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Original Research

Effect of Ropivacaine Combined with Sufentanil on Hemodynamics and the Expression of Serum TNF-α and IL-6 in Parturients Undergoing Cesarean Section

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Abstract

Background: This study aims to investigate the effect of ropivacaine combined with sufentanil on hemodynamics and expression levels of serum tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) in parturients undergoing cesarean section. **Methods**: The clinical data of 135 parturients undergoing cesarean section were retrospectively collected. After anesthesia, 135 parturients were divided into observation group (68 cases) and control group (67 cases). The observation group was anesthetized with ropivacaine combined with sufentanil before operation, while the control group was anesthetized with ropivacaine. Anesthesia related indexes, hemodynamics at different times and arterial blood gas analysis indexes of the two groups were observed and recorded. The peripheral venous blood of the two groups was taken 1 day before delivery, 12 hours after delivery and 24 hours after delivery to detect expression levels of TNF-α and IL-6. The Apgar scores of the two groups of newborns were recorded at 1 and 5 minutes after delivery, respectively. **Results**: Compared with the control group, the observation group had a shorter time to reach the maximum block plane, a longer time to maintain analgesia, and a lower visual analog scale (VAS) score at 6 h postpartum ($p < 0.05$). Moreover, the mean arterial pressure (MAP) and heart rate (HR) during skin resection (T_1) in the observation group were higher ($p < 0.05$), and the cardiac output (CO), stroke volume (SV) and systemic circulation resistance (SVR) during T_1 and end of surgery (T_2) in the observation group were higher ($p < 0.05$). $PaCO_2$ was increased and PaO_2 in the control group at T_1 and T_2 was decreased after anesthesia ($p < 0.05$). Compared with 1 day before delivery, the serum levels of TNF-α and IL-6 increased at 12 and 24 hours after delivery. Compared with the control group, the serum levels of TNF-α and IL-6 in the observation group were lower at 12 and 24 hours after delivery ($p < 0.05$). **Conclusions**: The anesthetic effect of ropivacaine combined with sufentanil before cesarean section is better, which can effectively stabilize the mean arterial pressure, heart rate and other hemodynamic indicators of the puerpera, inhibit the inflammation in the puerpera, and have no adverse effects on the newborn.

Keywords: ropivacaine; sufentanil; cesarean section; hemodynamics; inflammatory reaction; tumor necrosis factor-α; interleukin-6; anesthesia

1. Introduction

Cesarean section provides an effective solution for dystocia and serious obstetric complications. Women during pregnancy have different anatomy and higher sensitivity to anesthetics. Reasonable anesthesia method is a key factor to ensure successful completion of cesarean section as well as good maternal and infant outcomes [1]. Clinical operation of cesarean section may cause abnormal stimulation of the sympathetic nerves of pregnancy body, rapid increase in the levels of norepinephrine and blood glucose, leading to higher heart beat and more violent contraction of the systemic blood vessels, and various complications. Moreover, cesarean section affects the uterine contraction, incision pain and postpartum recovery of the women [2]. At the same time, surgical wounds can stimulate the body to release tumor necrosis factor-α (TNF-α) [3], interleukin-6 (IL-6) [4] and other cellular inflammatory factors, which further aggravates postoperative pain of parturients [5]. Therefore, choosing a safe and reliable anesthesia method with rapid onset can ensure good maternal and infant outcomes after cesarean section. Ropivacaine, as long-acting amide local anesthetic, has a rapid anesthesia onset and fewer adverse reactions in the application process. However, when it is used alone, parturients often have a relatively strong stress response, which is unconducive to maternal and infant outcomes. Sufentanil is a class of opioids with strong analgesic activity, which can stabilize cardiovascular status while exerting anesthetic effect. Local anesthetics combined with opioids can improve the anesthetic effect, reduce the applied drug dose and stabilize the body hemodynamics [6]. The anesthetic effect of ropivacaine combined with sufentanil before cesarean section remains unclear, and its effect on maternal hemodynamics and inflammatory response needs to be further verified. Hence, this study investigates the effect of ropivacaine combined with sufentanil before cesarean section.

