A comprehensive analysis of continuous epidural analgesia’s effect on labor and neonates in maternal hypertensive disorder patients

Bin Han, Mingjun Xu *

Department of Anesthesiology, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing, China

Article history:
Received 15 July 2016
Received in revised form 21 December 2016
Accepted 22 December 2016
Available online 24 December 2016

Keywords:
Continuous epidural analgesia
Labor analgesia
Maternal hypertensive disorder
Neonate

Abstract

Background: Maternal hypertensive disorder is one of the most common and severe medical complications during pregnancy. Epidural analgesia administration is widely used during labor process.

Aim: To evaluate the potential advantage or disadvantage of continuous epidural analgesia’s on labor and neonates for maternal hypertensive disorder patients comprehensively.

Methods: We have retrospectively analyzed 232 patients who diagnosed as maternal hypertensive disorder in our hospital since 2015. Among which, 126 patients including 28 cases of severe preeclampsia were administrated with continuous epidural analgesia (Analgesia group), the other 106 patients were untreated (Control group). We have compared the maternal age, body weight, gestational weeks, period for the first and second labor stage; the incidence of eclampsia, natural labor, cesarean section, forceps delivery and postpartum hemorrhage between these two groups respectively; furthermore, we recorded patients who received oxytocin and antihypertensive treatment during the delivery progress as well as evaluated the neonate body weight, Apgar score and performed umbilical cord blood gas analysis.

Results: Continuous epidural analgesia does not affect the first and second labor stage period (p = 0.36), However, there is a significantly higher demand for oxytocin treatment (36.5% Vs 19.8%, p < 0.01) and a significantly lower requirement for antihypertensive treatment (22.2% Vs 81.1%, p < 0.001) in analgesia group compared to control group.

We also notice that the natural delivery ratio in analgesia group is higher than control group and most importantly, continuous epidural analgesia can increase 1 min Apgar score and has no other effect on neonates’ body weight, umbilical cord blood gas parameters, 5 min and 10 min Apgar score.

Conclusions: Our result based on a large cohort comprehensive analysis indicates that continuous epidural analgesia can benefit both maternal hypertensive disorder patients and neonates without any side effect.

1. Introduction

Maternal hypertensive disorder is a special disease during pregnancy, which occurred about 10% of pregnancies globally [1], and it is one of the most serious complications during pregnancy [2]. The patients usually exhibit high blood pressure and proteinuria, which normally disappear after delivery [3]. Clinically, the routine therapy includes antispasmodic, antihypertensive and some other supportive treatment, or in some scenario, terminating the pregnancy at the right time [3]. In western countries, the major complications result from maternal hypertensive disorder are hemolysis, elevated liver enzymes, low platelet count (HELLP syndrome) and Disseminated intravascular coagulation (DIC) [4]; cardiovascular complications and cerebrovascular accidents are rarely reported; whereas in China, it is documented that maternal hypertensive disorder usually induces severe complications such as cerebrovascular accident, heart failure, acute renal failure, HELLP syndrome and pulmonary edema [5].

Many studies have confirmed that continuous epidural anesthesia administration is a safe and efficient way for labor analgesia and can benefit both pregnant women and neonate [6,7]. This approach allows the analgesic to release plane and steady, reduces the motor block and the occurrence of hypotension. Furthermore, patients can adjust dosage and frequency for the administration themselves according to their own demand, therefore the administration is more personalized, and the outcome is much better with fewer side effects.
The basic pathological character for maternal hypertensive disorder is systemic small artery spasm [8]. The stress response induced by the pain during labor process can aggregate patients' condition, or even cause some severe complications such as eclampsia [9]. For pregnancies with such symptoms, obstetric doctors are prone to choose cesarean section in order to reduce the risk for the delivery. Recently, some studies have indicated that labor analgesia can ameliorate the stress response and control blood pressure caused by the pain [10]. Effective labor analgesia can increase the blood supply of the uterus and placenta as well as reduce the occurrence of fetal distress in uterus. However, the advantage or disadvantage of epidural labor analgesia for maternal hypertensive disorder patients based on a large cohort investigation is still unclear. Here, we retrospectively analyzed 232 patients who diagnosed as maternal hypertensive disorder (including 28 cases of severe preeclampsia) in Beijing Obstetrics and Gynecology Hospital since 2015 and evaluated the therapeutic outcome of epidural labor analgesia.

2. Material and methods

2.1. Patients

We collected 232 patients who diagnosed as maternal hypertensive disorder (including 28 cases of severe preeclampsia) in our hospital since 2015. The patients are ranging from 20 to 35 years old who are pregnant for the first time, single embryo, and the gestational weeks are between 36 and 41 weeks. 126 patients were given continuous epidural labor analgesia, including 28 cases of severe preeclampsia; the other 106 patients were untreated as controls.

