The optimal dose of intrathecal sufentanil to be added to low-dose intrathecal ropivacaine during anesthesia for cesarean delivery

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Decreasing the spinal dose of local anesthetics for cesarean section has been advocated to improve maternal hemodynamic stability, and decrease the incidence of hypotension.[1] However, reducing the local anesthetic dose runs the risk of inadequate anesthesia. Sufentanil, a high-lipophilic opioid, is known to augment the quality of intrathecal block,[2] but effective anesthesia must be balanced against fetal respiratory depression and bradycardia, as well as maternal respiratory depression, emesis, and pruritus caused by intrathecal opioids. Chen et al[3] found that the ED_{50} was 10.37 mg, and was 15.39 mg for ED_{95} of the spinal hyperbaric ropivacaine for cesarean section. Qian et al[2] reported that 10 mg of hyperbaric ropivacaine produced a less complete motor block than 15 mg. We hypothesized that 11.25 mg intrathecal hyperbaric ropivacaine combined with sufentanil, may offer more effective anesthesia than ropivacaine alone. In addition, our purpose was to find the optimal dose of sufentanil to add to 11.25 mg intrathecal hyperbaric ropivacaine to increase its analgesic efficacy, and minimize its side effects during cesarean delivery.

The study was conducted between November 2008 and December 2009, and was approved by the Ethics Committee of the Third Xiangya Hospital of Central South University. After obtaining a written informed consent from each patient, we conducted this prospective double-blind and randomized controlled trial on 144 full-term singleton parturients, undergoing elective cesarean delivery, all having American Society of Anesthesiologists (ASA) physical status I-II. Parturients were excluded if they had psychiatric illness, coagulation disorders, chronic pain, allergies to opiates or local anesthetics, drug or medication abuse, suspected fetal abnormality, pregnancy-induced hypertension, bronchial asthma requiring regular therapy, cardiac problems associated with dyspnea, or any other significant medical condition. The parturients were randomly allocated to 4 groups of 36 each, using a computer-generated random number list. All parturients received a 2.5-mL admixture that included 1.5 mL (11.25 mg) of hyperbaric ropivacaine 0.75% (AstraZeneca, Södertälje, Sweden), and the following: Control group A - 1.0 mL 10% dextrose; Group B - 0.95 mL 10% dextrose + 0.05 mL (2.5 mcg) sufentanil (YiChang Humanwell Pharmaceutic, China); Group C - 0.90 mL 10% dextrose + 0.10 mL (5.0 mcg) sufentanil; Group D - 0.85 mL 10% dextrose + 0.15 mL (7.5 mcg) sufentanil. Combined spinal-epidural anesthesia was administered, with patients in the right lateral position. Using the needle-through-needle method, the epidural space was identified with the loss of resistance to air technique. After identification, a 27-gauge Tuohy spinal needle was inserted into the subarachnoid space at the L2-L3 interspace. Once the free flow of clear cerebrospinal fluid was obtained, the test solution was injected over 30 seconds. After removing the spinal needle, an epidural catheter was advanced 4 cm into the epidural space and aspirated, and no test dose was given. Syringes containing the study drug were prepared by one researcher, and administered by a second who remained blinded to their contents. Parturients were assessed and cared for, and the study data recorded by a blinded researcher.

Blood pressure, heart rate, and oxygen saturation was documented and sensory and motor block was assessed at 2-minute intervals for 10 minutes, and then at 5-minute intervals until the end of surgery. Surgery was allowed to start when the upper dermatome level of loss of discrimination to pinprick was at, or above T7. If this was not achieved within 20 minutes, 2% lidocaine was administered through the epidural catheter in incremental doses at 10-minute intervals until a T7 block was achieved. Pain was assessed with a 10-cm linear visual analogue scale (VAS), where 0 represented "no pain", and 10 represented "most severe pain". The VAS was recorded at 5-minute intervals during the operation. Patients who reported intraoperative pain (VAS 4-6) were treated with a 0.1-mg intravenous bolus dose of fentanyl. If pain remained intolerable (VAS more than or equal to 7), epidural top-up was given, spinal anesthesia was considered to have failed, and the patient was excluded from this study.

The duration of complete analgesia was defined as the time from the intrathecal injection to a VAS score more than 0. Motor block in the lower limbs was graded according to the modified Bromage Scale (that is: 0 - able to flex extended leg at the hip; 1 - able to flex knee, but not flex extended leg; 2 - able to move foot only; and 3 - unable to move foot). Duration of complete motor block was the time interval between intrathecal injection and recovery to a Bromage score of 0. Effectiveness of surgical anesthesia was graded on a 4-point scale: 4 - excellent, no intraoperative pain, abdominal muscle loose; 3 - good, pain was minimal, and no additional analgesics were needed, a little tight

Table 1 - Comparison of clinical data among the 4 treatment groups.

