

COMPARISON OF ANALGESIC EFFECT OF ROPIVACAINE WITH ALFENTANIL AND SUFENTANIL IN LABOR

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ABSTRACT

Introduction: To compare the efficacy of ropivacaine with alfentanil and sufentanil in labor analgesia.

Materials and methods: 240 parturients nulliparous women who were requesting labor analgesia were enrolled in the double-blind study and randomly divided into two groups. Group alfentanil(A) received 15 μ g/ mL alfentanil with 0.075% ropivacaine, and group sufentanil(S) received 0.4 μ g/ml sufentanil with 0.075% ropivacaine. Pain relief, duration of analgesia, the onset of epidural analgesia, the time of first urination after delivery, duration of stages of labor, delivery outcome, blood loss, neonatal Apgar scores, umbilical artery blood gas analysis and side effects, such as fever, dizziness, nausea, vomiting, pruritus, urinary retention were recorded.

Results: Compared with the control group, The onset time of analgesia was shorter in group A(8.7 \pm 2.7 VS 13.4 \pm 2.6, P<0.05), and the pain score in the group A was significantly lower at 5 and 10 minutes after labor analgesia (P<0.05). There were no significant differences between the 2 groups in neonatal Apgar score and umbilical arterial blood pH.

Conclusion: Alfentanil and sufentanil have a similar analgesic effect in epidural labor analgesia. Alfentanil is associated with a faster onset of analgesia with no significant neonatal side effects.

Keywords: Alfentanil, sufentanil, ropivacaine, epidural, labor analgesia.

DOI: 10.19193/0393-6384_2022_5_468

Received July 15, 2022; Accepted July 20, 2022

Introduction

Labor pain is reported to be one of the most severe pains that have ever been evaluated⁽¹⁾. Epidural analgesia is regarded as one of the most effective methods for labor pain relief⁽²⁾. The combination of opioids with local anesthetics is commonly used for epidural labor analgesia⁽³⁾. The structure and pharmacological properties of alfentanil are similar to fentanyl, and Alfentanil has been successfully used for epidural labor analgesia⁽⁴⁾. Previous studies compared the analgesic effect of fentanyl and sufentanil in combination with a lower dose of anesthetics in labor⁽⁵⁾, while few studies compared the effects between alfentanil and sufentanil in

labor. Therefore, the present study was designed to compare the effects of alfentanil and sufentanil as adjuvants to local anesthetic for epidural labor analgesia.

Materials and methods

General information

The ethics committee of third affiliated Hospital of Guangzhou Medical University approved this study. A written informed consent was obtained from all patients. From June 2021 to January 2022, 240 participants were enrolled in this prospective, double-blind study. Inclusion criteria included aged 20-35 years, gestational age 37 weeks or above,

American Society of Anesthesiologists grade II, and following assessment, the patient was able to undergo vaginal delivery. Exclusion criteria were as follows: patients with severe cardiopulmonary diseases, cervical dilatation >3 cm, induced labor, contraindications to epidural analgesia, and allergy to opioids. Patient was randomly divided into the control group (group S, n=120) and the alfentanil group (group A, n=120) using a computer-generated random-number table.

Methods

After entering the delivery room, patients' vital signs, such as blood pressure, heart rate, and SpO₂, were monitored, and fetal heart rate was also monitored using a Doppler fetal heart monitor, and intravenous access was established. Epidural analgesia was carried out when cervical dilatation was about 3 cm. An epidural catheter was inserted 3-4 cm cephalad into the epidural space at the estimated level of L2-3 interspace while the patient was positioned in the left lateral decubitus position. The lidocaine (1.5%) with a dose of 45mg in 3.0 mL containing 5µg/mL epinephrine was injected epidurally to all patients as a test dose.

Group A received 10 mL 15 µg/mL alfentanil combined with 0.075% ropivacaine and meanwhile group S received 10 mL 0.4 µg/mL sufentanil combined with 0.075% ropivacaine as loading dose for epidural analgesia, and this mixed solution was infused continuously by a patient-controlled epidural analgesia pump. The parameters of the pump were set as follows: background dose of 4 mL/h, pulse dose of 6ml/h at interval of 45min, a bolus of 6 mL, and locked time of 15 minutes, maximum dose 28mL /h. The women were instructed to use the pump to inject an additional bolus to relieve pain. A rescue bolus of 6 mL (lockout 15 minutes) was administered by using an electronic analgesia pump when visual analog scale (VAS) score was >3 (0=no pain, 10=maximum pain). The analgesic solutions were prepared by nurses who were blind to this study, and investigators were blind to these solutions.

