Prospective Study

ED_{90} of Sufentanil in Epidural Initiation for Labor Analgesia in Latent Phase and Active Phase During the First Labor Stage

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Background: The standard solutions for epidural labor analgesia include both local anesthetics and opioids. The concept of the standard epidural use of local anesthetics in labor analgesia has shifted from high concentrations to high volumes with low concentrations. However, the optimal dosage of opioids needed to initiate and maintain epidural labor analgesia in different phases during the first labor stage has rarely been studied.

Objective: The present study aimed to determine the optimal sufentanil dose for epidural initiation in the latent and active phases during the first stage of labor.

Study Design: A prospective, double-blind, sequential dose-finding study.

Setting: A Class A tertiary obstetrics and gynecology hospital.

Methods: The study included 80 nulliparae with cervical dilatation of 2-4 cm and 5-6 cm, with 40 nulliparae in each group. A research dose of sufentanil combined with ropivacaine 13 mg in epidural initiation with a volume of 15 mL was administered to the puerperant. A 1-μg sufentanil dose and a 2.5-μg sufentanil dose were used for the first puerperant of each group. The dose of sufentanil for the subsequent puerperant was determined by the response of the previous puerperant according to the biased coin up-and-down design in each trial. The primary outcome was a visual analog scale score of ≤3 at 15, 30, and 45 minutes after epidural administration, including the given dose of sufentanil. According to the response of each puerperant, the 90% effective doses and their 95% confidence intervals were estimated by isotonic regression and bootstrapping according to the response of each puerperant.

Results: The 90% effective doses of sufentanil for puerperants were 1.91 μg (95% confidence intervals 1.82-2.35 μg) and 4.90 μg (95% confidence intervals 4.82-5.35 μg) in epidural initiation in the latent and active phases, respectively. The 90% effective doses were 62.5% (95% confidence intervals 50.8-64.0%) lower in the latent phase than that in the active phase during the first stage of labor.

Limitations: Both spontaneous labor and induced labor were included in this study, and the degree of pain in these 2 types of labor is different. Further, only nulliparae were recruited in the study.

Conclusions: Different sufentanil doses should be adopted in epidural initiation in different phases during the first stage of labor due to the large differences in the demand for sufentanil.

Key words: Sufentanil, 90% effective dose, epidural initiation, labor analgesia, active phase, latent phase, first labor stage

The work was attributed to: a. The International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; b. Shanghai Key Laboratory of Embryo Original Diseases, Shanghai, China; c. Shanghai Municipal Key Clinical Specialty, Shanghai, China

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The standard solutions for epidural labor analgesia consist of both local anesthetics and opioids. The concept of the standard epidural use of local anesthetics in labor analgesia has shifted from high concentrations (1-3) to high volumes with low concentrations (4,5). However, the optimal dosage of opioids needed to initiate and maintain epidural labor analgesia in different phases during the first labor stage has rarely been studied. Although a reduced sufentanil concentration of 0.3 $\mu g \cdot mL^{-1}$ was adopted in the latent phase during the first labor stage in some studies (6,7), the precise sufentanil dose or concentration in the epidural solution for the latent or active phases is still unknown.

We hypothesized that the requirements of sufentanil are different between the latent phase and the early active phase in both the initiation and maintenance of epidural labor analgesia. Furthermore, the study was designed to determine the optimal sufentanil dose required for epidural initiation in the latent and early active phases during the first stage of labor.

Methods

The prospective, double-blind, sequential dose-finding study described here was approved by the Institutional Review Board of the International Peace Maternity and Child Health Hospital (GKLW2017-131). The study was registered prior to the patient enrollment at http://www.chictr.org.cn (CTR1900021683; Principal investigator: Tao Xu, Date of registration: 5/3/2019). Written informed consent was obtained from all the study patients after recruitment.