2. Data and Methods

2.1 Clinical Data

The clinical data of 135 women who received cesarean section in our hospital from March 2021 to June 2022 were retrospectively collected (the case screening process is shown in Fig. 1), and all of them were single pregnancy. Inclusion criteria: ① Full-term pregnancies; ② No contraindications to intravertebral anesthesia. Exclusion criteria: ① Complicated with severe gestational hypertension and diabetes; ② Twin or multiple pregnancies; ③ Allergy to anesthetic drugs; ④ Complicated with mental diseases. Through anesthesia, 135 parturients were divided into observation group and control group. In the observation group, there were 68 patients (41 cases of primiparum and 27 cases of multiparum) aged 21~36 (28.64 $\pm$ 3.45) years old, with body weight of (64.78 $\pm$ 3.16) kg, gestational age of (39.16 $\pm$ 1.07) weeks. There were respectively 45 cases and 23 cases of grade I and grade II in accordance with classification by American Society of Anesthesiologists (ASA). In the control group, there were 67 patients (43 cases of primiparum and 24 cases of multiparum) aged 22~37 (28.07 $\pm$ 3.62) years old, with body weight of (65.09 $\pm$ 3.28) kg, gestational age of (39.48 $\pm$ 1.12) weeks. There were respectively 45 cases and 22 cases of grade I and grade II in accordance with ASA classification. There were no significant differences between two groups in age (t = 0.937, p = 0.351), body weight (t = 0.559, p = 0.577), gestational age (t = 1.698, p = 0.092), primiparum or not (χ^2 = 0.217, p = 0.642) and ASA classification (χ^2 = 0.015, p = 0.903). This study was approved by the Ethics Committee of our hospital.

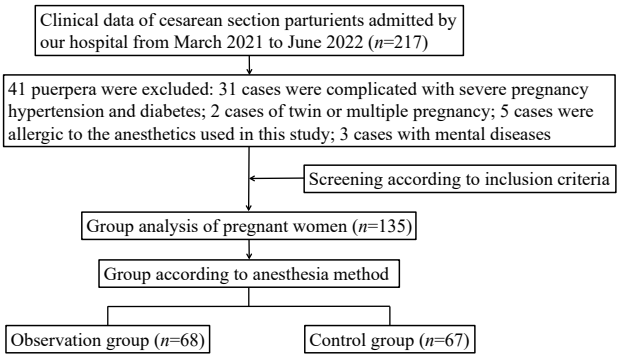

Fig. 1. Case screening flow chart.

2.2 Anesthesia Methods before Cesarean Section

The two groups were given elective cesarean section, with all examinations completed before the surgery. The parturients were instructed to abstain from drinking and fasting, taking the left lateral position. The control group was given ropivacaine for lumbar anesthesia, the puncture site was $L_{2\sim3}$ or $L_{3\sim4}$ intervertebral space. Then, 0.75% ropivacaine (Zhejiang Xianju Pharmaceutical Co., Ltd., National Drug Approval Number H20163208, specifications: 10 mL: 75 mg, Batch Number 20180516, Taizhou, Zhejiang, China) was injected obliquely upward with the puncture needle into the subarachnoid space at the rate of 0.2 mL/s at the dosage of 1–2 mL. The observation group was given ropivacaine combined with sufentanil for lumbar anesthesia. The puncture method was consistent with the control group. 5 μg of 0.75% ropivacaine (1~2 mL) + sufentanil (Jiangsu Enhua Pharmaceutical Co., LTD., National Drug Approval Number H20203653, specifications: 10 mL: 50 μg, Batch Number 20190125, Xuzhou, Jiangsu, China) were injected into the subarachnoid space at the rate of 0.2 mL/s.

2.3 Observation of Anesthesia Effect

① The time for anesthesia to reach the highest block level and analgesic maintenance time were recorded in both groups. Visual analog scale (VAS) was used to evaluate the degree of pain in parturients at the 6th hour after delivery. ② The mean arterial pressure (MAP), heart rate (HR), cardiac output (CO), stroke volume (SV) and systemic circulation resistance (SVR) of the two groups were recorded before anesthesia (T_0), during skin resection (T_1) and end of surgery (T_2). ③ The arterial partial pressure of carbon dioxide ($PaCO_2$) and arterial partial pressure of oxygen (PaO_2) were recorded before anesthesia (T_0), during skin resection (T_1) and end of surgery (T_2). ④ 3 mL of venous blood was collected from patients 1 d before delivery, 12 hours after delivery and 24 hours after delivery, respectively, and then serum TNF-α and IL-6 were detected by enzyme-linked immunosorbent assay (ELISA). All procedures were carried out according to the kit instructions. ⑤ Apgar score was used to evaluate neonates at 1 and 5 minutes after delivery.

