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Original Research Article

Effect of intraspinal dexamethasone on intrapartum fever, and maternal and infant outcomes

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Abstract

Purpose: *To study the effect of intraspinal injection of dexamethasone (DXMS) on intrapartum fever and maternal and infant outcomes.*
Methods: *A total of 200 puerperal women who gave birth in The Fourth Hospital of Shi Jia Zhuang from May 2020 to September 2021 were randomly selected and randomly divided into two groups: routine group (control group) and study group, with 100 women in each group. The routine group received epidural block anesthesia. In addition to the treatment given to the routine group, mothers in the study group were injected with 5 mg of dexamethasone in the spinal canal through an epidural catheter. Pain, fever, as well as maternal and infant outcomes were evaluated.*
Results: *There were no statistically significant differences in the degree of pain between the two groups, before and 1 h after anesthesia ($p > 0.05$). However, visual analogue scale (VAS) scores at the end of the first and second stage of labor were significantly lower in the study group (1.76 ± 0.56 and 3.41 ± 0.39, respectively) than in the control group (4.73 ± 0.48 and 6.11 ± 0.63, respectively; $p < 0.05$). In the control group, 23 puerperal women (23 %) had body temperature ≥ 37.5 °C but < 38 °C, while 19 puerperal women (19 %) had body temperature ≥ 38 °C. There was no statistically significant difference in Apgar scores between the two groups at 1 min and 5 min after delivery ($p > 0.05$). In the control group, there were 9 (9 %) cases of headache, 5 (5 %) cases of prolonged labor, and 7 (7 %) cases of weak contractions, while the corresponding numbers in the study group were 2 (2 %), 0 (0 %) and 1 (1 %), respectively.*
Conclusion: *The use of intrathecal dexamethasone in women reduced maternal pain and likelihood of fever during labor, with no significant effect on the newborn.*

Keywords: *Intraspinal injection, Dexamethasone, Intrapartum fever, Maternal and infant outcomes*

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INTRODUCTION

Intrapartum fever is defined as maternal oral temperature ≥ 38 °C [1]. Due to improvements in standard of living and medical care in recent years, the demand for comfort during labor has increased. Thus, more and more women are opting for analgesia during labor so as to reduce labor-associated pain. Clinical evidence has demonstrated that the most clinically used and more definitive form of labor analgesia is spinal anesthesia which is safe, although it also results in problems of fever during labor [2]. Moreover, with increased use of neurasthenia in recent

decades, the prevalence has increased several folds to the current incidence of 6.8 % of intrapartum fever, and the figure in China is as high as over 20 % [3].

The causes of intrapartum fever can be roughly divided into two categories, namely infectious and non-infectious causes. Infectious causes comprise other systemic infections such as urinary tract infections and respiratory tract infections, the most common of which are intra-amniotic infections. In 2017, the SMFM and ACOG classified amniotic cavity infections into three categories: (a) simple fever in pregnant women, i.e., a single oral temperature ≥ 39 ^{o}C or persistent oral temperatures ranging from 38 to 38.9 ^{o}C; (b) suspected amniotic cavity infection defined as maternal fever in combination with maternal leukocytosis, cervical drainage and fetal tachycardia (meeting at least one of the three), and (c) confirmed amniotic cavity infection defined as positive amniotic fluid infection or pathology of the placenta confirming infection or inflammation of the placenta. Non-infectious conditions are often caused due to anesthesia (including epidural and combined spinal epidural) [4,5]. They are difficult to identify clinically due to the multiple pathogenesis of intrapartum fever, which in many cases is not clearly diagnosed until after birth, and the possible adverse consequences of intrapartum fever for the mother and the newborn which may lead to adverse health effects.