Inclusion and Exclusion Criteria

A total of 91 nulliparae in the study aged 18-40 years, with a full-term (> 37-weeks' gestation) singleton pregnancy and vertex fetal presentation, American Society of Anesthesiologists II, normal fetal heart rate, cervical dilatation within 2-6 cm, visual analog scale scores ≥ 60 mm, and request for labor analgesia were recruited from November 2019 to February 2021 in the author's hospital. After providing signed informed consent, the participants were enrolled in the study and divided into 2 groups by the cervical dilatation: Group 1 with cervical dilatation of 2-4 cm and Group 2 with cervical dilatation of 5-6 cm. The exclusion criteria were severe cardiac or respiratory disease with American Society of Anesthesiologists > II, allergy or contradiction to local anesthetics and opioids, visual analog scale scores < 60 mm before analgesia, fetal heart rate abnormalities, multiple gestations, body mass index > 36 $kg \cdot m^{-2}$, previous intravenous or intramuscular analgesia with opioids, rapid cervical changes (cervical dilatation increases out of the range of each group in the first hour), and patient refusal.

Analgesia Procedures

Each participant signed informed consent before analgesia. Subsequently, each puerperant underwent a puncture using an 18-guage catheter on the left forearm to establish intravenous access. Then, 500 mL of lactated Ringer's solution was quickly administered (8 $mL \cdot kg^{-1} \cdot h^{-1}$) to prevent hypotension after analgesia. Routine monitoring included electrocardiography, noninvasive blood pressure, heart rate, pulse oximetry, uterine activity, and fetal heart rate by external tocodynamometry; these parameters were measured and recorded every 5 minutes. A midwife performed a cervical examination to confirm that the cervical dilatation met the requirements of the study and arranged the grouping before analgesia. Only the midwife and a research assistant knew the degree of cervical dilatations. All anesthesiologists and puerperants were blinded to the grouping. An epidural puncture was performed at L2-3 or L3-4 by a practiced anesthesiologist with over 10 years of working experience while the puerperant was in the right lateral decubitus position. A 17-guage Touhy needle was used for epidural puncture; a paramedian approach was applied. After confirming the entrance into the epidural space, an epidural catheter (Arrow FlexTip Plus Epidural Catheterization Set, Arrow International, Reading, PA, USA) was inserted into the epidural space with 5 cm advancing through the Tuohy needle. Then the catheter was fixed by a sterile dressing. After the puerperant changed to a supine position by a pillow under the right hip, a 3-mL research solution was administrated first to exclude subarachnoid catheterization. The left 12 mL research solution was injected 3

minutes later. A patient-controlled epidural analgesia pump (AM3300, ACE Medical Equipment Inc., Korea) was connected to the patient once the visual analog scale score was > 30 mm at 15, 30, or 45 minutes after epidural initiation. A patient-controlled epidural analgesia bolus was administered in failed analgesia cases; in cases that showed successful analgesia (visual analog scale scores ≤ 30 mm) within the first 45 minutes after the initiation of epidural anesthesia, the patient-controlled epidural analgesia pump was connected at 45 minutes, and the epidural bolus was not administrated. The patient-controlled epidural analgesia fluid consisted of ropivacaine 75 mg, sufentanil 30 μg, and normal saline with a total volume of 75 mL. An 8 $mL \cdot h^{-1}$ background infusion and a 5-mL patient-controlled epidural analgesia bolus dose with a 15-minute lockout interval were set as the parameters of the pump. All puerperants were instructed to press the patient-controlled analgesia button if their visual analog scale scores were > 30 mm. The pump wasn't stopped until delivery. The midwife performed the cervical examination again in the failed cases. The participants were excluded from the analysis if rapid cervical changes were detected.

A total of 1 mL of umbilical arterial blood was collected and assessed immediately after delivery.

