Effectiveness of Single Shot Intra Thecal Analgesia in Multiparous Women Scheduled for Normal Vaginal Delivery

Original Article

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ABSTRACT

Background and Aims: Spinal analgesia is used as pain relief method during labor. This cross-sectional study was conducted to assess the effect of adding dexmedetomidine, fentanyl to low-dose bupivacaine for intrathecal labour analgesia in multiparous women.

Methodology : A total of 75 women in the active phase of labor were randomly allocated to have intrathecal bupivacaine with dexmedetomidine (group D), fentanyl (group F), or saline (placebo) (group C). The duration of analgesia, intrathecal block characteristics and maternal and foetal outcomes were assessed and analysed**.**

Results: The longest analgesia duration and S1 regression time was recorded in group D followed by groups F and C. The shortest analgesia onset time and the highest sensory levels were recorded in both group D and group F then group C. Visual analogue scale values were comparable among groups F and D at most of the measurement time points and at the peak of the last uterine contraction before delivery while being significantly lower than those in group C. However, there were similar motor block characteristics and normal neonatal outcomes in all groups**.**

Conclusion: Single-dose intrathecal analgesia is a safe, fast, and efficient technique for labor analgesia, which can be easily performed, In comparison to fentanyl, dexmedetomidine addition to intrathecal bupivacaine significantly prolonged the duration of labour analgesia, with a good maternal and neonatal outcome.

Key Words: Bupivacaine, dexmedetomidine, fentanyl, intrathecal, labour analgesia, neonatal outcome

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INTRODUCTION

Labour pain is a stressful condition on both the mother and the foetus. painful uterine contractions can lead to hyperventilation, with a subsequent risk of maternal and foetal hypoxaemia[1].

Intense labour pain was reported to be associated with posttraumatic stress, postpartum depression and chronic pain[2].

Effective analgesia during labour can prevent or decrease these hazardous consequences[3].

Several medical analgesic methods have been proposed, and neuraxial techniques are considered as the most acceptable and practical ways to reduce labor pain[4].

Intrathecal analgesia using local anaesthetics or opioids is a rapid onset and effective technique for pain management in labouring women. It provides a symmetrical neurologic blockade with a high success rate covering the episiotomy and forceps delivery[5].

Pain of the first stage of labour is visceral in origin and can be effectively managed by neuraxial opioids alone. However, pain of the second stage is of both visceral and somatic origins due to distention and tearing of the perineal tissues; thus, neuraxial opioids alone are presumably ineffective in its management. In recent years, a growing body of evidence has suggested that sustainable and assured analgesia during the entire labour process can be achieved by adding adjuvants (e.g. morphine, fentanyl and dexmetedomidine) to the local anaesthetics[6].

These adjuvants can improve the neuraxial block characteristics while reducing the required local anaesthetic doses, thus minimising the motor component of the block[7].

The Aim of this study was to assess the effectiveness of intrathecal labour analgesia by adding dexmedetomidine, fentanyl to low-dose bupivacaine in multiparous women.

Secondary outcomes include maternal hypoxemia, hemodynamic instability, maternal adverse effects (nausea, vomiting, shivering and post-delivery urine retention),fetal heart rate and Apgar score.

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METHODOLOGY

The study protocol gained the approval of the local ethics committee of the Anaesthesia Department, Faculty of Medicine, Ain Shams University (FMASU MD282/2022) and clinical trial registration at ClinicalTrials.gov (registration number NCT05998551), this prospective, randomized, study was conducted on 75 Multiparous women admitted for normal vaginal delivery of uncomplicated term pregnancy in the active phase of labor (cervical dilatation ≥ 5 cm by examination), aged 22–45 y old, singleton term pregnant with normal fetal heart rate and requesting neuraxial analgesia. An informed signed written consent was obtained from all parturients. Sample size was calculated using PASS 15 program for sample size calculation, setting power at 90% and alpha error at 0.05, it is estimated that sample size of 25 women per group (total 75) were needed to detect difference between groups regarding duration of analgesia assuming that duration of analgesia among study groups were as follows: Group D: 199.9+ 25.3 minutes, Group F: 171 13.8 minutes, Control group: 139.6+ 3.8 minutes. Parturients who refused to participate, had pre-existing or pregnancy-induced hypertension, abnormal foetal heart rate (FHR) tracings, obesity, endocrinal diseases and/or diagnosed foetal abnormalities were excluded. Other exclusion criteria included preexisting neurologic deficits, or any contra-indication to epidural/spinal anesthesia, including spinal deformity or previous spine surgery, the occurrence of wet tap during epidural placement, allergy to any of the study drugs, and parturients who were scheduled for emergency cesarean section due to any reason were excluded from the study (Figure 1).

