Intrathecal sufentanil as the sole agent in combined spinal-epidural analgesia for the ambulatory parturient

Alex Tiong Heng Sia MB BS MMED Anaesthesia,
Jin Long Chong MB BS MMED Anaesthesia,
Dicky Hock Beng Tay MB BS MMED Anaesthesia,
Wai Kit Lo MB BS MMED Anaesthesia,
Lin Han Chen MB BS MRCOG (London),
Jen Wun Chiu MB BS MMED Anaesthesia

Purpose: To compare the effect of a combination of intrathecal (IT) sufentanil plus bupivacaine with IT sufentanil alone, on the incidence of hypotension and the success of ambulation in parturients.

Methods: This was a controlled, double-blind prospective trial involving 50 parturients in early labour who had received combined spinal-epidural analgesia (CSE). They were divided equally into two groups; group A received 10 μg IT sufentanil while group B received IT 10 μg sufentanil plus 2.5 mg plain bupivacaine. The blood pressure, pain scores, the highest sensory block and the degree of motor blockade were documented over the first 30 min by an unbiased anaesthetist. The ability and the desire to ambulate was studied 30 min after CSE. The side effects were documented throughout labour.

Results: Group B had a higher incidence of hypotension; (12 *vs* 3: $P < 0.01$). Fewer parturients in group B could ambulate (19 *vs* 25: $P < 0.05$). Group B also had a higher sensory blockade than group A (median T_4 *vs* $T_{7\text{-}8}$: $P < 0.01$). Of all the 44 parturients who could ambulate, 13 desired not to do so, usually due to sedation.

Conclusion: The quality of analgesia in all subjects in the study was excellent. Side effects were more common in the IT sufentanil-bupivacaine combination group.

Objectif : Comparer l'effet d'une combinaison de sufentanil intrathécal (IT) et de bupivacaïne avec le sufentanil IT employé seul, sur l'incidence de l'hypotension et le succès de la déambulation chez des parturientes.

Méthode : Cet essai prospectif, contrôlé et en double aveugle porte sur 50 parturientes, en début de travail, qui ont reçu une analgésie rachidienne et péridurale combinée (RPC). Elles ont été réparties également en deux groupes; le groupe A a reçu 10μg de sufentanil IT pendant que le groupe B a reçu 10μg de sufentanil IT plus 2,5 mg de bupivacaïne simple. La tension artérielle, le score de la douleur, le bloc sensitif le plus haut et le degré de blocage moteur ont été vérifiés pendant les 30 premières minutes par un anesthésiste impartial. La capacité de marcher et le désir de le faire ont été étudiés 30 minutes après la RPC. Les effets secondaires ont été vérifiés tout au long du travail.

Résultats : Le groupe B a présenté une plus grande incidence d'hypotension (12 *vs* 3 : $P < 0,01$). Moins de parturientes dans le groupe B ont pu marcher (19 *vs* 25 : $P < 0,05$). Le groupe B présentait aussi un blocage sensitif plus haut que le groupe A (médiane T_4 *vs* $T_{7\text{-}8}$: $P < 0,01$). Des 44 parturientes qui pouvaient marcher, 13 n'ont pas voulu le faire, en général à cause de la sédation.

Conclusion : La qualité de l'analgésie chez tous les sujets de l'étude a été excellente. Les effets secondaires ont été plus fréquents dans le groupe ayant reçu la combinaison de sufentanil IT-bupivacaïne.

From the Departments of Anaesthesia and Maternal and Fetal Medicine, Kandang Kerbau Women And Childrens Hospital, Singapore.
Address correspondence to: Alex Sia Tiong Heng, Department of Anaesthesia, 100 Bukit Timah Road, Singapore 229 899
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INTRATHECAL (IT) sufentanil provides effective analgesia in labour but sometimes results in systemic hypotension.[1,2] The addition of bupivacaine may enhance the quality and duration of analgesia but it may increase the risk of hypotension due to increased sympatholysis. The success of ambulation after CSE (with its purported advantages) may be hindered by a greater impairment of muscle power in the lower limbs due to IT bupivacaine.[3] Although the use of bupivacaine was advocated in an earlier study, the ability (as well as the desire) of the parturients to ambulate was not evaluated.[1]

In this study, we tried to determine if addition of IT 2.5mg bupivacaine produced an increased incidence of hypotension. Also, the ability of parturients to ambulate safely after CSE was assessed.