Visual analog scale scores were used to evaluate pain, with 0 mm representing no pain and 100 mm representing the worst pain. Modified Bromage scores (0 = no impairment; 1 = unable to raise the extended leg, but able to move the knees and feet; 2 = unable to raise the extended leg as well as flex the knees, but able to move the foot; 3 = not able to flex the ankle, knees or feet) were used to assess motor block of the lower limb. The upper sensory level was tested by assessing the cold sensation in response to an alcohol cotton ball. Hypotension after analgesia with a systolic blood pressure < 80% of the baseline value was treated with intravenous ephedrine 6 mg. Maternal bradycardia with a heart rate < 50 bpm was treated with atropine 0.5 mg. If fetal bradycardia happened, i.e., fetal bradycardia with abrupt fetal heart rate < 90 bpm for at least 2 minutes and occurring within the first 30 minutes after analgesia (8), intrauterine resuscitation was performed. Intrauterine resuscitation includes posture change, rapid intravenous fluid administration, high-flow mask oxygen by midwives; intravenous atropine or ephedrine by anesthesiologists. If the resuscitation failed, an emergency cesarean section was performed by obstetricians.

Biased Coin Up-and-Down Design of the Study

In this study, 15 mL of epidural initiation fluid included ropivacaine 13 mg, and a research dose of sufentanil that was prepared in a 20-mL syringe by the research assistant previously mentioned, who was the only person who knew the exact sufentanil dose. All anesthesiologists and puerperants were blinded to the sufentanil dose. A sufentanil dose of 1 μg was used for the first puerperant in Group 1, while a dose of 2.5 μg was used for the first puerperant in Group 2. The sufentanil dose for the subsequent puerperant was increased or decreased by 0.5 μg, which depended on the response of the previous puerperant. The range of sufentanil dose was from 1 to 4.5 μg in Group 1 and 2.5 to 6 μg in Group 2. If all the visual analog scale scores of the puerperant were all ≤ 30 mm at 15, 30, and 45 minutes, the sufentanil dose was treated a success, and the assigned dose for the next puerperant was with a 1/9th chance of decreasing by 0.5 μg or with an 8/9th chance of remaining the same dose of the previous puerperant. If any of the visual analog scale scores of the puerperant were > 30 mm at 15, 30, or 45 minutes, the dose was treated as a failure, and the assigned dose for the subsequent puerperant was increased by 0.5 μg. This was implemented using the biased coin up-and-down scheme designed by a statistician in a Microsoft Excel file. The file could only be accessed by the research assistant in order to keep the double-blind nature.

Outcomes

The primary outcome was a visual analog scale score of ≤ 3 at 15, 30, and 45 minutes after administration of epidural initiation with the given dose of sufentanil. The secondary outcomes were maternal and fetal observations. Maternal observations were as follows: the accumulated sufentanil and patient-controlled epidural analgesia bolus times in the first hour of analgesia, total patient-controlled epidural analgesia bolus times during analgesia, modified Bromage scores, oxytocin used after analgesia, fetal bradycardia, pruritus in the first 60 minutes, hypotension, bradycardia, nausea, vomiting, cesarean and forceps delivery rate, lateral episiotomy, upper sensory level, duration of the 3 stages of labor, duration of epidural analgesia, and postpartum hemorrhage. Neonatal observations were as follows: birth weight, Apgar scores at 1 minute and 5 minutes, neonatal intensive care unit admission, and pH of umbilical arterial blood. Maternal demographics before analgesia, such as age, weight, height, gesta-

tional period, gravidity, parity, membrane rupture, induced or spontaneous labor, cervical dilatation, and visual analog scale scores, were also recorded.

Statistical Analysis and Sample Size Calculation

The dose-finding study based on a biased coin up-and-down design and the suggestion of enrolling 20-40 patients could provide stable estimates of the target dose according to a simulation study (9). Therefore, the study included 40 puerperants in each group.

The 90% effective dose (ED_{90}) was defined as the sufentanil dose in epidural initiation that could fulfill a successful analgesic effect for 90% of the puerperants; it was estimated using the isotonic regression method (9,10). The 95% confidence interval (CI) of ED_{90} was obtained by a bias-corrected percentile method using 2000 bootstrap replications (11). The study statistician performed isotonic regression and bootstrapping using R version 3.4.4. software (R Foundation for Statistical Computing, Vienna, Austria).