Dexamethasone (DXMS) [6], which was first synthesized in 1957, is listed in the WHO Model List of Essential Medicines as one of the essential medicines in the basic public health system [7]. It is an inexpensive synthetic corticosteroid with strong anti-inflammatory effects, and it inhibits the release of histamine and the production of other toxicants [8,9]. However, there is much debate both nationally and internationally about its benefits in pregnancy. For instance, in the USA, its pregnancy classification is C, which implies that it requires an assessment to show that the effectiveness of the drug outweighs the side effects before it can be administered. In contrast, DXMS is rated A in Australia, indicating that it is frequently used in pregnant women, with no evidence of fetal harm [10]. Based on this, the present study randomly selected a total of 200 puerperal women who gave birth in our hospital from May 2020 to September 2021 and divided them into the conventional method group (control) and intraspinal injection dexamethasone intervention group (study group). The effect of intraductal injection of dexamethasone on intrapartum fever and maternal and infant outcomes might provide a useful reference for subsequent clinical applications or provide data support for subsequent research.

METHODS

Patients

A total of 200 full-term singleton pregnant women aged 20 - 40 years (mean age = 27.58 ± 2.96 years) who gave birth at our hospital between May 2020 and September 2021, were randomly selected. The patients were divided into control group and study group using random number sorting method, with 100 puerperal women in each group. In addition to the use of epidural block anesthesia in both groups, patients in the routine group and the study group were treated with conventional and intraspinal injection of dexamethasone.

Inclusion and exclusion criteria

The included subjects were all singleton, full-term pregnant women in cephalic labor delivered in our hospital, puerperal women with pre-labor body temperature in the range of 36 to 37.5 ^{o}C , and those who voluntarily accepted to participate in the study and signed informed consent form, or had them signed on their behalf by their family members.

Puerperal women in the following categories were excluded from the study: subjects who had complications involving gestational hypertension, gestational diabetes mellitus, renal function damage and other diseases; women with history of drug abuse, and those who were in labor for < 2 h or > 8 h, or who were switched to cesarean section midway.

Treatments

The routine group received epidural block anesthesia. In this process, when the pregnant woman entered the active phase of labor with regular uterine contractions, and the cervix opened by 3-5 cm, a combination of spinal-epidural anesthesia and spinal anesthesia was routinely administered at L3-4. The spinal anesthesia needle was inserted into the subarachnoid space, and the puncture was considered successful if the cerebrospinal fluid fluxed smoothly after the needle was withdrawn. Then, an epidural catheter was placed at the site of the puncture at the backside of each subject.

Lidocaine (1 %, 5 mL) was injected into the epidural tube, and the signs of spinal anesthesia drug poisoning and local anesthesia drug

poisoning were monitored. Moreover, 90 mg of 0.75 % ropivacaine hydrochloride, 50 µg of sufentanil (0.4 µg/mL), and 100 mL of 0.9 % sodium chloride were injected through an epidural catheter. In addition to the treatment given to the routine group, mothers in the study group were injected with 5 mg of dexamethasone in the spinal canal through an epidural catheter. Both groups were given additional drugs as appropriate according to the degrees of cervical dilatation and weakening of analgesic effect. Epidural anesthesia was stopped when the fetus was delivered.

Evaluation of parameters/indices

Pain

The pain level of the patients was scored using the VAS at four time points before anesthesia, 1 h of anesthesia, at the end of the first stage of labor, and at the end of the second stage of labor. Comparison was made between the two groups. The VAS score was in the range of 0 - 10, and the score was proportional to the degree of pain: ≤ 3 points indicate mild pain, that is, pain that was mild but had no impact on daily life; 4-6 points indicate moderate pain, that was, obvious but tolerable pain, while a score of ≥ 7 indicated severe and unbearable pain.

Fever

An infrared cochlear thermometer was used to measure the temperature of the ear drum and tympanic membrane of the parturient during labor. If the temperature of the eardrum and tympanic membrane during labor was ≥ 38 ^{o}C, it was recorded that the parturient had fever during labor.

