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Original Research Article

Effect of epidural pre-injection of low-dose chloroprocaine on analgesia during second parturition

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Abstract

Purpose: *To investigate the anesthetic effect of epidural pre-catheterization with low-concentration chloroprocaine during the second parturition.*
Methods: *180 second-trimester primiparas undergoing epidural analgesia in Maanshan Maternal and Child Health Care Hospital, Ma'anshan, China were randomly divided into 3 groups, viz, pre-catheterization with chloroprocaine (group A), routine chloroprocaine (group B), and routine ropivacaine (group C), with 60 patients per group. The time of onset of analgesia, visual analogue scale (VAS) scores, modified Bromage score (MBS) scores, neonatal 1- and 5-min Apgar scores, oxytocin use, number of cesarean sections, volume of postpartum hemorrhage, and incidence of anesthesia-related complications were compared among the three groups.*
Results: *Onset time of anesthesia was significantly shorter in women in groups A and B than in group C ($p < 0.05$). The VAS scores at 5 and 15 min after analgesia were lower in groups A and B than in group C ($p < 0.05$). There were no significant differences in VAS scores among the three groups from 30 min after analgesia to the end of the first stage of labor ($p > 0.05$). There were also no significant differences in MBS scores, neonatal Apgar scores, oxytocin use, number of cesarean sections, volume of postpartum hemorrhage, and incidence of adverse reactions among the three groups ($p > 0.05$).*
Conclusion: *Individualized mode of analgesia involving the administration of low-concentration chloroprocaine to primiparas using an epidural catheter has timely onset of analgesia, good efficacy, high safety, rapid metabolism, and minimal adverse reactions. Further studies involving multiple centers and long-term follow-up are necessary.*

Keywords: *Epidural prepositioning tube, Low-dose chloroprocaine, Multiparous women, Labor analgesia*

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INTRODUCTION

Since the liberalization of the two-child policy in China in 2015 and the release of the three-child policy in 2021, more and more families have joined the ranks of second and even third childbirths. With increases in the number of parturients, there has been an increasing number of clinical studies on delivery and analgesia methods. In the clinics, it has been found that many parturients enter the labor stage too quickly, without enough time for labor analgesia. Moreover, the cervix may be too dilated or even

fully dilated during the waiting process, resulting in poor clinical outcomes.

Intrathecal labor analgesia is currently the most widely used method for labor analgesia in clinical practice [1]. For instance, epidural analgesia is used in clinical practice due to its many advantages such as good efficacy, high degree of satisfaction experienced by parturient women, and precise analgesic effect [2,3]. The pain of waiting for the cervix to dilate during labor causes anxiety and stress in parturient women, leading to series of physiological effects such as increases in blood pressure and heart rate, which in severe cases, may result in dystocia and postpartum hemorrhage [4]. Therefore, it is important to identify how to quickly alleviate pain in parturient women, as well as the timing of medication and administration of labor analgesia, so as to give these women emotional relief.

The present study compared the analgesic onset time between epidural pre-catheterization based on the parturients' wishes and conventional intraoperative administration. Moreover, the efficacy of low-concentration chloroprocaine was compared with that of ropivacaine. The overall aim was to determine the effect of low-concentration chloroprocaine injection through epidural pre-catheterization on labor analgesia in parturient women.

METHODS

Subjects and ethical approval

A total of 180 subjects were selected from second-trimester women who received epidural labor analgesia in the Maanshan Maternal and Child Health Care Hospital, Ma'anshan, China from December 2022 to June 2023. This study was approved by the Ethical Committee of Maanshan Maternal and Child Health Care Hospital (approval no. PJ-2023-06) and conducted according to the guidelines of Declaration of Helsinki promulgated in 1964 as amended in 1996 [5].

Inclusion criteria

The pregnant women were aged 24 - 36 years, with a gestational age of 38 - 40 weeks. All the women had no contraindications to epidural anesthesia, no long-term use of analgesic drugs, no indications for cesarean section, and no other serious complications. All the women were taller than 150 cm, and each woman weighed less than 95 kg, with the fetus having normal physiological indicators after examination. The women were informed about the details and purpose of the study, and each subject voluntarily signed an informed consent form.