After epidural analgesia, pain score (measured by VAS), the onset of epidural analgesia, duration of analgesia, duration of labor stages, blood pressure (systolic, diastolic), HR, delivery outcome, time of first urination after delivery, blood loss were recorded. Umbilical arterial blood was collected for analysis and neonatal Apgar scores were assessed at 1 and 5 minutes. Onset of analgesia was defined as time from epidural administration to VAS, 3, and

duration of the first stage of labor was defined as time from epidural administration to 10 cm cervical dilatation. Side effects, such as fever, dizziness, nausea/vomiting, pruritus, urinary retention were also recorded and managed. Motor block was evaluated using a Bromage score (0=no motor loss, 1=unable to move hip, 2=unable to move hip and knee, 3 =unable to move hip, knee, and ankle).

Statistical analysis

Data were analyzed using SPSS software version 16. The data are expressed as the mean ± SD and normally distributed quantitative variables were analyzed using a t-test. Count data were analyzed using a χ^2 or Fisher's test. Non-normally distributed parameters were analyzed using the nonparametric Mann-Whitney U test. P<0.05 was considered significant.

Results

240 patients were initially enrolled in the study. 201 patients completed the study and 39 patients were excluded from the study that required cesarean

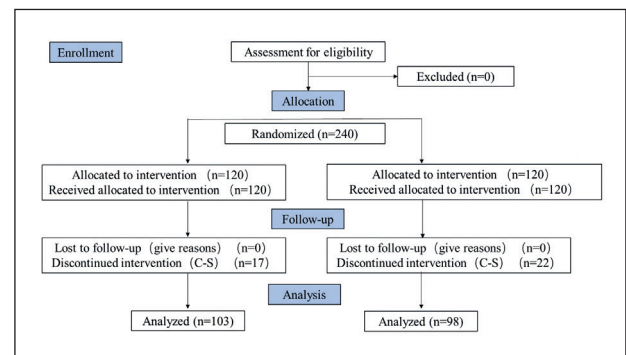


Figure 1: Flow diagram of study.

Notes: C-S, Cesarean section.

section (Figure 1).

There were no significant differences in age, body mass index (BMI), gestational weeks, delivery outcome, oxytocin use, estimated blood loss, duration of analgesia, or the duration of the stages of labor between the groups ($P>0.05$, Table 1). The VAS values of group A at 5 and 10 minutes were significantly lower than that of the group S ($P<0.05$). But there was no significant difference between the two groups after 30 minutes following epidural analgesia to the time period of 10 cm cervical dilatation. The analgesia began significantly sooner in the group A (8.7 ± 2.7) than group S (13.4 ± 2.6) ($P<0.05$). (Figure 2).

There were no significant differences in the

incidence of motor block (Bromage score >0), dizziness, nausea and vomiting between the two groups ($P>0.05$), but the incidence of Pruritus and Urinary retention in group A was significantly lower than that of group S ($P<0.05$). (Table 2)

There were no significant differences in neonate umbilical artery pH and Apgar between the two groups ($P>0.05$, Table 1), all the Apgar scores at the 1 and 5 minutes were >7, and umbilical artery pH was not <7.2 in both groups. However, the time of first urination after delivery in group A was shorter

Index	Group A (n=103)	Group S (n=98)	P
Motor block	0(0)	0(0)	1
Nausea and vomiting	3(2.9%)	5(5.1%)	0.49
Dizziness	2(1.9%)	3(2.4%)	0.677
Pruritus	6(5.8%)	10(10.2%)	0.303
Urinary retention	8(7.8%)	7(7.1%)	0.866

Table 2: Side effects of epidural analgesia. than group A ($P<0.05$).

Index	Group A	Group S	P
Age(years)	31.2±3.7	30.2±3.4	0.648
BMI(kg/m ²)	26.1±3.0	26.5±2.9	0.267
Gestational age (weeks)	38.9±1.1	38.7±1.5	0.674
Onset of analgesia(minutes)	8.7±2.7	13.4±2.6	0.000*
Duration of analgesia (hours)	5.3±3.7	5.2±3.7	0.593
Duration of the first stage (hours)	9.7±4.6	10.1±4.4	0.697
Duration of the second stage (hours)	1.2±0.9	1.2±1.0	0.567
Mode of delivery (vaginal/cesarean)	103/17	98/22	0.599
Blood loss(mL)	253.3±94.4	268.5±145.3	0.379
Oxytocin use(n%)	53	62	0.245
1-min Apgar score	9.9±0.4	9.8±0.8	0.139
5-min Apgar score	10.0±0.1	9.9±0.2	0.165
Umbilical artery pH	7.30±0.06	7.29±0.06	0.286
Time of first urination after delivery(h)	5.0±1.5	5.6±2.6	0.035*

Table 1: Data of patients.

Notes: Compared with the group A, * $P<0.05$. Data were presented as the mean ± standard deviations or numbers.