The diagnostic criteria for maternal hypertensive disorder complicating pregnancy are described as follows:

Gestational hypertension is defined as that hypertension is only detected for the first time during pregnancy, systolic blood pressure \( \geq 140 \) mmHg and/or diastolic blood pressure \( \geq 90 \) mmHg, urine protein is negative, the symptoms are disappeared and patients are back to normal within 12 weeks after delivery.

Severe preeclampsia is defined as: (1) blood pressure is persistently rising: systolic blood pressure \( \geq 160 \) mmHg and/or diastolic blood pressure \( \geq 110 \) mmHg; (2) persistent headache, visual disturbances or other central nervous system abnormalities; (3) persistent upper abdominal pain and liver subcapsular hematoma or symptoms of liver rupture; (4) liver enzyme abnormalities: increased serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels; (5) impaired renal function: urine protein \( \geq 2.0 \) g/24 h; oliguria (24 h urine output <400 ml, or hourly urine output <17 ml); or serum creatinine \( >109 \) /L; (6) hyperbilirubinemia with ascites, pleural or pericardial effusion; (7) blood abnormalities: sustained decreased platelet count (<100 \( \times 10^9 \)/L); microvascular hemolysis (anemia, jaundice, or increased blood lactate dehydrogenase (LDH) levels); (8) heart failure; (9) pulmonary edema; (10) fetal growth restriction or oligohydramnios, fetal death, early placenta abruption and so on.

Mild preeclampsia is defined as: systolic blood pressure \( \geq 140 \) mmHg and/or diastolic blood pressure \( \geq 90 \) mmHg after 20 weeks of gestation, and accompanied with any of the following symptoms: proteinuria \( \geq 0.3 \) g/24 h, or urine protein/creatinine \( \geq 0.3 \), or random urine protein positive (when proteinuria determination is not applicable); when proteinuria is negative but associated with any of the following organ or system dysfunction: such as heart, lung, liver, kidney, or blood system, digestive system, nervous system, or placenta – fetus abnormality.

2.2. Continuous epidural analgesia administration

Patients in the analgesia group requested analgesia after entering the first labor stage voluntarily, when fetal heart rate were normal, patients were informed and consent agreements were signed with the anesthesiologist, continuous epidural anesthesia was administered at lumbar 2–3 or 3–4 gap by puncture and cephelic epidural catheter 3 cm, 5 ml of 2 mg/ml ropivacaine was given first and patients were monitored for 5 min, followed with 10–15 ml mixture of 1 mg/ml ropivacaine and 0.5 mg/ml sufentanil, 30 min later, epidural analgesia pump was connected to the epidural catheter, the analgesia mixture in the pump was 1 mg/ml ropivacaine and 0.5 \( \mu \)g/ml sufentanil, the baseline infusion dose was 5 ml/h, the PCA was 5 ml every time and fixed for 15 min. Patients were encouraged to rest or move appropriately to facilitate fetal loss and labor process, when the analgesic effect diminished, patients could adjust epidural administration by controlling micro-pump. When the cervix was almost fully open, the analgesia administration was terminated.

For the control group: patients refused any continuous epidural labor analgesia during delivery progress.

We documented maternal patients' age, body weight and gestational weeks; the period for the first and second labor stage; the incidence of eclampsia, natural labor, cesarean section, forceps delivery, postpartum hemorrhage; recorded the usage of oxytocin and antihypertensive during the delivery progress; recorded the neonate weight, Apgar score and performed the umbilical cord blood gas analysis. Postpartum hemorrhage was defined as vaginal bleeding over 500 ml after delivery in 24 h.

3. Statistics

Data was shown as mean ± SEM and analyzed using unpaired t-test. For categorical data like adverse events, Chi-square test was applied. In this study, \( P < 0.05 \) was accepted to be statistically significant.

4. Results

We had compared patients' age, body weight, gestational weeks between analgesia and control group, but didn't detect any difference (Fig. 1), which indicated that our study was unbiased.

4.1. No difference was detected for the period of first and second labor stage between analgesia and control group

We had compared the periods for the first and second labor stage between control and analgesia group respectively, and we noticed that both first and second labor stage were slightly prolonged in analgesia group, but there was no significant difference detected (Fig. 2).

4.2. Continuous epidural analgesia treated maternal hypertensive disorder patients required more oxytocin but much less antihypertensive treatment

21 patients (19.8%) in control group were treated with oxytocin, while 46 patients (36.5%) in analgesia group required oxytocin treatment, in contrast, 86 patients (81.1%) in control group compared to 28 patients (22.2%) in analgesia group required antihypertensive treatment (Fig. 3), this result suggested that patients treated with continuous epidural analgesia usually need treatments to induce labor but much less measures to control blood pressure.
4.3. The natural delivery ratio is higher in continuous epidural analgesia treated maternal hypertensive disorder patients

We had analyzed all patients for their delivery methods and categorized them into 3 subgroups, natural delivery, forceps and cesarean section. We noticed that the ratio for natural delivery was higher in analgesia group compared to control group (Fig. 4). Furthermore, no difference was detected for postpartum hemorrhage (4.71% in control group compared to 4.76% in analgesia group) and eclampsia (no occurrence in both groups) between analgesia and control group.