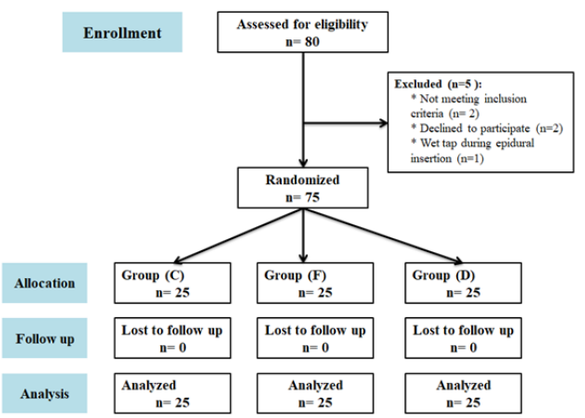

Fig. 1 : Flow chart of the studied cases

All patients were assessed and routine preoperative investigations were done: CBC, PT, PTT, INR, liver function tests, kidney function tests, fasting blood sugar, ECG and Portogram to exlude any incidence of fetal distress.

The eligible parturients were randomly allocated into three groups according to the additive added to a fixed dose of local anesthetic (1ml=5mg of 0.5% hyperbaric bupivacaine).Total volume of 2 ml was given to each patient: Group D (Dexmedetomidine): received intrathecal injection of 5mg (1ml) of 0.5% hyperbaric bupivacaine + 1 ml contain 5µg dexmedetomidine (0.05ml dexmedetomidine in insulin syringe+ 0.95ml normal saline). Group F (Fentanyl): received intrathecal injection of 5 mg (1ml) of 0.5% hyperbaric bupivacaine + 1 ml contain 12.5µg fentanyl (0.25ml fentanyl in insulin syringe+ 0.75ml normal saline). Group C (Control): received intrathecal injection of 5mg (1ml) of 0.5% hyperbaric bupivacaine + 1 ml normal saline then epidural catheter was inserted.

On arrival to the operating room, pulse oximetry, electrocardiography and non-invasive blood pressure monitors were applied. An 18 G IV cannula was inserted, and Ringer infusion (7 ml/kg/hr) was started. All patients were put in the sitting position with leaning forward. Sterilization was done by Povidone Iodine (Betadine) in a circular manner with covering the back by sterilized towels just exposing the spinal segments to be injected. Local anesthesia 2ml of lidocaine 1% was given at L3–L4 and 5ml of lidocaine 1% at L2–L3 then Dural puncture will be performed in paramedian approach at L3–L4 interspace with a 27G Quincke spinal needle. Each participant were received an intrathecal injection of 5 mg bupivacaine 0.5% (1 ml) plus an adjuvant (1 ml). The adjuvants (1 ml) was either fentanyl (12.5 µg) in group F, dexmedetomidine (5 µg) in group D or normal saline (placebo) in group C (control group). All these drugs were preservative-free and were prepared by an anaesthetist not involved in the study. Then Epidural analgesia was performed while with 18G Touhy needle (Braun, Germany), via midline approach at the L2–L3.

After returning the parturient to supine position, oxygen (5 L/min) was provided through a face mask. Uterine contractions and FHR were monitored with cardiotocography. Intraoperative hemodynamic data (HR, MAP) and visual analogue scale (VAS) score for pain were recorded baseline, 15 and 30 minutes till 6 hours after delivery.