Methods

Patient selection and protocol

This was a randomised, double-blind controlled study (with the approval of the Hospital Research Ethics Committee) comprising 50 parturients of ASA physical status I in established labour (at least one painful contraction in five minutes) who had given written consent to CSE.

The exclusion criteria were: cervical dilatation > 5 cm, weight > 90 kg, age > 40 yr, previous administration of meperidine in the last three hours and the presence of obstetric complications (e.g. preeclampsia, high unengaged fetal head, multiple pregnancy, preterm pregnancy and past history of abdominal delivery).

Baseline pain score (100 point VAS, 0 = no pain, 100 = worst pain imagined), systolic blood pressure (measured non-invasively on the left arm) and fetal heart tracing were obtained.

After an intravenous preloading with 0.5 l Ringers lactate solution over five minutes, CSE was instituted in the left lateral position at the L_{2-3} or L_{3-4} level with a #17 Weiss needle followed by a #27 Whitacre spinal needle (Becton Dickinson *Durasafe* set), with the epidural needle serving as the "introducer" for the spinal needle.

Each parturient in group A received IT 10 μg sufentanil (Janssen) while group B received a combination of IT 10 μg sufentanil plus 2.5 mg plain bupivacaine (Astra). In both groups, the drugs were diluted to 4 mL with normal saline solution and injected over 20 sec. The epidural catheter was then inserted, with 3 cm left in the epidural space and, after negative aspiration for blood, was flushed with 1 mL of normal saline.

Unsuccessful dural taps (i.e. no cerebral spinal fluid seen at the hub of the spinal needle after two attempts) would exclude the parturient from the study and epidural analgesia would be instituted accordingly. In the first minute after CSE, the parturients were turned to the semi-supine position with a wedge on the left to effect uterine displacement.

Assessment

During the first 30 min after CSE, the parturients were assessed as follows:

1. Blood pressure every five minutes
2. Pain scores at 5, 15 and 30 min after CSE
3. Highest sensory block to cold (cold spirit) at 5, 15 and 30 min after CSE
   Maximum degree of motor block in the lower limbs at 5, 15 and 30 min after CSE by the modified Bromage scale i.e. 0 = no impairment, 1 = unable to raise extended leg (either) but able to move knees and feet, 2 = unable to raise extended leg as well as knees, able to move feet, 3 = not able to flex ankle, feet or knees (complete block)
4. Posterior column sensory loss by distal joint position sense of the big toes at 5, 15 and 30 min
5. Presence of shivering, pruritus, nausea, vomiting or sedation. Sedation was defined by a Ramsay score of 4 i.e. patient asleep but with brisk response to a light glabellar tap or loud auditory stimulus[4] (monitoring of side effects was continued throughout labour)

Any reduction of systolic blood pressure of > 20% of the baseline value was promptly treated with 3 mg boluses ephedrine *iv*. The blood pressure was checked one minute later and the dose repeated if necessary. Respiratory depression (shallow respiration of 8 bpm) or severe sedation (Ramsay score ≥ 5) provided justification to abandon the study and to administer 0.4 mg naloxone *iv*. If the pain score was still > 30, 15 min after CSE, the block was considered a "failure" and epidural analgesia was reinstituted with 8 mL bupivacaine 0.25% (after a test dose of 50 mg lidocaine) via the epidural catheter.