4.4. Continuous epidural analgesia administration increases 1min Apgar score but does not have any other effect in neonates

We had carefully evaluated and compared the neonates’ body weight in both control and analgesia group, our result suggested that continuous epidural analgesia administration did not affect the neonates’ body weight. Furthermore, we analyzed 1 min, 5 min, 10 min Apgar score and umbilical cord blood gas analysis result. of note, 1 min Apgar score in analgesia group was significantly higher than control group, none of the other characters were significantly different between analgesia group and control group, thus, we conclude that continuous epidural analgesia administration can improve neonates condition immediately after delivery but has no further effect in maternal hypertensive disorder patients (Fig. 5).

5. Discussion

The major pathological features for maternal hypertensive disorder are systemic small blood vessel spasm and decreasing organ perfusion [7]. During delivery progress, patients are usually anxious and painful, which induces catecholamine release and increases blood pressure, and may cause severe cardiovascular accidents or eclampsia in some cases. Therefore, the maternal hypertensive disorder patients have a higher risk when they take vaginal delivery. Currently, in our department, the obstetricians...
usually choose cesarean section to terminate such pregnancy as it is safer for patients and neonates according to our experience, however, cesarean section does not significantly improve neonates’ condition [8], and can cause some complication such as neonatal respiratory distress syndrome, neonatal transient tachypnea and allergic asthma [11]. Furthermore, cesarean section can induce much more postpartum hemorrhage and amniotic embolism than natural delivery, and incidences for uterine scar pregnancy, placenta previa or placental abruption are also higher for cesarean section patients when they are pregnant for next time [12].

Continuous epidural analgesia administration can block damage stimulation input and sympathetic output, therefore effectively reduce catecholamines, β-endorphin, adrenocorticotropic hormone (ACTH) and cortisol release, it can also reduce cardiac output and blood pressure which increased by pain, furthermore, it can decrease stress response and maternal oxygen consumption, epinephrine level in plasma and can the incidence of fetal acidosis [13]. For maternal hypertensive disorders in pregnancy, efficient analgesia can block the sympathetic, dilate blood vessels and help to control blood pressure, moreover, it can increase kidney and uterine blood flow and perfusion, and it can control blood pressure which induced by stress response [11]. Recently, many studies have reported that labor analgesia can reduce stress response in maternal hypertension disorders patients during vaginal childbirth induced by pain stimulation, especially in the first stage of labor, it can significant decrease catecholamines, endorphins, ACTH and cortisol release as well as improve uteroplacental blood flow, which might be relevant to NO and PGI elevation [14]; small doses of low concentration drugs can also avoid low blood pressure and protect placental switching function, thus improve blood flow between among fetal villus. Pregnancies with less maternal stress response during delivery process can maintain better physiological homeostasis and normal lung ventilation, thus to reduce oxygen consumption to avoid acidosis and facilitate fetal oxygen supply [15,16].

Many studies have proved that continuous epidural anesthesia during labor process is safe and beneficial for both mothers and neonates [10,11]. Some studies have focused on the placenta – fetal endocrine function, which they show that labor analgesia can reduce maternal cortisol level in peripheral blood, thereby reduce the stress response, while the cortisol concentration has not been affected in umbilical cord blood and amniotic fluid before and after
or even cesarean section [20], however, our results suggest that may result in prolonged active period, more oxytocin requirement. Some reports indicate that application of analgesia in latency stage should be introduced until cervix opening to 4–5 cm. Iccan College of Obstetrics and Gynecology (ACOG) in 2000 suggest introduce analgesia too early. Thus, the clinical guidelines of Amer-
tically considered to apply neuraxial analgesia during active stage when cervix opening to 3 cm, it is also concerned the first lab stage but can prolong the second labor stage, and increase oxytocin requirement [7]. Another study has shown that epidural labor analgesia can decrease uterine contractility but not the uterine contraction hormone, and have no adverse effects on the whole delivery process [19]. Sharma et al. have suggested that labor analgesia can increase oxytocin requirement, prolong the first and second labor stage, increase instrumental delivery ratio but efficiently reduce the ratio of cesarean section [8]. Regarding the timing of analgesia implementation, it is generally considered to apply neuraxial analgesia during active stage when cervix opening to 3 cm, it is also concerned the first lab stage will be prolonged and cesarean section risk will be increased if introduce analgesia too early. Thus, the clinical guidelines of American College of Obstetrics and Gynecology (ACOG) in 2000 suggest analgesia should be introduced until cervix opening to 4–5 cm. Some reports indicate that application of analgesia in latency stage may result in prolonged active period, more oxytocin requirement or even cesarean section [20], however, our results suggest that labor analgesia during early stage of labor can relieve pain, control blood pressure, increase uterine blood perfusion and improve fetal oxygen supply in maternal hypertensive disorder patients, even with preeclampsia.