Groups

The women were randomly divided into a pre-catheterization chloroprocaine group (group A), a conventional chloroprocaine group (group B), and a conventional ropivacaine group (group C). There were 60 parturients in each group. There were no significant differences in age, gestational age, body weight, and other aspects among the three groups of multiparous women ($p > 0.05$).

Administration of analgesia

Group A

When the cervical canal disappeared and regular uterine contractions occurred, epidural catheters were put in place. When the patient voluntarily requested analgesia during labor, epidural analgesia comprising 0.8 % chloroprocaine and sufentanil (0.5 μg/mL) was administered. After regular uterine contractions when the cervix was close to disappearing, blood pressure, heart rate, fetal heart rate, and intensity of uterine contraction in the parturient were measured. The parturients were instructed to lie on their left sides to enable epidural puncture at the L2-3 space. After successful insertion, a tube was placed on the head side and each of the parturients was moved to a relaxed position. Once the parturient felt pain and requested analgesia without any obstetric emergency surgery indications, upper limb venous access was established for the delivery of the baby. The drugs were initially given as test dose consisting of 3 mL of 1.5 % lidocaine and adrenaline (1:200,000). This was injected in-between contractions and monitored for 45-60 sec to see if the heart rate increased. After observing for 5 min without finding any signs of sub-arachnoid block or local anesthetic intoxication, sufentanil (0.5 μg/mL) plus 0.8 % chloroprocaine were administered.

Group B

When the cervix was dilated to 2 - 3 cm, epidural analgesia was administered using 0.8 % chloroprocaine combined with 0.5 μg/mL sufentanil.

Group C

When the cervix was dilated to 2 - 3 cm, epidural analgesia consisting of 0.067 % ropivacaine + 0.5 μg/mL sufentanil was administered.

Table 1: Comparison of basic information on the three groups of pregnant women (mean ± SD, n = 60)

Group	Age (years)	Weight (kg)	Gestational age (weeks)	BMI (kg/m^2)
A	27.20±2.51	69.11±6.98	39.42±0.58	25.32±2.16
B	27.38±2.44	69.05±7.23	39.13±0.46	25.71±2.70
C	27.56±2.73	69.53±7.08	39.28±0.51	25.38±2.66

In groups B and C, when the first stage of labor approached the active phase (i.e., cervix opening to 2 - 3 cm), epidural puncture was performed at the L2-3 space, and a tube was placed on the head side to a distance of 3 - 4 cm. The drugs were given initially as test doses consisting of 3 mL of 1.5 % lidocaine and adrenaline at a ratio of 1:200,000. This was injected in-between contractions, and the parturient was monitored for 45 - 60 sec to see if the heart rate increased. After observing for 5 min and finding no signs of subarachnoid block or local anesthetic intoxication, a PCA pump was connected to the epidural catheter for epidural self-controlled labor analgesia. In group B, the parturient was given sufentanil (0.5 µg/mL) plus 0.8 % chloroprocaine, while in group C, each parturient received sufentanil (0.5 µg/mL) and 0.067 % ropivacaine. The first dose given in each group was 10 mL at a basic injection rate of 7 mL/h. The patient-controlled analgesia dose rate was 5 mL at a time, with a lockout time of 30 min until delivery was complete.

Evaluation of parameters/indices

Onset time of anesthesia

The onset time of anesthesia was recorded in the three groups of multiparous women administered the different analgesic drugs.

Severity of pain

The severity of pain was scored using the visual analog scale (VAS) at 5, 15, and 30 min after administration of anesthetic drug, and at the end of the first stage of labor. The severity of pain was scored on a scale of 0 to 10, with higher scores indicating more severe pain.

Modified Bromage score

The modified Bromage score (MBS) was used to evaluate the limb activity of the multiparous women, with scores ranging from 1 to 4. The higher the score, the lower the activity level.