After 30 min, provided the parturient was not hypotensive, was not in pain and had neither impairment of motor power or position sense loss, she was asked to do the following:

- sit up and then stand up, after which the systolic blood pressure was measured to exclude postural hypotension
- close her eyes to test for any degree of unsteadiness i.e. Rombergism
- perform the partial knee bending test while bearing weight as the inability to do so would render ambulation unsafe[5]

Fulfilment of the above criteria was taken to signify that the parturient was able to ambulate. Those who desired to do so would be allowed to remove their monitors for up to five minutes to walk within the confines of the labour room with assistance.

The duration from CSE to the time when the parturient asked for additional analgesia was noted. Aliquots of 4 mL bupivacaine 0.25% (total 8-12 mL) were given via the epidural catheter after a test dose of 50 mg lidocaine. Once the pain score was < 30, the epidural infusion of bupivacaine 0.125% was started at 10 $mL \cdot hr^{-1}$.

Data on the following were also collected for each group:

- mode of delivery
- duration of second stage
- total amount of spinal and epidural bupivacaine
- neonatal birthweights and Apgar scores (one and five minutes after birth)
- overall satisfaction with analgesia (immediately post delivery on a 0-100 scale, 0 = very dissatisfied and 100 = extremely satisfied)
- post-dural puncture headache before discharge from the hospital (36 hr or more after CSE)
- fetal heart tracing one hour before and one hour after CSE. This was reviewed by the obstetrician who was "blinded" to the drugs received. The cardiotocogram was categorised as "normal" (reactive) based on the following criteria: at least two accelerations (>15 beats for > 15 sec) in 20 min, baseline heart rate 110 -150 bpm, baseline variability 5-25 bpm and early decelerations. Any deviation from the above was classified as "abnormal" (non-reassuring) and the appropriate obstetric intervention was effected if necessary. All the fetal cardiotocograms were confirmed to be reactive prior to labour analgesia.

Statistics

The following tests were used for the comparison of the data between the two groups:

a students t test for the demographic profile and the total amount of ephedrine used.

b Fisher exact test for the incidence of hypotension and the ability to ambulate 30 min after CSE. It was also used to compare the incidence of shivering, nausea and vomiting.

c Wilcoxon Rank-Sum test for pain scores, systolic blood pressure, extent of sensory block, the time for the first request for analgesia, the duration of second stage, the satisfaction score and Apgar scores of the neonates.

d χ^2 test was used to compare the differences in parity, use of oxytocin before CSE, incidence of pruritus and sedation, desire to ambulate in parturients who could do so, fetal heart rate changes and mode of delivery.

The sample size was computed to detect, with a power of 0.8 and P value of < 0.05, a difference of 40% reduction in the incidence of hypotension between the two groups.

Results

Both groups were similar in terms of weight, height and age and no differences were detected in baseline values of systolic blood pressure, pain scores, cervical dilatation, parity or use of oxytocin before CSE. Ten parturients in each group received the CSE at L_{2-3} level while the rest at L_{3-4}. (Table I)

There was an increase in the incidence of hypotension in group B ($P < 0.01$) resulting in a greater amount of ephedrine used ($P < 0.01$). However, no differences in the absolute values of blood pressure were detected at any particular time interval due to the designed rescue regimen of the study. The mean systolic blood pressure ranged from 108-120 mmHg in group A and 106-122 mmHg in group B at the assigned five minute intervals after CSE.

Fewer parturients in group B could ambulate ($P < 0.05$) even though the desire to ambulate for those who could was not reduced.

In terms of reduction of pain scores, there was no difference in the treatment effect between the groups. The median pain score ranged from 0-6 in group A and 0-4 in group B five minutes after CSE for the first 30 min. All parturients in both groups had pain scores

TABLE I Demographic profile (mean±sd), baseline systolic blood pressure (mean ±sd), pain scores (median (range)), cervical dilatation (median (range)), the proportion of parturients who were primiparous and the proportion of parturients that had oxytocin infusion before CSE in the two groups.