2.4 Statistical Methods

SPSS 22.0 software (IBM Corp., Armonk, NY, USA) was used for statistical processing. The measurement data were expressed as $\bar{x} \pm s$. Two-factor repeated measurement ANOVA was used for comparison at multiple time points between the two groups. The HF coefficient method was used for sphericity correction of data. *LSD-t* test was used for fine comparison between groups. The count data were expressed as %, and comparison between the two groups was conducted by χ^2 test or Fisher exact probability method. $p < 0.05$ indicates statistically significant difference.

3. Results

3.1 Time for Anesthesia to Reach the Highest Block Level, Analgesic Maintenance Time and VAS Score at the 6th Hour after Delivery of the Two Group

Table 1 shows the time for anesthesia to reach the highest block level, analgesic maintenance time and the

Table 1. Time for anesthesia to reach the highest block level, analgesic maintenance time and VAS score at the 6th hour after delivery of the two groups ($\bar{x} \pm s$).

Group	Time to reach the maximum block plane (min)	Time to maintain analgesia (h)	VAS score at 6 h postpartum (score)
Observation group	9.79 ± 2.15	6.48 ± 1.74	4.06 ± 1.27
Control group	13.26 ± 3.04	5.24 ± 1.61	4.75 ± 1.32
t	7.666	4.296	3.095
p	0.000	0.000	0.002

VAS, visual analog scale.

Table 2. MAP, HR, CO, SV and SVR of the two groups at different time ($\bar{x} \pm s$).

Group	MAP (mmHg)	HR (times/min)	CO (L/min)	SV (mL/times)	SVR (dyne/(s·cm^{-5}))
Observation group					
T_0	92.78 ± 7.32	76.34 ± 11.23	6.20 ± 0.41	76.46 ± 3.85	1235.84 ± 121.37
T_1	89.65 ± 6.94	75.07 ± 10.48	5.53 ± 0.58	71.32 ± 4.08	1092.63 ± 112.19
T_2	93.83 ± 7.75	77.92 ± 9.53	4.87 ± 0.35	63.59 ± 5.16	1018.53 ± 128.46
Control group					
T_0	93.14 ± 6.85	75.86 ± 10.64	6.16 ± 0.54	75.48 ± 4.23	1249.36 ± 131.07
T_1	81.47 ± 8.30	66.58 ± 8.47	5.13 ± 0.47	67.31 ± 4.64	1002.54 ± 108.87
T_2	95.83 ± 9.26	79.15 ± 11.63	4.52 ± 0.49	59.27 ± 3.95	943.48 ± 105.62
F	$F_{interaction}$ = 16.662, F_{time} = 6.297, $F_{between\ groups}$ = 53.611	$F_{interaction}$ = 8.427, F_{time} = 6.249, $F_{between\ groups}$ = 19.445	$F_{interaction}$ = 5.586, F_{time} = 30.555, $F_{between\ groups}$ = 326.154	$F_{interaction}$ = 6.095, F_{time} = 51.707, $F_{between\ groups}$ = 379.261	$F_{interaction}$ = 7.552, F_{time} = 18.464, $F_{between\ groups}$ = 178.143
p	$p_{interaction}$ = 0.001, p_{time} = 0.012, $p_{between\ groups}$ = 0.000	$p_{interaction}$ = 0.000, p_{time} = 0.013, $p_{between\ groups}$ = 0.000	$p_{interaction}$ = 0.004, p_{time} = 0.000, $p_{between\ groups}$ = 0.000	$p_{interaction}$ = 0.003, p_{time} = 0.000, $p_{between\ groups}$ = 0.000	$p_{interaction}$ = 0.001, p_{time} = 0.000, $p_{between\ groups}$ = 0.000

MAP, mean arterial pressure; HR, heart rate; CO, cardiac output; SV, stroke volume; SVR, systemic circulation resistance; F, analysis of variance.

VAS score at the 6th hour after delivery of the two groups. Compared with the control group, the observation group had a shorter time to reach the highest block level, longer analgesic maintenance time and lower VAS score at the 6th hour after delivery (all $p < 0.05$).

3.2 Comparison of MAP, HR, CO, SV and SVR Levels between the Two Groups at Different Time

Table 2 shows the MAP, HR, CO, SV and SVR levels of the two groups at different time. Compared with the control group, observation group had higher MAP and HR at T_1 (all $p < 0.05$), as well as higher cardiac output of CO, SV and SVR at T_1 and T_2 (all $p < 0.05$).

3.3 Comparison of $PaCO_2$ and PaO_2 Levels between the Two Groups at Different Time

Table 3 shows the $PaCO_2$ and PaO_2 levels of the two groups at different time. Compared with T_0 (control group), $PaCO_2$ level was increased while PaO_2 level was decreased at T_1 and T_2 ($p < 0.05$).