The primary outcome of the present study was the duration of pain relief. Other intrathecal block characteristics such as the analgesia onset time, the maximum level of sensory block, the visual analogue scale (VAS) of the labour pain and S1 regression time were recorded. The duration of pain relief was defined as the duration from intrathecal injection till the VAS became more than 4. The analgesia onset time was defined as the time from intrathecal injection until the VAS became less than 4. The VAS (ranging from 0 = pain-free up to 10 = worst imaginable pain) of the labour pain was recorded before the intrathecal injection, every 15 min till delivery , then every 1 hour for 6 hours. VAS of the pain during the

last uterine contraction before delivery was also recorded. Temperature was assessed using methylated soaked swabs on both sides of the body (15 min after the intrathecal injection). S1 regression time was defined as the time from intrathecal injection to sensory regression to S1 dermatome. The need for epidural activation with 10 ml bupivacaine 0.125% (if VAS become ≥4 before delivery) was recorded. If epidural was activated the case was excluded.

After delivery epidural catheter was removed.

The secondary outcomes included SpO_2, maternal mean arterial pressure (MAP), heart rate (HR), and maternal adverse effects (nausea, vomiting, shivering and post-delivery urine retention), FHR and Apgar score. All the outcomes were assessed by a blinded anaesthetist who was not involved in the study.

Hypotension (a decrease in systolic blood pressure of greater than 20% from the baseline value or a fall of systolic blood pressure below 90 mmHg) was treated with injection of IV ephedrine 5-10mg increments, bradycardia (pulse rate < 60 beats per minute) was treated by injecting IV atropine increments of 0.3-0.6mg.

After delivery the Patients were received paracetamol 1gm and ketorolac 30 mg if VAS score more than 4.

RESULTS

Patient recruitment and flow are presented in Figure 1. 75 eligible women were included in the present study after excluding 5 parturients not meeting inclusion criteria or declined to participate or had a wet tap during epidural insertion, 25 parturients were allocated in each of dexmeditomidine group, fentanyl group and control group.

There were no significant differences in age, weight, height, gestational age, cervical dilatation, time to full cervical dilatation and duration of second stage among the three groups (Table 1).

Group C showed significantly shorter duration of analgesia and S1 regression time than the other two groups with statistically significantly delayed onset time. Although Group D showed significantly longer duration of analgesia and S1 regression time than group F, Both groups showed no statistically significant difference regarding analgesic onset time. Maximum level of sensory block was comparable between all groups with no statistically significant difference. VAS score at the peak of the last contraction before delivery was significantly higher in group C than the other 2 groups with no significant difference between group D and F (Table 2).

All patients before intrathecal injection experienced pain with comparable VAS scores, VAS scores at 15 and 30 minutes were nearly the same in all three groups. VAS scores at 1 and 2 hours were significantly higher in group C than the other 2 groups while group D and F showed no statistically significance difference. Group F showed significantly higher VAS scores at 3 hrs than group D (Table 3).

All study groups were comparable regarding maternal heart rate at baseline, 15 and 30 minutes till 6 hours with no statistically significant difference (Figure 2).

Dexmedetomidine group showed statistically significant lower MAP at 30 minutes 60 minutes and 2 hours, than control and fentanyl groups (Figure 3).

Comparing the three studied groups regarding maternal side effects, 6 patients in group F experienced nausea and vomiting compared to only 1 patient in both other groups with no statistically significant difference, also incidence of post-delivery urine retention was slightly higher in Group F but with no statistical significance. Maternal shivering showed no statistically significant difference (Table 4).

Regarding the foetal outcomes, there was no significant difference in FHR also Apgar score at 1 and 5 min, 3 groups were comparable and within the normal ranges (Table 5).

Table 1: Comparison between groups according to demographic data and labour progress.