The maternal characteristics and secondary outcomes were reported as mean ± standard deviation, numbers, numbers (proportions), and median (interquartile range). Parametric data were compared by the t-test, and nonparametric data were compared by the Mann-Whitney test. Proportions were analyzed by the Chi-square or Fisher's exact test. Statistical comparisons were made using SPSS version 18.0 for Windows (Chicago, IL). Significance was defined as a *P*-value < 0.05.

Results

The flow diagrams of the study are shown in Fig. 1. A total of 191 puerperants were enrolled in the study. One hundred cases were excluded because of greater cervical dilatation (n = 39), high body mass index (n = 8), multiparity (n = 17), multiple gestations (n = 3), or patient refusal (n = 33). One patient dropped out of the study during the allocation because of difficulties during epidural puncture, and 3 cases dropped out of the study during the follow-up due to the administration of a wrong dose of sufentanil (n = 1) and fast cervical dilatations (n = 2) during the follow-up in Group 1; 7 cases dropped out of the study due to fast cervical dilatation during the follow-up in Group 2. Finally, 40 cases from Group 1 and 40 from Group 2 were included in the final analysis.

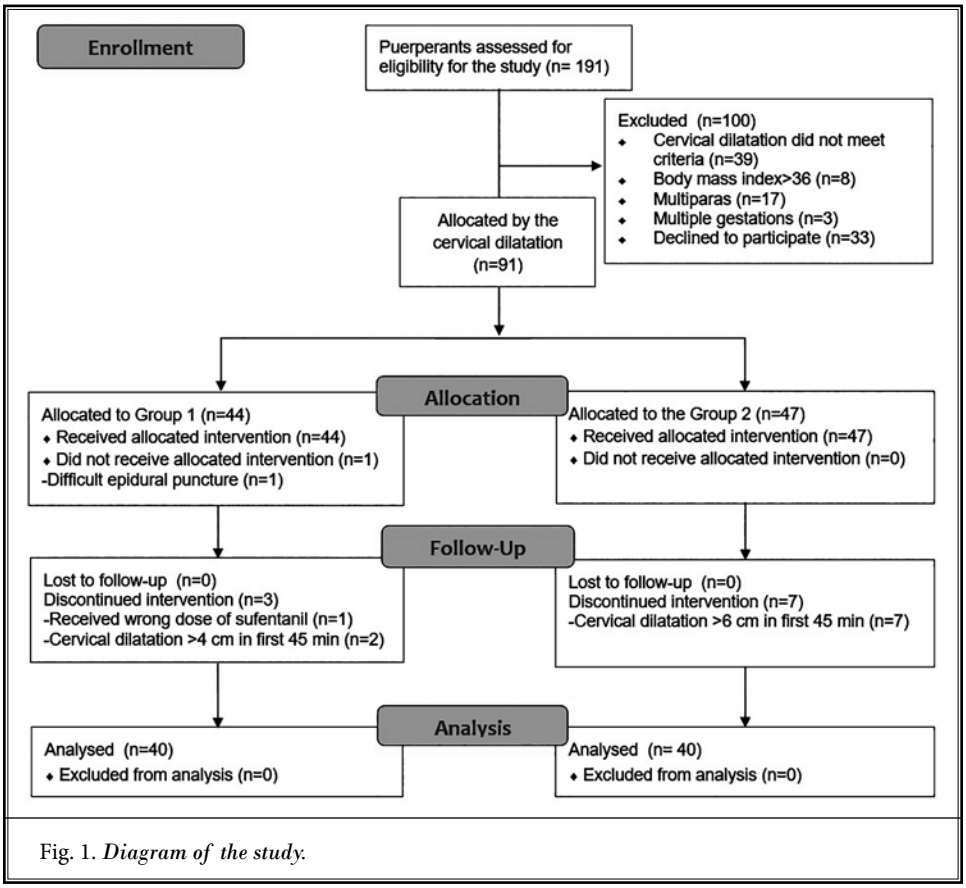

Fig. 1. *Diagram of the study.*

Table 1 shows the maternal characteristics. Cervical dilatations were different between the 2 groups (*P* < 0.001), though the other characteristics were similar.