Maternal and infant outcomes

Apgar scores

Apgar scores were used to evaluate the health of newborns based on the five signs of skin color, heart rate, respiration, muscle tone, movement and reflex at two time points, i.e., 1 min and 5 min after delivery. The full score was 10 points. Neonates with scores < 7 were considered to have mild asphyxia, and a score of < 4 was considered indicative of severe asphyxia. The Apgar scoring method and standard involved: (a) evaluation of the oxygen exchange in blood in the lungs of newborns *via* skin color, with 2 points for pink body skin, 1 point for blue hands and feet, 1 point for cyan, and 0 point if the whole body was blue/pale.

Heart rate and rhythm

Moreover, heart rate and rhythm of the newborns were evaluated. Heart rates > 100 beats/min were scored 2 points, heart rates < 100 beats/min (weak heart rates) were scored 1 point, and inaudible heart sounds were scored 0 point. Neonatal center and lung maturity were evaluated through inhalation, with 2 points for regular breathing, 1 point for irregular breathing rhythm, and 0 point for no breathing. The central reflex and muscle strength of newborns were evaluated using muscle tension and exercise, with 2 points for normal muscle tone, 1 point for abnormal hypertension or hypotension, and 0 point for relaxed muscle tension. The ability of the neonate to respond to external stimuli was determined using reflex: severe crying due to leg swings or other stimuli was scored 2 points, soft sobbing or frowning was scored 1 point, while weak responses were scored 0 point. In addition, adverse reactions in the two groups, including headache, prolonged labor, and uterine atony, were recorded, and the total incidence was calculated and compared between the two groups.

Statistical analysis

Data analysis was done with SPSS 22.0 software. Measurement data are expressed as mean ± SD, and were compared between the two groups using independent sample *t*-test. Enumeration data are expressed as numbers and percentages [n (%)], and chi-square test was used for comparison between the two groups. Statistical significance was set at $p < 0.05$.

RESULTS

Profiles of participants

There were 100 puerperal women in the routine group aged 20 - 40 years (mean age = 27.23 ± 3.11 years), with gestational ages of 36-42 weeks (mean gestational age = 39.17±1.23 weeks), mean basal body temperature of 36.68 ± 0.32 ^{o}C, mean cervix dilation length of 1.73 ±0.35 cm, mean height of 164.17 ± 3.29 cm, and mean weight of 70.28 ± 5.47 kg. In the study group, there were 100 puerperal women aged 20 - 40 years (mean age = 39.39 ± 2.83 years), with gestational periods of 36 - 42 weeks (mean gestational period = 39.39 ± 1.27 weeks), mean basal body temperature of 36.61 ± 0.37 ^{o}C, mean cervical dilation length of 1.75 ± 0.35 cm, mean height of 164.65 ± 3.48 cm, and mean weight of 70.11 ± 5.37 kg.

Table 1: Comparison of general data of puerperal subjects in the two groups (mean ± SD, n = 100)

Group	Age (years)	Gestational weeks	Body temperature (°C)	Cervical dilation length (cm)	Height (cm)	Weight (kg)
Routine	27.23 ± 3.11	39.17 ± 1.23	36.68 ± 0.32	1.73 ± 0.35	164.17 ± 3.29	70.28 ± 5.47
Study	27.69 ± 2.83	39.39 ± 1.27	36.61 ± 0.37	1.75 ± 0.35	164.65 ± 3.48	70.11 ± 5.37
T	1.094	1.244	1.431	0.404	1.002	0.222
P-value	0.275	0.215	0.154	0.687	0.318	0.825

Key: Age range, 20 – 40 years; Gestational range: 36 – 42 weeks

Table 2: Comparison of VAS scores between the two groups of subjects at different times (mean ± SD, n = 100)

Group	Before anesthesia	Anesthesia for 1 h	End of first stage of labor	End of second stage of labor
Routine	8.68 ± 0.47	2.94 ± 0.42	4.73 ± 0.48	6.11 ± 0.63
Study	8.71 ± 0.35	2.81 ± 0.39	1.76 ± 0.56	3.41 ± 0.39
t	0.512	2.212	40.268	36.44
P-value	0.609	0.051	<0.001	<0.001