Ropivacaine is a long-acting amide like local anesthetic which has very low heart and central nervous system toxicity. Ropiva-
caine can block sensory and motor nerve separately without affecting placental blood supply. Sufentanil is a strong analgesic with long term effect, which can enhance the effect and reduce the dosage of local anesthetics when used together. Thus, combination of ropivacaine and sufentanil can efficiently block sensory neuron with limited effect on motor neuron, which can reduce the impact on pregnant women compared to other anesthetics, however, some studies have reported that long labor analgesia can increase the dural of labor period and usage of oxytocin and reduce the natural delivery ratio [11,20]. This is consistent to our study, which we also find that the usage of oxytocin is significantly more often in analgesia group, indicating that uterine smooth muscle contraction is suppressed while pain relieved, which might be relevant to decline of prostaglandin in uterus upon analgesia treatment [9]. Once withdrawal the analgesia, the effect will gradually disappear and have less and less impact on the second stage of labor. According to conventional clinical requirement, it is important to actively take some measures during second stage of labor to prevent eclampsia for maternal hypertension patients when give vaginal childbirth, thus without prolonged second stage of labor and fetal distress, doctors usually will use forceps to facilitate delivery, this is the reason why forceps delivery ratio is relatively higher in both groups in our study.

Importantly, in our study, the use of antihypertensive drugs in control group is significantly more than analgesia group, suggesting the blood pressure in patients without continuous epidural analgesia increase significantly during delivery process, and obstetricians need to give additional antihypertensive drugs to control it, which further confirmed that continuous epidural analgesia is beneficial for maternal hypertensive patients.

**Fig. 5.** Quantification results of neonate body weight, blood pH, blood pCO2, blood pO2, BE, 1 min Apgar, 5 min Apgar, 10 min Apgar in both control and analgesia group. Note continuous epidural analgesia administration increases 1 min Apgar score but does not have any other effect in neonates. P values are indicated for each bar graph. P < 0.05 was accepted to be statistically significant (unpaired, two-sided t-test).
In the present study, we didn’t find any uterus hypertonic in our patients in both analgesia group and control group, however, Preston et al. have reported that uterus hypertonic may be a special complication of intrathecal injection of opioids, and there is no method to eliminate this effect so far [15], moreover, intrathecal injection of sufentanil can induce respiratory distress [21], so it is very important to avoid simple intrathecal administration of opioids.

We have noticed that the ratio of cesarean section in analgesia group is significantly less than control group (P < 0.05), one important reason is the disease-related symptoms getting worse during labor process in control group, which makes both doctors and patients lose their confidence to try vaginal delivery. There are 3 cases of forceps delivery in analgesia group and 7 cases in control group; the main reason is the significantly elevated blood pressure and fetal heart rate changes during second stage of labor which requires the termination of the whole labor process. Furthermore, we also realize that continuous epidural analgesia administration can reduce patient stress response to a certain extent, which also reduce the risk of eclampsia in the second stage of labor. Although oxytocin usage is higher in analgesia group, (P < 0.05), it does not affect the analgesic effect and the success ratio of vaginal delivery, and a proper dosage of oxytocin can avoid prolonged delivery time.

Taken together, we conclude that continuous epidural analgesia has no significant effect on the period for the first and second labor stage, but it indeed increases the demand for oxytocin usage and significantly decreases the requirement for antihypertensive treatment, moreover, our results suggest that labor analgesia can significantly increase natural delivery ratio compared to non-analgesia treated patients. Finally, our results indicate that labor analgesia can benefit 1 min Apgar score for neonates, but has no other effects on neonates’ body weight, umbilical cord blood gas parameters, as well as 5 min and 10 min Apgar score. Our conclusion is slightly different from some previous studies; we speculate that this is due to the difference of patients’ sample size and ethnics.

Finally, our results suggest that continuous epidural analgesia is a safe and efficient treatment for maternal hypertensive disorder patients during delivery process.

Conflict of interest

The authors declare that there is no conflict of interest associated with this manuscript.

Acknowledgements

This study was approved by Ethics Committee of Beijing Obstetrics and Gynecology Hospital, Capital Medical University and supported by Promotion program of appropriate scientific and technological projects, Beijing Municipal Health and Family Planning Commission (TG-2014-12).

References