The puerperant allocation sequence and the response to the assigned sufentanil dose in epidural initiation in Group 1 and Group 2 are shown in Fig. 2 and Fig. 3, respectively. The observed and pooled-adjacent-violators algorithm-adjusted response rates for each sufentanil dose level in Group 1 and Group 2 are shown in Table 2.

Table 1. *Maternal characteristics*.

Characteristics	Group 1 (n = 40)	Group 2 (n = 40)	*P* value
Age, years	30.3 ± 3.1	30.6 ± 2.9	0.633
Weight, kg	69.6 ± 8.1	69.4 ± 8.4	0.909
Height, cm	161.8 ± 4.1	162.3 ± 8.4	0.748
Gestational period, weeks	39.6 ± 0.9	39.2 ± 1.0	0.088
Gravidity, n	1(1-1)	1(1-2)	0.055
Parity, n	0(0-0)	0(0-0)	1.000
Membrane rapture, %	22(55%)	20(50%)	0.823
Induced/Spontaneous labor	5/35	12/28	0.099
Cervical dilation, cm	4(3.25-4)	6(5-6)	< 0.001
VAS scores before analgesia, mm	8.3 ± 1.1	8.4 ± 1.1	0.773

Values are mean ± SD, median (IQR), n (%), or count numbers.
VAS, visual analog scale; SD, standard deviation; IQR, interquartile range.

Table 2. *Observed and PAVA-adjusted response rates in Group 1 and Group 2*.

Assigned Dose (ug)	Number of Successes	Number of Patients	Observed Response Rate (%)	PAVA-adjusted Response Rate (%)
Group 1				
1.0	3	4	0.750	0.667
1.5	5	8	0.625	0.667
2.0	21	22	0.955	0.955
2.5	6	6	1.000	1.000
Group 2				
2.5	0	1	0.000	0.000
3.0	0	1	0.000	0.000
3.5	0	1	0.000	0.000
4.0	0	1	0.000	0.000
4.5	7	12	0.583	0.583
5.0	17	18	0.944	0.944
5.5	6	6	1.000	1.000

PAVA-adjusted response rates were estimated using the weighted isotonic regression method. PAVA, pooled-adjacent-violators algorithm.

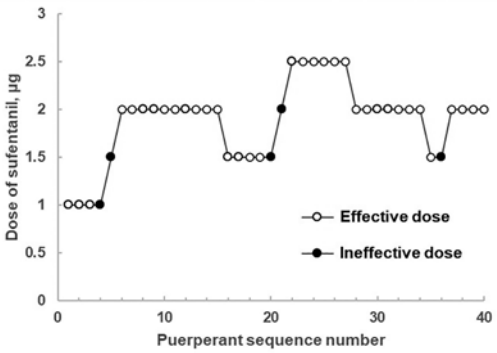

Fig. 2. *The puerperant allocation sequence and the response to the assigned sufentanil dose in epidural initiation in Group 1. The puerperant's sequence number (X-axis) is the order of all puerperants exposures using a biased coin up-and-down design. The assigned sufentanil dose in epidural initiation is displayed on Y-axis. An effective dose is denoted by a hollow circle, while an ineffective dose is denoted by a solid circle.*

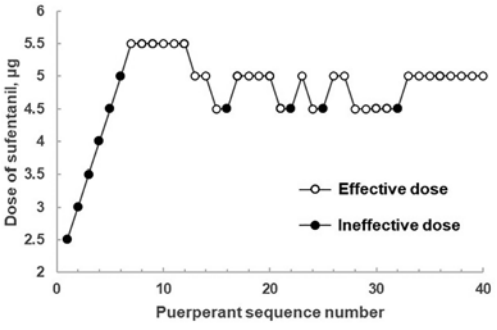

Fig. 3. *The puerperant allocation sequence and the response to the assigned sufentanil dose in epidural initiation in Group 2. The puerperant's sequence number (X-axis) is the order of all puerperants exposures using a biased coin up-and-down design. The assigned sufentanil dose in epidural initiation is displayed on Y-axis. An effective dose is denoted by a hollow circle, while an ineffective dose is denoted by a solid circle.*

The ED_{90} of sufentanil in epidural initiation was 1.91 µg (95% CI 1.82-2.35 µg) and 4.90 µg (95% CI 4.82-5.35 µg) in Group 1 and Group 2, respectively, as estimated by isotonic regression. The ED_{90} of sufentanil was 62.5% lower (95% CI 50.8-64.0%) in Group 1 than that in Group 2.