Table 3: Comparison of maternal fever between the two groups {n (%)}

Group	≥37.5 °C but <38 °C	≥38 °C
Routine	23 (23.00)	19 (19.00)
Study	5 (5.00)	2 (2.00)
χ^2	13.455	15.376
P-value	<0.001	<0.001

Table 4: Comparison of Apgar scores between two groups at different times (mean ± SD, n = 100)

Group	1 min after delivery	5 min after delivery
Routine	9.53 ± 0.33	9.88 ± 0.09
Study	9.48 ± 0.41	9.91 ± 0.08
t	0.95	1.661
P-value	0.343	0.098

There were no statistically significant differences in profiles between the two groups ($p > 0.05$). These data are presented in Table 1.

Pain

Pain condition was comparable in the two groups before and one hour after anesthesia ($p > 0.05$). However, the VAS score at the end of the first and second stages of labor were significantly lower in the study group (1.76 ± 0.56 and 3.41 ± 0.39, respectively) than in the conventional group (4.73 ± 0.48 and 6.11 ± 0.63, respectively; ($p < 0.05$). These results are presented in Table 2.

Fever

In the routine group, there were 23 (23 %) subjects with body temperatures ≥ 37.5 °C but < 38 °C, and 19 (19 %) subjects with body temperature ≥ 38 °C, while 5 subjects (5 %) in the study group had body temperatures ≥ 37.5 °C but < 38 °C, and 2 subjects (2 %) with body temperatures ≥ 38 °C. Moreover, the number of febrile puerperal women in the study group was less than that in the routine group ($p < 0.05$; Table 3).

Maternal and infant outcomes

Apgar scores

There were no statistically significant differences in Apgar scores between the two groups at 1 min and 5 min after birth ($p > 0.05$; Table 4).

Incidence of adverse reactions

In the routine group, there were 9 (9 %) cases of headache, 5 (5 %) cases of prolonged labor, and 7 (7 %) cases of weak contractions, while in the study group, there were 2 (2 %) cases of headache, 0 (0 %) case of prolonged labor, and 1 (1 %) case of weak contraction. The overall incidence of maternal adverse conditions in the study group (3 %) was significantly lower than that in the conventional group (21 %; $p < 0.05$), with no other adverse effect such as lower limb motor nerve block in either group. These results are shown in Table 5.

DISCUSSION

The maternal need to reduce pain during childbirth has increased with today's improved standards of living. The fear of labor pain is an important reason why women who do not have an indication for caesarean section choose to deliver by caesarean section.

Table 5: Comparison of the incidence of maternal adverse reactions between the two groups {n (%)}

Group	N	Headache	Prolonged labor	Uterine fatigue	Total incidence
Routine	100	9（9.00）	5（5.00）	7（7.00）	21（21.00）
Study	100	2（2.00）	0（0.00）	1（1.00）	3（3.00）
χ^2	-			15.341	
P-value	-			<0.001	

The use of labor analgesia is effective in reducing the frequency of socially-induced caesarean sections, while decreasing obstetric complications. Currently, the most effective and widely used postpartum analgesia is spinal block [11]. Spinal block not only effectively relieves severe labor pain, but also psychologically relieves anxiety in pregnant women, and mitigates other negative emotions caused by severe labor pain. These positive effects stabilize blood pressure and stroke volume in pregnant women, and relax pelvic and pubic muscles, thereby facilitating the delivery process.

However, the results obtained in the present study indicate that anesthesia during labor led to febrile symptoms, and that the incidence of fever was significantly higher in pregnant women who received intralesional analgesia than in those given non-vertebral analgesia [12]. Fever is caused by the effect of fever activator. The endogenous pyrogen (EP) produced by the fever activator is attached to the thermoregulatory center of the brain, resulting in the release of mediators which eventually lead to fever. There are many causes of fever, the most common being bacterial, viral and *Mycoplasma* infections [13]. However, the mechanism underlying fever symptoms during childbirth is not completely clear.