	Group A	*Group B*
Age (yr)	27.5 ±4.9	28.2 ±4.6
Weight (kg)	65.3 ±8.7	65.7 ±8.7
Height (cm)	156.8 ±4.2	155.6 ±4.6
Systolic blood pressure (mmHg)	119.7 ±12.3	121.8 ±12.0
Pain scores (0-100 visual analogue scale)	85 (60-100)	83 (72-100)
Cervical dilatation (cm)	3 (2-5)	3 (2-5)
Proportion of primiparas	15/25	14/25
Use of oxytocin	8/25	11/25

P: NS.

TABLE II Incidence of hypotension, total amount of ephedrine used (mean ±sd), the ability to ambulate and the desire to ambulate after CSE, the highest sensory level of thoracic (T) or cervical (C) dermatomal block to cold spirit (median (range)) after CSE and the time to the first request for analgesia after the initial intrathecal dose (mean ±sd).

	Group A	*Group B*
Systolic blood pressure reduction by 20%	3	12*
Total ephedrine used (mg)	0.25 ±0.84	2.1 ±2.6
Satisfied criteria for walking	25	19†
Satisfied criteria for walking and desired to walk	17	14
Highest sensory block	T_7 (T_{2-12})	T_4 (C_7- T_{10})*
Time to first request for analgesia (min)	125 ±33.2	160 ±33.1*

*($P < 0.01$)
†($P < 0.05$)

TABLE III Total mass of bupivacaine used (mean±sd), duration of second stage of labour (mean±sd), changes in fetal heart rate one hour after CSE, the proportion of neonates with Apgar scores greater than 7 at one and five minutes after birth, the numerical breakdown of the modes of delivery, neonatal birthweight (mean±sd) and the analgesia satisfaction scores.

	Group A	*Group B*
Total spinal/epidural bupivacaine used (mg)	125 ±33	112 ±52
Duration of second stage (min)	72.0 ±43	93.4 ±4
Intrapartum Fetal Heart Tracing		
Normal	18	20
Suspicious	7	5
Apgar score > 7 at		
One minute	23/25	22/25
Five minutes	25/25	25/25
Mode of delivery		
Normal	13	10
Instrumental (forceps/vacuum)	7	6
Abdominal	5	9
Neonatal birthweight (g)	3265 ±371	3481 ±384*
Analgesia satisfaction score (0-100 VAS)	87 (75-100)	85(65-100)

*$P < 0.05$

< 30 at 15 min after CSE: there were no "failures" with regard to analgesia. The duration of analgesia as reflected by the time to the first request for epidural "top-up" after the IT doses was longer in group B ($P < 0.05$). The level of sensory block to cold was higher in group B throughout the duration of assessment ($P < 0.01$). (Table II)

There were no differences in the duration of second stage of labour, the total bupivacaine used, intrapartum fetal heart rate changes, the distribution of the modes of delivery or the neonatal Apgar scores. Group B had a higher birth weight ($P < 0.05$). The satisfaction scores were high but were not different between the groups. (Table III)

The profile of side effects was similar. The commonest side effects were self-limiting pruritus (13 parturients in group A and 9 in group B) and sedation (8 in group A and 14 in group B). Only 10% of all the parturients had nausea and vomiting (2 in group A and 3 in group B, alleviated by 10 mg metoclopramide) while one parturient from group B shivered. None of the parturients had respiratory depression or postdural puncture headache. Failure to obtain cerebral spinal fluid was experienced in one parturient who was excluded from the study.

Discussion

Our study showed that the addition of 2.5 mg bupivacaine to IT 10 μg sufentanil produced more hypotension and hampered the ability of the parturients to ambulate. Although the duration of analgesia was prolonged, the satisfaction score was not enhanced, possibly because the epidural analgesia was started as soon as the spinal analgesia wore off.

As demonstrated by Riley et al, systolic blood pressure could decrease after administration of 10 μg IT sufentanil in labouring women. Even though the mechanism involved remains undetermined, the near immediate relief of labour pain with resultant inhibition of the sympathetic arc and the decrease of circulating catecholamines probably contributed.[2] We attributed the increased incidence of hypotension in group B partially to either an additive or synergistic effect of local anaesthetic and sufentanil (which also possessed local anaesthetic properties) on sympatholysis.