Table 3 shows the maternal and neonatal outcomes in the 2 groups. The accumulated sufentanil dose in the first hour (3.19 ± 1.04 µg vs. 6.40 ± 1.12 µg, $P < 0.001$), rate of oxytocin use after analgesia (67.5% vs. 35%, $P = 0.004$), duration of the first stage of labor (524 ± 186 min vs. 350 ± 120 min, $P < 0.001$), and duration of epidural analgesia (300 ± 96 min vs. 238 ± 111 min, $P = 0.009$) were significantly different between the 2 groups in maternal outcomes. In neonatal outcomes, there were no differences in birth weight, Apgar scores

at 1 and 5 minutes, rate of Apgar scores ≤ 7 at 1 minute, neonatal intensive care unit admission, and pH of umbilical arterial blood between the 2 groups.

Figure 4 shows the sequence allocation number of each case and the corresponding accumulated sufentanil dose during the first hour of analgesia in Groups 1 and 2. The figure also shows 2 reference lines representing the recommended total sufentanil dose to be used in the first hour of analgesia according to the normal practice at the author's hospital and that recommended by Stanford University.

Table 3. *Maternal and neonatal outcomes*.

	Group 1 (n = 40)	Group 2 (n = 40)	*P* value
Maternal Outcomes			
Accumulated sufentanil in 1st hour, μg	3.19 ± 1.04	6.40 ± 1.12	< 0.001
PCEA bolus times in 1st hour	0 (0-0)	0 (0-1)	0.156
Total PCEA bolus times	0 (0-1)	1 (1-2)	0.297
Modified Bromage scores	0 (0-0)	0 (0-0)	1.000
Oxytocin used after analgesia, n (%)	27 (67.5%)	14 (35%)	0.004
Fetal bradycardia, n (%)	0 (0%)	0 (0%)	1.000
Pruritus in first 60 min, n (%)	0 (0%)	0 (0%)	1.000
Hypotension, n (%)	0 (0%)	0 (0%)	1.000
Bradycardia, n (%)	0 (0%)	0 (0%)	1.000
Nausea, n (%)	0 (0%)	0 (0%)	1.000
Vomiting, n (%)	0 (0%)	0 (0%)	1.000
Cesarean delivery, n (%)	8 (20%)	5 (12.5%)	0.363
Forceps delivery, n (%)	3 (7.5%)	4 (10%)	0.692
Lateral episiotomy, n (%)	12 (30%)	13 (32.5%)	0.809
Upper sensory level	T9 (T8-T10)	T9 (T8-T10)	0.521
Labor stage 1, min	524 ± 186	350 ± 120	< 0.001
Labor stage 2, min	41 ± 28	50 ± 45	0.229
Labor stage 3, min	6.3 ± 5.3	9.4 ± 8.5	0.052
Duration of epidural analgesia, min	300 ± 96	238 ± 111	0.009
Postpartum hemorrhage, mL	312 ± 144	305 ± 85	0.079
Neonatal Outcomes			
Birth weight, g	3381 ± 392	3283 ± 373	0.105
Apgar scores at 1 min	10 (10-10)	10 (10-10)	0.355
Apgar scores at 5 min	10 (10-10)	10 (10-10)	1.000
Apgar scores at 1 min ≤ 7, n (%)	1 (2.5%)	1 (2.5%)	1.000
Admission to NICU, n (%)	8 (20%)	9 (22.5%)	0.785
pH of UA blood	7.28 ± 0.03	7.29 ± 0.05	0.340

Values are n (%), mean ± SD, median (IQR).
PCEA, patient-controlled epidural analgesia; NICU, neonatal intensive care unit; UA, umbilical artery.