Fever during anesthesia-assisted labor may be associated with reduced respiratory rate and respiratory intensity, as well as airway heat dissipation following analgesia, relative to pregnant women who did not use analgesia [14]. Moreover, it may be associated with factors such as increased ambient temperature in the labor room, suppression of local anesthesia and interference with central thermoregulatory function by peripheral thermoreceptors [14]. Therefore, the present study determined the effect of intraspinal injection of dexamethasone on intrapartum fever and maternal and infant outcomes. The findings showed that the differences in pain condition between the two groups before and 1 h after anesthesia were not statistically significant. However, VAS at the end of the first and second stage of labor were significantly lower in the study group than in the conventional group. In the routine group, there were 23 (23 %) subjects with body temperature ≥ 37.5 ^{o}C but < 38 ^{o}C, and 19 (19 %) subjects with body temperature ≥ 38 ^{o}C, while 5 (5 %) subjects in the study group had body temperature ≥ 37.5 ^{o}C but < 38 ^{o}C, and 2 (2 %) subjects had body temperature ≥ 38 ^{o}C. At present, the most popular medical view is that the administration of anesthesia to the pregnant women in labor negatively affects vascular regulation and interferes with their body temperature control center, thereby leading to increases in body temperature.

Dexamethasone is a synthetic adrenal hormone with good analgesic, anti-inflammatory and anti-allergic properties [15]. Based on the results of this study, it can be concluded that intraspinal injection of dexamethasone may be an effective strategy during labor. On the one hand, it is reasonable to suggest that intraspinal injection of dexamethasone might prolong maternal peripheral nerve block, stabilize the structure of maternal cell membranes, and increase the pain threshold of peripheral nerves, thereby reducing pain and possibility of fever during labor. Moreover, intraspinal injection of dexamethasone may reduce the serum levels of pain-causing substances and interleukin-6, thereby mitigating maternal fever and pain during childbirth.

The effects of fever on the mother and baby during labor are manifested mainly in increased amounts of acidic metabolites in the baby due to accelerated metabolism; these metabolites tend to cause disorders in acid-base and electrolyte homeostasis in body fluids. Secondly, the accumulation and proliferation of acids in the intraluminal environment also increase the temperature of the uterus, and may even cause fetal death in severe cases, leading to adverse birth outcomes and increasing the number of caesarean sections [16].

The results of this study show that there were no statistically significant differences in Apgar scores between the two groups at 1 min and 5 min after birth. Furthermore, the overall incidence of maternal adverse conditions in the study group (3 %) was significantly lower than that in the conventional group (21 %). However, there was no serious adverse effect such as lower limb

motor nerve block in either group. This demonstrates the high safety profile associated with the use of intralesional dexamethasone in women, as evidenced by the lack of significant negative effects on the newborns, and the reduction in maternal complications which improved maternal and infant outcomes. This is because dexamethasone prevents or suppresses cell-mediated immune responses, delays allergic reactions, and reduces immune responses by decreasing the number of T lymphocytes, monocytes, and eosinophils, thereby minimizing the likelihood of maternal complications. In addition, the concentration of the drug used in this study was in line with the concentration range recommended by the consensus of experts in obstetric analgesia [17]. Furthermore, there was no motor nerve block in both groups, indicating good anesthesia, which is also consistent with the findings in a previous study [18].

Limitations of this study

There are several limitations in this study. First, the observed indices were limited to assess the reliable outcomes. Second, there is a limitation in generalizing to other population due to the results on the small number of participants. Finally, the intervention time might not be enough. Thus, further studies are suggested to secure a larger population of subjects.

CONCLUSION

The use of intraspinal dexamethasone in women might be a viable approach to reduce maternal pain and lower the possibility of fever during labor, drive down maternal complications, and improve maternal and infant outcomes. It has no significant impact on the newborn. Therefore, the use of intraspinal dexamethasone has benefits, but further clinical trials are required prior to application in practice.

DECLARATIONS

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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

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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