Apgar scores of newborns

The Apgar scores of newborns were recorded in the three groups at 1 min and 5 min after delivery. The Apgar score, which ranges from 0 to 10, evaluates five criteria: heart rate, respiratory effort, muscle tone, reflex irritability, and skin color. Each criterion is scored on a scale of 0 to 2, with higher scores indicating better health.

Clinical indicators of labor

The frequency of use of oxytocin, the number of cesarean sections, and the volume of postpartum hemorrhage (bleeding volume greater than 500 mL within 24 h) were recorded in the 3 groups.

Incidence of maternal anesthesia-related complications

Moreover, the incidence of maternal anesthesia-related complications such as nausea and vomiting, itching, hypotension, difficulty in passing urine, and numbness and weakness in the lower limbs after analgesia, were carefully recorded in each group.

Statistical analysis

The data obtained in this study were processed using SPSS 20.0 statistical analysis software. Independent sample t-test and Chi-square test were used for comparison of quantitative data among the 3 groups. Statistical significance was assumed at $p < 0.05$.

RESULTS

Onset time of anesthesia and VAS scores

The onset times of anesthesia in groups A and B were significantly shorter than that in group C ($p < 0.05$). The VAS scores at 5 and 15 min after analgesia in groups A and B were markedly lower than those in group C ($p < 0.05$). The difference in VAS scores between groups A and B at 5 min after analgesia was statistically significant ($p < 0.05$), but there was no significant difference in VAS scores between both groups at 10 min after analgesia ($p > 0.05$). There were no significant differences in VAS scores among the three groups from 30 min after analgesia to the end of the first stage of labor ($p > 0.05$).

Table 2: Comparison of onset time of anesthesia and VAS scores at different time points in the three groups (mean ± SD, n = 60)

Group	Anesthesia onset time (min)	VAS Score			
		5 min	*15 min*	*30 min*	*End of the first stage of labor*
A	5.11±0.96[a]	3.32±1.20*[#]	2.16±1.20*	1.15±0.72	1.08±0.29
B	5.20±1.12[a]	5.68±1.03*	2.33±1.11*	1.24±0.87	1.02±0.48
C	7.48±1.31	6.21±0.98	3.69±1.57	1.34±0.79	1.11±0.33

Note: *$P < 0.05$ vs group C; [#]$p < 0.05$ vs group B

Table 3: The modified Bromage score (MBS) scores of limb activities of the 3 groups at different time points (mean ± SD, n = 60)

Group	MBS scores			End of the first stage of labor
	5 min	*15 min*	*30 min*	
A	0.21±0.39	0.18±0.24	0.20±0.14	0.23±0.81
B	0.19±0.22	0.17±0.30	0.18±0.28	0.26±0.93
C	0.19±0.42	0.18±0.28	0.19±0.42	0.21±0.89

MBS scores for limb activity at three different time points

There were no significant differences in MBS scores on physical activity among the three groups of women at different time points (5, 15, and 30 min, and at the end of the first stage of labor) ($p > 0.05$).

Apgar scores of newborns

There were no significant differences in the Apgar scores of the three groups of newborns at 1 and 5 min ($p > 0.05$).

Clinical indicators of delivery

There were no significant differences in the amount of oxytocin used, number of cesarean sections, and volume of postpartum hemorrhage among the three groups of mothers ($p > 0.05$).

Incidence of adverse reactions

There were no significant differences in the incidence of adverse reactions such as nausea and vomiting, itching, hypotension, difficulty urinating, numbness in the lower limbs, and weakness among the three groups of women ($p > 0.05$).

DISCUSSION

The pain of giving birth is the highest level of pain which instils fear and anxiety in many women. In clinical practice, the combination of intense physical pain and nervousness is not conducive to the delivery of a parturient: it is a serious threat to the safety of the pregnant woman and newborn. With the advancement of medicine, it has been recognized that anesthetic drugs alleviate labor pain, a process known as "labor analgesia" or "painless childbirth."