Discussion

In the current study, the ED_{90} of sufentanil in epidural initiation for puerperants with a cervical dilatation of 2-4 cm was 1.91 μg (95% CI 1.82-2.35 μg), while that for puerperants with a cervical dilatation of 5-6 cm was 4.90 μg (95% CI 4.82-5.35 μg), as estimated by isotonic regression. The ED_{90} of sufentanil in epidural initiation was 62.5% lower (95% CI 50.8-64.0%) in the latent phase than that in the active phase during the first stage of labor. As per our knowledge, no studies have reported the optimal dose of sufentanil in both the latent and active phases during epidural labor analgesia in the first stage of labor, while our results revealed a large difference in the dose of sufentanil requirement between the 2 phases; if the dose of sufentanil in epidural initiation was transformed into the concentration (0.157 $\mu g \cdot mL^{-1}$) of the epidural solutions, the concentration of sufentanil in the latent phase would be much less than the normal concentration (with sufentanil concentration of 0.4-0.5 $\mu g \cdot mL^{-1}$) used in clinical practice.

It is noteworthy that the doses or estimated concentrations of sufentanil employed in both the phases of labor in the study were much lower than those in current clinical use/suggested in most studies (12-16). For example, in the Department of Anesthesia of Stanford University School of Medicine, sufentanil 10 μg and 0.125% bupivacaine with a volume of 15 mL was suggested as the regimen for epidural initiation in epidural labor analgesia (16). In the current study, compared to the above-mentioned dosage, the sufentanil dose was reduced by 75% and 50% in the latent and active phases, respectively. Most studies used a sufentanil concentration of 0.3 $\mu g \cdot mL^{-1}$ in the latent phase during labor analgesia (17,18), which is about 2 times higher than the concentration estimated in the latent phase in Group 1. We also compared the total accumulated dose of sufentanil administered in the first hour of labor analgesia in the 2 groups of the study; the dose as per the standard practice at the author's hospital and that as per the Stanford University School of Medicine guidelines were higher than the doses used in either of the groups described herein (Fig. 3). Of course, we recognize that the recommendations for epidural initiation as per the

Stanford University School of Medicine must be appropriate for all nulliparae and multiparae and all stages of labor; the recommendation was presumably a solution to address the issue of shortage of anesthesiologists by providing satisfactory analgesic effects as per the demands of puerperants.

However, according to the authors, the solution is sub-optimal, given the safety of puerperants and fetuses. There are many side effects of epidural use of high doses of opioids, including maternal pruritus, fetal bradycardia, nausea and vomiting, and a higher cesarean rate (19-21). It was also reported that consuming a higher dose of total epidural fentanyl during labor might result in lower neonatal Neurologic and Adaptive Capacity Scores and lower breastfeeding success rates at 6 weeks postpartum (22). Thus, to reduce the total consumption of opioids and their influence on the puerperants and fetuses and to increase the safety of epidural analgesia, sufentanil doses need to be optimized in both epidural initiation and epidural maintenance. A low concentration of sufentanil with local anesthetics tailored to cervical dilatation conditions may be a solution to balance the analgesic effect and side effects of epidural analgesia. Thus, this study may constitute preliminary research on this aspect.