Similarly, prolongation of the duration of analgesia in the sufentanil-bupivacaine group could be explained by potentiation of neural inhibitory effects by the combination of the opioid and the local anaesthetic agent.[1] A possible local anaesthetic mechanism could also explain the consistently higher level of dermatomal sensory block. Although it would be very unlikely that the local anaesthetic effect produced by 10 μg sufentanil on its own was of any clinical importance (albeit decreased isolated neural conduction had been demonstrated at higher sufentanil concentrations), its effects when used in combination with bupivacaine as well as the degree of positive interaction warrants further investigation.[6]

The additional value of adding bupivacaine to IT sufentanil is debatable. We found a higher "failure" rate with regard to fulfilling the criteria for safe ambulation in parturients who had received this bupivacaine-sufentanil combination (four parturients had

motor block, one had postural hypotension and one could not perform "knee-bending"). Our findings are in contrast to an earlier report that used the same dose of sufentanil-bupivacaine combination but found no evidence of motor block.[1]

Therefore, if the aim of the clinician is to administer a "walking epidural"successfully, we suggest that bupivacaine at the dose employed in the current study be reduced. We could not detect motor weakness in parturients who had received IT sufentanil although we did not use the sensitive isometric testing by mechanotransducers.[7] None of the parturients in this study had any loss of position sense in the lower limbs and no unsteadiness could be detected in parturients who could stand after the CSE. Our results showed that all the parturients in the group that had received IT sufentanil only were categorically "safe" to ambulate.

However, of all the parturients who could ambulate (44 in total; 25 in group A and 19 in group B), 13 chose not to do so. The reasons cited included: "drowsiness/sedation" (in six of the 13 parturients who could but would not walk), "sleepiness and fatigue" (5/13) and "abnormal sensation of the lower limbs and the feeling of insecurity" (2/13). Moreover, in our study, all the parturients who could ambulate only did so once. Most of the parturients preferred to remain in bed once they became comfortable. This relatively low ambulation rate was in contrast to the results of Collis *et al.*[8] Indeed, the presence of sedation (associated with the use of intrathecal opioids, notably sufentanil) probably rendered ambulation undesirable as well as unsafe.[9] We recommend that parturients always ambulate with the assistance of trained medical/nursing staff. Although respiratory depression has been reported with the use of IT sufentanil, none of the parturients in our study had this complication.[10] In spite of this, we recommend close vigilance and monitoring to be applied when this technique of analgesia is used.

In our study, new "abnormal" fetal heart tracings were detected in 12/50 parturients who had had CSE (no difference between groups), although unlike an earlier report, none of our cases required operative interventions.[11] Neonatal outcome was favourable. As the majority of the Caesarean sections were done for "dystocia"(8/12), the higher birthweight could have contributed to the apparently, but not significantly higher Caesarean delivery rate in group B (9 *vs* 5). The establishment of a cause-effect relationship between spinal/epidural analgesia and dysfunctional labour leading to increased intervention at delivery is an issue for continuing debate.[12]

The satisfaction scores for analgesia were very high for both groups of parturients, hence, IT sufentanil (with or without the addition of bupivacaine) should remain as a good option for labour analgesia.

Conclusion

Our study showed that 10 μg IT sufentanil provided excellent analgesia in early labour. Although the addition of 2.5 mg bupivacaine prolonged analgesia, we recommend that the dose of local anaesthetic be reduced or omitted to improve the haemodynamic profile as well as the success of maternal ambulation in labour. On the other hand, IT sufentanil at the current dose still falls short as a solution providing optimal analgesia for early labour due to its side effects. Finally, one must recognise that it is not always possible to induce a "walking epidural", however great the social indication, as the ultimate safety of the parturient must never be compromised for the sake of ambulation.

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