismul acestui fenomen, dacă ar trebui considerat febră sau hipertermie, și cum ar putea fi prevenit.

Cu toate acestea, nu sunt motive pentru a nu recomanda analgezie neuraxială pe baza acestor rezultate, dat fiind faptul că parturientele fără dureri sunt mai cooperante și pot înregistra un grad mai ridicat de satisfacție. Metodele analgezice alternative, cum ar fi analgezia cu opioide controlată de pacient, pot de asemenea afecta evoluția nou-născutului.

Cuvinte cheie: analgezie, peridurală, hipertermie, travaliu, maternal, neonatal