		N	Mean	SD	95% Confidence Interval for Mean		*p-value*
					Lower Bound	Upper Bound	
Age	C	25	28.92	4.415	27.10	30.74	0.397
	D	25	27.40	3.948	25.77	29.03	
	F	25	28.20	3.354	26.82	29.58	
	Total	75	28.17	3.926	27.27	29.08	
Weight	C	25	90.20	9.183	86.41	93.99	0.856
	D	25	91.40	9.188	87.61	95.19	
	F	25	91.40	7.842	88.16	94.64	
	Total	75	91.00	8.660	89.01	92.99	
Height	C	25	167.60	7.047	164.69	170.51	0.654
	D	25	169.44	7.752	166.24	172.64	
	F	25	169.24	8.303	165.81	172.67	
	Total	75	168.76	7.658	167.00	170.52	
Gestational age (weeks)	C	25	39.04	.790	38.71	39.37	0.171
	D	25	38.68	.852	38.33	39.03	
	F	25	39.08	.812	38.74	39.42	
	Total	75	38.93	.827	38.74	39.12	
Cervical dilatation (cm)	C	25	5.32	.476	5.12	5.52	0.942
	D	25	5.28	.458	5.09	5.47	
	F	25	5.32	.476	5.12	5.52	
	Total	75	5.31	.464	5.20	5.41	
Time to full cervical dilatation (min)	C	25	108.00	20.616	99.49	116.51	0.523
	D	25	102.80	21.510	93.92	111.68	
	F	25	109.20	21.000	100.53	117.87	
	Total	75	106.67	20.946	101.85	111.49	
Duration of 2nd stage (min)	C	25	11.68	6.706	8.91	14.45	0.442
	D	25	10.00	5.276	7.82	12.18	
	F	25	12.00	5.657	9.66	14.34	
	Total	75	11.23	5.897	9.87	12.58	

Using: t-Independent Sample t-test for Mean±SD; x2: Chi-square test for Number (%) or Fisher's exact test, when appropriate

Table 2: Comparison between groups according to intrathecal block characteristics.

	Group C	Group D	Group F	*p-value*
Duration of pain relief (min)	130.00†(124.81-135.19)	188 (181.37-194.63)	174.80* (166.98-182.62)	<0.001
analgesic onset time (min)	4.56‡(3.96-5.16)	3.00(2.6-3.4)	3.00(2.55-3.45)	<0.001
VAS at the peak of the last contraction before delivery	3(2-3)†	2(1-2)	2(1-2)	<0.001
Maximum level of sensory block	T9(8-10)	T8(8-9)	T9(8-9)	0.112
S1 sensory regression time (min.)	120.3(111.3-129.3	181.2(173.1-189.1)	158.2(150.2-166.2)	<0.001

*significantly lower than Group D; † significantly lower than the other two groups; ‡ significantly higher than the other two groups

Table 3: Comparison between groups according to VAS score.

	Group C	Group D	Group F	*p-value*
VAS score before injection	9(8-9)	8(7.5-9)	9(8-9)	0.565
VAS 15 min	1(1-2)	1(0-1.5)	1(0.5-2)	0.306
VAS 30 min	0(0-1)	0(0-1)	0(0-0)	0.143
VAS 1 hr	3(2-4)†	0(0-0)	0(0-0)	<0.001
VAS 2 hrs	5(3-6)†	1(1-2)	1(0-1)	<0.001
VAS 3 hrs	3(2-4)	3(2-4)	5(3.5-5)†	<0.001
VAS 6 hrs	1(1-2)	2(1-2)	2(1-2.5)	0.032

† significantly higher than the other two groups

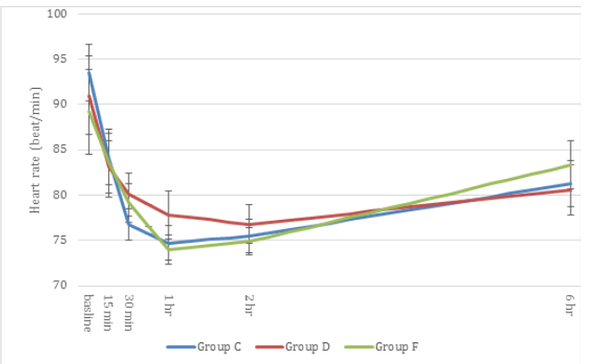

Fig. 2: Comparison of the studied groups according to maternal heart rate.