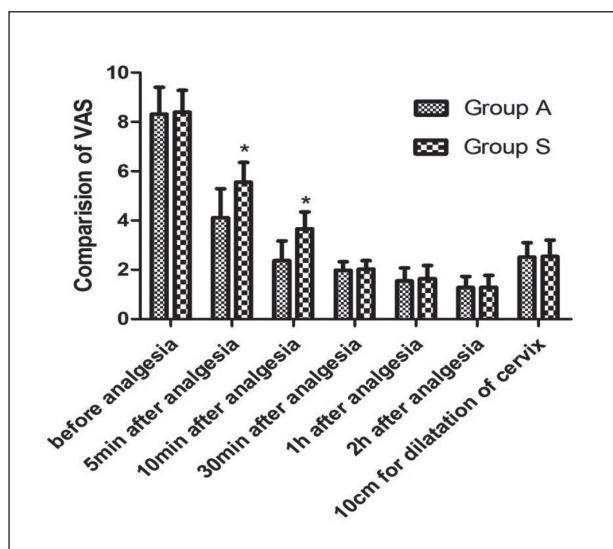


Figure 2: Comparison of pain visual analog scale (VAS) values at different time points.

Notes: Compared with the group A, * $P<0.05$.

Discussion

The results of this study showed that the onset time of analgesia was significantly lower for the alfentanil. This can be attributed to differences in physicochemical, pharmacokinetic and pharmacodynamic characteristics of both the drugs. Alfentanil is a structural analogue of fentanyl, and it has the most rapid analgesic onset and time to peak effect as well as the shortest distribution and elimination half-lives. Compared with sufentanil, alfentanil has lower lipid solubility so that it reaches a higher serum concentration more rapidly and has a smaller volume of distribution and total body clearance. Due to the shorter time of elimination half-lives, tissue accumulation is rare among alfentanil⁽⁶⁾.

This study compared the quality of analgesia and side-effects of continuous epidural infusion with 0.075% Ropivacaine in combination with either of 150µg/h of alfentanil or 4µg/h sufentanil. The early studies of continuous epidural infusion of alfentanil proved to be unsatisfactory for pain relief in labor⁽⁷⁾, but other studies found that alfentanil provided superior pain relief when comparing fentanyl⁽⁸⁾. There some studies reported that the analgesic potency ratio between sufentanil and fentanyl is 10:1^(6,9,10), and meanwhile the ratio between fentanyl and alfentanil is 10:1^(11,12), but it did not apply to epidural administration because of direct spinal effect mechanism. Geller et al⁽¹³⁾ suggested that the analgesic potency of epidural sufentanil compared with fentanyl was about 4.2, and Capogna et al⁽¹⁴⁾ showed it was about 5.9. Simultaneously, the potency of alfentanil was reported varies widely in the literature. White et al⁽¹⁵⁾ found a dose ratio varying from 1:6 to 1:40 between fentanyl and alfentanil. Chrubasik et al⁽¹⁶⁾ confirmed that the dose ratio of epidural fentanyl relative to alfentanil was about 10:1, If this figure is correct, the does we used in this study is equivalent. The results showed that the pian score in the alfentanil group was

significantly lower than the sufentanil group at 5 and 10 minutes, but there was no significant difference between the two groups after 30 minutes, 1 hour, 2 hours following epidural analgesia to the time period of 10 cm cervical dilatation. Epidural alfentanil and sufentanil have a similar analgesic effect on labor, but more rapid analgesic onset.

The use of a combination of opioids and local anesthetic in epidural labor analgesia must consider the influence on neonates. Opioids could rapidly transfer across the placenta⁽¹⁷⁾. Neonates with parenteral opioid exposure may result in decreased Apgar scores, neonatal respiratory depression⁽¹⁸⁾. However, Wang et al⁽¹⁹⁾ found the common doses of fentanyl and sufentanil used with an epidural/spinal technique in labor analgesia were safe for neonates. Wen et al⁽²⁰⁾ indicated that ropivacaine combined with sufentanil in epidural labor analgesia had less adverse effects on mother and infant. A systemic review found that fetal oxygenation is not affected in the use of opioids in epidural labor analgesia⁽²¹⁾. A study pointed out that the shorter acting and rapidly metabolized opioid was less likely to cause neonatal depression⁽²²⁾. Alfentanil has a shorter elimination half-life than sufentanil; We demonstrated no difference in Apgar scores Apgar score and neonatal pH between the two groups.

In conclusion, this study shows that Alfentanil provided a comparable analgesic efficacy as sufentanil in epidural labor analgesia with no significant neonatal side effects, and alfentanil is associated with a faster onset of analgesia. The use of a combination of opioids and local anesthetic in a continuous infusion epidural during labor has been shown to decrease the dose of local anesthetic required resulting in decreased motor blockade.

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