Table 4: Comparison of Apgar scores among three groups of newborns (mean ± SD, n = 60)

Group	1 min Apgar score of newborns	5 min Apgar score of newborns
A	9.33±0.21	9.67±0.09
B	9.41±0.18	9.83±0.11
C	9.43±0.25	9.85±0.06

Table 5: Comparison of clinical indicators of delivery among three groups of mothers {n (%)}

Group	Use rate of oxytocin	Number of cesarean sections in transit	Volume of postpartum hemorrhage
A	25 (41.67)	4 (6.67)	1 (1.67)
B	27 (45.00)	5 (8.33)	0 (0.00)
C	24 (40.00)	7 (11.67)	1 (1.67)

Table 6: Comparison of incidence of adverse reactions in the three groups of mothers {n (%)}

Group	Nausea and vomiting	Pruritus	Hypotension	Dysuria	Lower limb numbness	Weakness	Incidence (%)
A	1 (1.67)	0 (0.00)	0 (0.00)	1 (1.67)	2 (3.33)	1 (1.67)	5 (8.33)
B	2 (3.33)	1 (1.67)	1 (1.67)	1 (1.67)	1 (1.67)	0 (0.00)	6 (10.00)
C	1 (1.67)	0 (0.00)	2 (3.33)	1 (1.67)	1 (1.67)	0 (0.00)	5 (8.33)

Labor analgesia helps alleviate the pain associated with delivery in pregnant women, it enhances natural delivery and increases the satisfaction of pregnant women with the delivery process. With the implementation of China's three-child policy and the resultant increase in the number of pregnant women, the promotion and implementation of labor analgesia have become particularly important.

Clinically, efforts have been made to find ideal analgesia methods. Ideal labor analgesia should have the following qualities: minimal impact on maternal and infant safety; non-interference with the progression of labor, minimal impact on motor nerves and low effect on uterine contractions; ease of administration, reliable efficacy, and rapid and effective pain relief; and it should ensure maternal consciousness and her active participation in the delivery process [6].

The most widely used local anesthetics for labor analgesia in clinical practice are lidocaine, bupivacaine, and ropivacaine. Lidocaine is often used in obstetric anesthesia as an experimental dose for epidural administration [7]. Bupivacaine and ropivacaine have many advantages such as significant efficacy and long-lasting analgesia, but studies have shown that when compared to chloroprocaine and ropivacaine, bupivacaine produces a higher degree of motor block [8]. When used in large doses, it may cause various adverse reactions in pregnant women and affect the efficacy of anesthesia [9]. It has been reported that ropivacaine separates sensory and motor blocks, with significantly lower cardiac toxicity and neurotoxicity, when compared to bupivacaine, resulting in fewer adverse reactions in pregnant women [10,11]. Ropivacaine produces better clinical effects than bupivacaine, and it is an ideal anesthetic drug for labor analgesia. However, in clinical practice, it has been found that, when compared to an ester local anesthetic such as chloroprocaine, ropivacaine has a longer onset time. Chloroprocaine results from the introduction of a -Cl group into the structure of procaine. This modifies the procaine structure to make it a fast-acting, metabolizable, lowly toxic, and highly effective anesthesia, especially for obstetric needs [12].

With improvements in medical standards, while clinical workers continue to carry out studies on labor analgesia drugs, they also pay attention to the importance of the timing of labor analgesia. The 2016 edition of the Consensus of Experts on Labor Analgesia in China [1] and related foreign guidelines [13] indicate that the timing of analgesia implementation should no longer be based on extent of traditional uterine dilation (greater than 3 cm), but should be primarily based on the needs of the parturient. In essence, when the parturient voluntarily requests analgesia, it should be implemented. In clinical practice, the placement of an epidural catheter is used to rapidly meet the needs of the patient and achieve a personalized mode of analgesia.