3.4 Comparison of Serum TNF-α and IL-6 Levels between the Two Groups at Different Time

Table 4 shows serum TNF-α and IL-6 levels between the two groups at different time. Compared with 1 d before delivery, serum TNF-α and IL-6 levels were increased in both groups at 12 and 24 hours after delivery. Compared with the control group, the serum TNF-α and IL-6 levels were lower in the observation group at 12 and 24 hours after delivery (all $p < 0.05$).

3.5 Comparison of Apgar Scores between the Two Groups at Different Time

The Apgar scores of neonates were (9.24 ± 0.36) and (9.63 ± 0.25) points in the observation group and (9.21 ± 0.32) and (9.55 ± 0.28) points in the control group at 1 min and 5 min after delivery, respectively. There was no statistically significant difference in Apgar score at different time (t = 0.511, 1.752, p = 0.610, 0.082).

4. Discussion

The cesarean section rate has been climbing in recent years [7,8]. Cesarean section means the fetus is taken out via abdominal incision without vaginal delivery, which is an important way to save the life of pregnant women and perinatal infants in obstetrics. Cesarean section as invasive midwifery practice can stimulate maternal abdominal organs, causing pain. The body released a large amount of catecholamines within 48 h after cesarean section, which could cause pain peaks, reduced secretion of oxytocin and decreased uterine contraction ability, resulting in affected

Table 3. $PaCO_2$ and PaO_2 levels of the two groups at different time (mmHg, $\bar{x} \pm s$).

Group	$PaCO_2$	PaO_2
Observation group		
T_0	50.21 ± 3.69	32.75 ± 2.51
T_1	48.87 ± 4.09	32.61 ± 3.08
T_2	49.28 ± 3.95	32.03 ± 2.78
Control group		
T_0	49.89 ± 3.72	32.68 ± 2.47
T_1	57.41 ± 4.82	28.82 ± 3.09
T_2	55.63 ± 3.08	28.36 ± 2.87
F	$F_{interaction}$ = 46.622, F_{time} = 154.903, $F_{between\ groups}$ = 23.060	$F_{interaction}$ = 19.091, F_{time} = 80.744, $F_{between\ groups}$ = 30.249
p	$p_{interaction}$ = 0.000, p_{time} = 0.000, $p_{between\ groups}$ = 0.000	$p_{interaction}$ = 0.000, p_{time} = 0.000, $p_{between\ groups}$ = 0.000

$PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; F, analysis of variance.

Table 4. Serum TNF-α and IL-6 levels in the two groups at different time ($\bar{x} \pm s$).

Time	TNF-α (pg/mL)	IL-6 (ng/mL)
Observation group		
1 d before delivery	1.65 ± 0.34	0.17 ± 0.04
The 12th hour after delivery	2.17 ± 0.48	0.26 ± 0.08
The 24th hour after delivery	2.76 ± 0.58	0.33 ± 0.12
Control group		
1 d before delivery	1.68 ± 0.37	0.18 ± 0.05
The 12th hour after delivery	3.13 ± 0.62	0.34 ± 0.10
The 24th hour after delivery	3.65 ± 0.84	0.41 ± 0.15
F	$F_{interaction}$ = 65.459, F_{time} = 235.818, $F_{between\ groups}$ = 379.876	$F_{interaction}$ = 14.252, F_{time} = 73.615, $F_{between\ groups}$ = 214.484
p	$p_{interaction}$ = 0.000, p_{time} = 0.000, $p_{between\ groups}$ = 0.000	$p_{interaction}$ = 0.000, p_{time} = 0.000, $p_{between\ groups}$ = 0.000

TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; F, analysis of variance.

maternal hemodynamics [9]. Appropriate anesthetics and anesthesia method can guarantee the smooth operation of cesarean section, and reasonable and effective anesthetic drugs can help reduce postpartum inflammatory reaction and stress reaction [10]. In cesarean section, anesthetic drugs enter the fetus through the placental barrier, producing certain effects on the fetus. Therefore, it is of great clinical significance to select appropriate anesthetics for cesarean section.