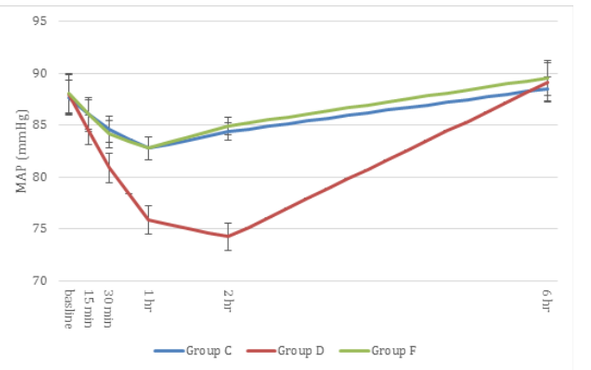

Fig. 3: Comparison of the studied groups according to Maternal Mean arterial pressure (MAP).

Table 4: Comparison of the three studied groups according to maternal side effects

	Group C	Group D	Group F	*p-value*
Maternal Nausea and Vomiting	1(4.0%)	1(4.0%)	6(16.0%)	0.196
Maternal shivering	2(8.0%)	2(8.0%)	1(4.0%)	0.807
Post-delivery urine retention	1(4.0%)	1(4.0%)	3(12.0%)	0.424

Table 5: Comparison of the four studied groups according to Neonatal parameters

	Group C	Group D	Group F	*p-value*
Fetal heart sounds 5 min after delivery	149.8 (146.2-153.2)	148.8 (146.68-152.92)	150.16 (145.86-153.46)	0.983
APGAR 1	8(7-9)	8(7-8.5)	8(7-8)	0.634
APGAR 5	8(8-9)	8(8-9)	8(8-9)	0.576

DISCUSSION

Labour analgesia has progressed throughout the last years towards avoiding adverse reactions on the progress of labour, maternal or foetal outcomes while providing adequate sensory blockade to provide safe and less painful experience during delivery. For these purposes spinal analgesia is commonly used in labor pain and preserve movement in labor, resulting in higher satisfaction among parturients[8,9].

In vaginal delivery, local anesthetics and opioids provide efficient and rapid onset method for analgesia when used as single shot via intrathecal route providing successful rates for symmetrical neurological block and also sufficient for episiotomy or forceps delivery[5].

In our study multiparous women planned for vaginal delivery received single shot intrathecal injection comparing a control group who received single shot intrathecal analgesia with bupivacaine only or dexmedetomidine added to bupivacaine or fentanyl added to bupivacaine, in aspects of effectiveness during and after delivery, side effects of each intrathecal medication on maternal outcomes and neonatal outcomes were all compared as endpoints.

We found that, in multiparous women undergoing vaginal delivery, there was significantly longer analgesia

duration with dexmedetomidine than fentanyl when added to intrathecal bupivacaine. Moreover, there was a significantly more rapid analgesia onset with dexmedetomidine and fentanyl than bupivacaine alone.

In recent years many adjuvants to local anesthetics have been used via intrathecal route to provide longer time of analgesia intra and post-operatively. Dexmedetomidine, a highly selective α2-adrenergic receptor agonist, one of the most frequently adjuvant used and many studies have reported that its use intrathecally as an additive to local anesthetics can provide longer high quality analgesia duration and more rapid onset with minimal side effects including hemodynamic stability[10].

Also many studies used intrathecal opioids as adjuvants to local anesthetics. Gian *et al*, concluded that when adding fentanyl and morphine to bupivacaine intrathecally as a single shot, efficient analgesia was achieved with adequate duration to cover labour, without affecting the outcomes of delivery regarding the incidence of instrumental delivery or progression to caesarean delivery[11].