In this study, group A mothers received 0.8 % chloroprocaine anesthesia through in-dwelling epidural catheters based on individualized needs, while group B mothers received 0.8 % chloroprocaine in line with the conventional model until the cervix was opened to 2 - 3 cm. Group C mothers were given 0.8 % ropivacaine according to the conventional model until the cervix was opened to 2 - 3 cm. The results showed that the onset times of anesthesia in groups A and B mothers were shorter than that in group C, and the VAS scores of group A and B mothers were lower than those of group C mothers after 5 min and 15 min of analgesia. It has been reported that the use of labor analgesia of 1 % chloroprocaine in combination with sufentanil produced a faster onset time than 0.1 % ropivacaine [14]. A study showed that for women with breakthrough pain, chloroprocaine produced a faster onset of analgesia than ropivacaine, as well as better anesthetic effect [15]. The onset time of local anesthetic is inversely proportional to its dissociation constant pka (the pka values of ropivacaine and chloroprocaine are 8.1 and 9.1, respectively). The results of this study also demonstrated that chloroprocaine had a faster onset of action than ropivacaine, and it quickly alleviated maternal pain. However, the VAS score of group A mothers after 5 min of analgesia was significantly lower than that of group B mothers. This suggests that administering analgesia based on the needs of mothers quickly alleviates maternal pain. The possible reason for this is that group A mothers were mentally anxious during the latent period and were highly sensitive to pain. Not only did the anesthesia provide protective effect on mental health, it also shortened the time of pain tolerance, which made it easier to alleviate pain. However, group B mothers endured pain until the active phase, and it took a longer period to alleviate pain after anesthesia administration. Therefore, after 5 min of anesthesia administration, the VAS score of group A mothers was lower than that of group B mothers. However, due to the faster onset of action of chloroprocaine, there was no significant difference in VAS scores between groups A and B after 15 min of anesthesia administration. From 30 min after administration to the end of the first stage of labor, there were no significant

differences in pain VAS scores among the three groups. It has been shown that epidural pre-catheterization improves the effectiveness of labor analgesia without affecting mother and child, as well as labor process [16].

In another study, it was reported that women who underwent epidural pre-catheterization for labor analgesia had enhanced satisfaction with the analgesia during the entire labor process [17]. Moreover, a study showed that epidural pre-catheterization for labor analgesia in multiparous women effectively reduced the rate of cesarean section and alleviated maternal pain [18]. In this study, the MBS scores, neonatal Apgar scores, oxytocin use during delivery, number of cesarean sections, volume of postpartum hemorrhage, and incidence of adverse reaction in limb activity were compared among the three groups of pregnant women at different time points. There were no statistically significant differences among the 3 groups, with respect to these parameters. This suggests that the clinical application of chloroprocaine does not produce adverse impact on pregnant women and infants, indicating that it has high safety and low adverse reactions.

In an actual setting, it takes at least half an hour from the signing of the consent form to the onset of anesthesia. Most multiparous women have characteristics of short labor, rapid progress, and high rate of emergency delivery [19]. Multiparous women with rapid progress may submit consent forms for labor analgesia indicating choice of individualized analgesia mode. Once the request for analgesia is made, sufentanil (0.5 μg/mL) plus 0.8 % chloroprocaine are quickly administered through a pre-placed tube. This greatly saves time that would otherwise be spent on conversation and puncture, and it shortens the onset time of drugs, thereby making analgesia more precise and timelier. Thus, maternal pain is rapidly alleviated, thereby saving the physical strength of the parturient.

Limitations of this study

This study was conducted at a single center, which regional factors and hospital management practices may have influenced. The follow-up period mainly focused on the labor process and short-term postpartum outcomes, lacking long-term maternal and infant health data.

CONCLUSION

This study has demonstrated that, for multipartite women with rapid changes in labor and high rates of emergency delivery, individualized analgesia using low-concentration of chloroprocaine with faster onset of action may be achieved by placing an epidural catheter in advance. This method results in timely onset of analgesia, good analgesic effect, high safety, fast metabolism, minimal adverse reactions, and low impact on mothers and infants. It provides parturients with a good medical experience and high degree of satisfaction. Future studies involving multiple centers and long-term follow-up are necessary.

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was performed by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Hong Xiaotian designed the study, supervised the data collection, and analyzed the data. Wu Yuexiang, Zhou Yike and Min Xinxin interpreted the data and prepared the manuscript for publication. Bao Jingying supervised the data collection, analyzed the data and reviewed the draft of the manuscript.

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