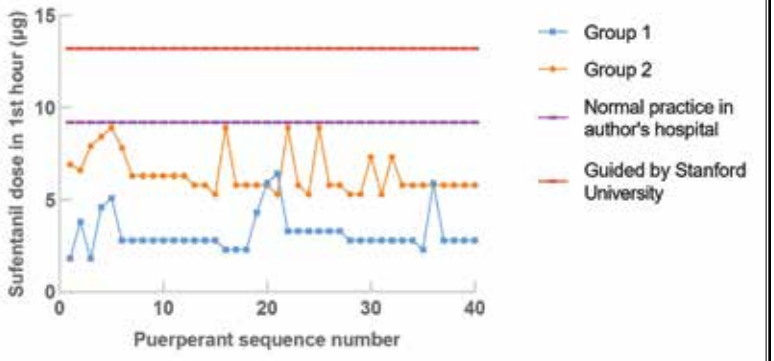

Fig. 4. *The puerperant allocation sequence (X-axis) and the corresponding accumulated sufentanil dose of puerperant during the first hour of analgesia (Y-axis) in Group 1 (blue square) and Group 2 (orange circle) with 2 reference lines representing the recommended total sufentanil dose to be used in the first hour of analgesia according to the normal practice at the author's hospital (purple line) and that recommended by Stanford University (red line).*

Several previous studies have reported on the use of low concentrations of sufentanil or fentanyl combined with a low concentration of local anesthetics during epidural labor analgesia (19,20,23). The reported concentrations of sufentanil (19) or fentanyl (20) were very close to those estimated in epidural initiations in the latent phase of the first stage of labor in Group 1. Moreover, among the 3 previous studies, the study by Bernard JM et al proved that a lower concentration of sufentanil used as the maintaining solution could fulfill the analgesia demand throughout the first labor stage. Therefore, we firmly believe that our findings from these 2 groups could also be applied to the maintenance of the latent and early active phase for labor analgesia. Furthermore, combined with the highest sufentanil concentration (17) (0.67 $\mu g \cdot mL^{-1}$), a new embryonic analgesia mode of variable concentrations of sufentanil throughout the first labor stage is formed. With this analgesia mode, the sufentanil would be saved to a maximum extent while the analgesic effect is ensured. Obviously, this analgesia mode should be further investigated.

This study has 2 limitations. First, both spontaneous labor and induced labor were included in this study, and the degree of pain in these 2 types of labor is different (24). Therefore, it is logical to assume that the required dose of opioids would also be different. Oxytocin was not used during the period from 15 minutes before to 45 minutes after epidural initiation in both groups; this strategy aimed to reduce the incidence of uterine hypertonus and fetal bradycardia in this study. Second, only nulliparae were included in the study, and the demand for sufentanil in epidural initiation for multiparous patients would be theoretically much higher. Therefore, further research should be conducted on multiparous individuals. Furthermore, in this study, the definitions of the latent phase and active phase were as follows: cervical dilatation of 2-4 cm and 5-6 cm, respectively, as per our hospital's normal clinical practice and several previous studies (25,26). However, the active phase was defined as cervical dilatation > 6 cm in a more recent study (27). Therefore, the threshold values for cervical dilatation to define latent and active phases should be standardized based on more research. However, the required sufentanil dose in epidural initiation was quite different between cases with a cervical dilatation of 2-4 cm and those with a cervical dilatation of 5-6 cm in this study.

Conclusions

The ED_{90} of sufentanil in epidural initiation was 1.91 μg (95% CI 1.82-2.35 μg) for puerperants in the latent phase and 4.90 μg (95% CI 4.82-5.35 μg) for those in the early active phase. Different sufentanil doses should be adopted for epidural initiation according to the different phases due to the large differences in sufentanil requirements between the 2 phases during the first stage of labor.

Contributions

Jing Zheng, MD helped with the data collection and interpretation, drafting the manuscript, and final approval of the manuscript to be published. Ting Shen, MD helped with the data collection, drafting the manuscript, and final approval of the manuscript to be published. Xiao-Hu An, MD helped with the data collection and final approval of the manuscript to be published. Yong Bian, MD helped with the data analysis and interpretation and final approval of the manuscript to be published. Ying Shen, MSN helped with the design of the study, data collection, revising the manuscript, and final approval of the manuscript to be published. Zifeng Xu, MD helped with the conception and design of the study, revising the manuscript, and final approval of the manuscript to be published. Tao Xu, MD helped with the conception and design of the study, data collection, analysis and interpretation, critical revising of the manuscript, and final approval of the manuscript to be published.

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