Clinical data	Treatment groups (n=36)				*P*-value
	A	B	C	D	
Duration of complete analgesia in minutes, mean ± SD	151.2 ± 79.0	230.4 ± 109.5	341.0 ± 186.8*,†	401.1 ± 255.8*,†	0.000
Effective surgical anesthesia (VAS scores 3 or 4), n (%)	17 (47.0)	28 (78.0)*	34 (94.0)*,†	35 (97.2)*,†	0.000
Intravenous supplementation, n (%)	16 (44.4)	7 (19.4)	2 (5.6)*,†	1 (2.8)*,†	0.000
Epidural supplementation, n (%)	3 (8.3)	1 (2.8)	0 (0.0)*	0 (0.0)*	0.007
Pruritus, n (%)	2 (5.6)	13 (36.1)*	17 (47.2)*	23 (63.9)*,†,‡	0.000

SD - standard deviation, *p<0.05 versus group A, †p<0.05 versus group B, ‡p<0.05 versus group C

abdominal muscle; 2 - fair, pain required treatment with 0.1-mg intravenous fentanyl, tight abdominal muscle; 1 - poor, larger doses of fentanyl were required, or epidural top-up was given. Grades 3 and 4 were considered evidence of effective anesthesia. Side effects such as hypotension, nausea and vomiting, shivering, pruritus, respiratory depression, and bradycardia were recorded during surgery, and the first postoperative day. At delivery, blood samples were collected from the umbilical vein for blood gas analysis. Apgar scores at one and 5 minutes were evaluated by the midwife who was unaware of the treatment group.

In this study, our results demonstrated that the addition of 5.0 mcg or 7.5 mcg sufentanil to hyperbaric ropivacaine significantly improved the efficacy of anesthesia, compared to ropivacaine alone or ropivacaine combined with 2.5 mcg sufentanil (**Table 1**). Qian et al[2] reported that a combination of 10 mg hyperbaric ropivacaine with 5 mcg sufentanil provided effective spinal anesthesia for cesarean delivery, but 10% of parturients felt mild pain at skin closure, and the study only compared 5 mcg with 0 mcg sufentanil. In our study, we increased the dose of ropivacaine and compared 0, 2.5, 5, and 7.5 mcg sufentanil. We found that the anesthesia effect was better, and the maximum VAS score during surgery was lower in all the sufentanil groups compared with the control group. It has been suggested that intrathecal sufentanil in combination with a local anesthetic greatly improves the anesthetic effect, and the effect increases with increasing the sufentanil dose.[4,5] However, our results show that there were no differences in the anesthetic effect and maximum VAS scores during surgery between the 5 mcg and 7.5 mcg sufentanil groups, and thus increasing the dose of intrathecal sufentanil above 5 mcg does not achieve a corresponding increase in anesthetic effect.

In our study, the duration of complete analgesia was defined as the time from the intrathecal injection to a VAS score more than 0. Our results were similar to Braga et al,[5] who found that there were no differences in duration of complete analgesia between the 2.5 mcg sufentanil group and the control. However, these findings conflict with another published study,[4] in which the authors found that the 2.5 mcg sufentanil group showed a significant increase in the duration of complete analgesia compared with the control. In our study, the duration of complete analgesia was longer in groups C and D than in groups A and B, but there were no differences between groups C and D. This suggests that increasing the dose of intrathecal sufentanil above 5 mcg does not achieve a corresponding increase in the duration of complete analgesia.[5] In the current study, pruritus was the main side effect in the groups receiving sufentanil. This is in agreement with a previous study.[5] Additionally, the incidence of pruritus and pruritus scores were higher for the 7.5 mcg sufentanil group than for the 2.5, and 5 mcg groups. Demiraran et al[4] reported that there was no difference in pruritus between the 2.5 and 5 mcg groups, and the incidence of pruritus was reported to range from 20-80% at different doses of intrathecal sufentanil. In our study, the incidence of pruritus increased from 36.1-63.9% over the range of sufentanil doses given, but even so this was lower than that reported in the Demiraran et al's study.[4] That research also found that pruritus treatment was required for 4 patients in their 2.5 mcg sufentanil group, and 7 patients in their 5 mcg sufentanil group.[4] In our study, pruritus treatment was required for 3 patients in the 5 mcg sufentanil group, and 5 patients in the 7.5 mcg sufentanil group, and no patients required pruritus treatment in the 2.5 mcg sufentanil group. Thus, it appears that increasing the sufentanil dose above 5 mcg increases the incidence and degree of pruritus without improving the quality, or duration of analgesia. There were no differences in the Apgar scores among neonates or umbilical venous blood gases among the groups.

In conclusion, the addition of 5 mcg sufentanil to 11.25 mg ropivacaine appears to be optimal, as it increases the efficacy of spinal analgesia without increasing the incidence of side effects.

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