Ropivacaine, as long-acting amide local anesthetic, plays an anesthetic role in inhibiting the flow of sodium ions in nerve cells, blocking ion exchange and blocking nerve conduction. This drug is less toxic to the central nervous system and cardiovascular system of the parturients, which is commonly used for local anesthesia during cesarean section [11]. Compared with other anesthetic drugs, ropivacaine has higher sensitivity and longer anesthetic duration, but the blocking effect needs to be improved. Opioids are powerful analgesics. Sufentanil is an opioid receptor agonist with high lipophilic properties. Sufentanil acts on opioid receptors and binds to blood proteins via the blood-brain barrier, and it is eliminated quickly and has a short half-life after infusion. At the same time, it can directly reach the subarachnoid space through the lipid dura mater, exerting rapid anesthesia block effect, without causing respiratory depression or affecting postoperative recovery [12]. Clinical studies [13–15] have confirmed that local anesthetics combined with opioids can play a synergistic role in analgesia, reduce the dosage of anesthetic drugs, stabilize hemodynamics, and reduce the adverse reactions caused by anesthetic drugs. In this study, women who underwent cesarean section received anesthesia using ropivacaine combined with sufentanil before surgery. Compared with the control group, the time for anesthesia to reach the highest block level was shorter, the analgesic maintenance time was longer and the VAS score at the 6th hour after delivery was lower in the observation group. It suggests that ropivacaine combined with sufentanil can accelerate the onset time of anesthesia, extend the analgesia duration and reduce postoperative pain, showing better anesthetic effect than using ropivacaine alone.

Wang *et al.* [16] reported that spinal epidural anesthesia after combined use of ropivacaine and sufentanil has shorter onset time, shorter labor process, more obvious analgesic effect and lower incidence of adverse reactions than continuous epidural anesthesia. Miao *et al.* [17] found

that combined administration of epidural ropivacaine and sufentanil could relieve pain after cesarean section. However, the effect of ropivacaine combined with sufentanil on the hemodynamics of cesarean section parturients remains to be verified. The changes of hemodynamic indexes (MAP, HR, CO, SV, SVR, etc.) are the focus of monitoring in clinical anesthesia during gynecological surgery. The results of this study showed that the hemodynamic stability was better in the observation group than in the control group. The reason may be that anesthesia can be stopped quickly after withdrawal regardless of how long sufentanil is administered. Moreover, sufentanil has good hemodynamic stability to effectively guarantee myocardial oxygen supply. The results of this study also showed that the change of arterial blood gas indexes was less significant in the observation group than in the control group, suggesting that ropivacaine combined with sufentanil could better stabilize blood gas indexes.

TNF-α generated by activated macrophages participates in the systemic inflammatory response of the body, and its expression level increased rapidly after trauma [18]. Secreted by T cells and macrophages, IL-6 is a chemotactic medium for a variety of inflammatory cells, which can stimulate the body's immune response and reflect the degree of inflammation in the body [19]. TNF-α and IL-6 jointly participate in the systemic inflammatory response of the body, and their expression levels increased rapidly after trauma. Good analgesia can inhibit the secretion of inflammatory cytokines and reduce postoperative stress response. Ren *et al*. [20] found that stress response was closely related to complications after cesarean section. Stress response can cause metabolic and endocrine disorders, which is a risk factor for postpartum massive hemorrhage and infection [21,22]. Moreover, strong and persistent stress response may also induce postpartum anxiety, depression and other adverse emotions. The results of this study indicated that serum TNF-α and IL-6 levels were higher at 12 and 24 hours after delivery in both groups compared to 1d before delivery, but serum TNF-α and IL-6 levels were lower in the observation group than in the control group at 12 and 24 hours after delivery. It suggests that ropivacaine combined with sufentanil can better reduce postpartum stress response. For its reason, the combination of the two can prolong analgesia time, reduce postoperative pain, and thus reduce the secretion of TNF-α and IL-6. There was no significant difference in Apgar score between the two groups at 1 min and 5 min after delivery, indicating that ropivacaine combined with sufentanil anesthesia has no adverse effects on neonates.

5. Conclusions

To conclude, ropivacaine combined with sufentanil has a good anesthetic effect on cesarean section, which can effectively stabilize maternal hemodynamic indexes and induce body inflammatory response without causing any adverse effects on the fetus, demonstrating certain clinical application value.

Availability of Data and Materials

The datasets used during the present study are available from the corresponding author upon reasonable request.

Author Contributions

ML—Manuscript writing, Project development, Data Collection. DM—Designed the research, revised the paper, Data analysis. BL and JZ—Data collection. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. This retrospective study involving human participants was conducted in accordance with the ethical standards of the institutional research committee and the 1964 Helsinki Declaration and its later amendments. The protocol was approved by the Ethics Committee of The First Affiliated Hospital of Shaoyang University (approval number: SYFY2021008).

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Conflict of Interest

The authors declare no conflict of interest.

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