The dose of Dexmedetomidine used in the current study was decided according to previous studies, as variable doses between 3 and 10 µg were described to be administered intrathecally Dilesh *et al*., [1]used the dose of 10µg while Liu *et al*.,[10]used the dose of 5µg intrathecally, both concluded that in comparison to other adjuvants to intrathecal anesthesia such as opiods, Dexmedetomidine provided safe, with minimal adverse effects, rapid onset and longer duration and more satisfactory analgesia during labour.

Consistent with our results, Khaled *et al*. concluded that dexmedetomidine added to intrathecal bupivacaine provide prolonged duration and more rapid onset of labour analgesia but in contrast, additives to intrathecal bupivacaine such as dexmedetomidine, fentanyl and morphine were found to allow higher level of sensory block, however our study revealed that adding fentanyl or dexmedetomidine to bupivacaine as in control group, didn't show significant difference in the level of sensory block[12].

Wong *et al*.,[13 reported that intrathecal analgesia results in a decrease in the first and second stages of labour in all groups regardless the additive used, this may be contributed to the preserved motor power, the frequency and more coordinated uterine contractions on the cervix after analgesia however, in consistency with the previously mentioned study cervical dilatation rate was comparable among all study groups with no significant difference.

Regarding level of analgesia many studies compared intrathecal adjuvants with variable results, as compared by VAS score Kiran *et al*., [14]found that fentanyl provided maximum analgesia, while Verma *et al*.,[15]found that both fentanyl and dexmedetomidine provided comparable level of analgesia. Whilst in correspondence to our results Mahendru *et al*., [16]found that dexmedetomidine provided deeper level of analgesia than fentanyl as compared by VAS score in the postoperative period.

Dexmedetomidine, an α2 agonist, may cause bradycardia and hypotension when used intrathecally, which are considered the most common side effects, owing to inhibition of preganglionic sympathetic activity in spinal medulla[17].

In our study MAP was significantly lower in dexmedetomidine group than other groups however this decrease in MAP was always clinically insignificant, and according to our study protocol no intervention was indicated.

Other investigators as, Wu *et al*.,[18]; Kanazi *et al*.,[19]; Weigl *et al*.,[20] found that higher incidences of maternal nausea and vomiting, shivering, and post-delivery urine retention occurred more frequently when narcotics were used, specially with morphine, however in our study morphine was not used, but incidence of maternal side effects were lower when using dexmedetomidine as an adjuvant,

Regarding fetal side effects, neuroaxial analgesia in general may be accompanied by maternal side effects as previously mentioned, however it was found that neuroaxial analgesia, not only, doesn't cause fetal acidosis or hypoxia compared with systemic analgesia it also may be partially protective against fetal hypoxia[21].

These were confirmed by other studies Owen *et al*., [22]; Al-Mustafa *et al*., [23], also in line with our study, as we found that FHR and Apgar score at 1 and 5 min were comparable and within the normal ranges with no differences between all groups supporting the safety of dexmedetomidine as an additive to intrathecal analgesia during delivery[24].

limitations

Our study has several limitations. First, is the limited number of parturients. Second, this study cannot involved women with serious medical or pregnancy-related illnesses since it only involved healthy and safe parturients. These comorbidities may affect obstetric management (impacting the rate of instrumental or cesarean deliveries) and neonatal outcomes. Third, all our parturients were multiparous; therefore, the results should not be generalised to primipara women.

CONCLUSION

We concluded that, single-dose intrthecal analgesia is a safe, fast, and efficient technique for labor analgesia, which can be easily performed with good duration of pain relief, a high level of maternal satisfaction, with a very few side effects, highly cost-effective and safe method for obstetric labor analgesia.

In comparison to fentanyl, dexmedetomidine seems to be a safe and efficacious adjuvant to intrathecal bupivacaine in multiparous women undergoing normal vaginal delivery. This may be helpful for parturients coming late to the delivery room, seeking rapid onset, long-lasting analgesia.

CONFLICT OF INTERESTS

There are no conflicts of interest

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