Original Article

# Outcomes of intrathecal analgesia in multiparous women undergoing normal vaginal delivery: A randomised controlled trial

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## ABSTRACT

**Background and Aims:** Although intrathecal analgesia is an effective option during labour, there is a need to establish sustainable and assured analgesia during the entire labour process. We aimed to assess the effect of adding dexmedetomidine, fentanyl or morphine to low-dose bupivacaine-dexamethasone for intrathecal labour analgesia in multiparous women. **Methods:** This was a triple-blind, randomised controlled trial that included 140 multiparous women. Eligible women were randomly allocated to have intrathecal bupivacaine-dexamethasone with dexmedetomidine (group D), fentanyl (group F), morphine (group M) 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 M, F and C, respectively, with statistical significance between all of them ($P < 0.001$). The shortest analgesia onset time and the highest sensory levels were recorded in group D followed by group F then group M with statistical significance between all of them ($P < 0.001$ and 0.003, respectively). Visual analogue scale values were comparable among groups M, F and D ($P > 0.05$) 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 ($P < 0.001$). However, there were similar motor block characteristics and normal neonatal outcomes in all groups. **Conclusion:** In comparison to morphine and fentanyl, dexmedetomidine addition to intrathecal bupivacaine-dexamethasone significantly prolonged the duration and accelerated the onset of labour analgesia, with a good maternal and neonatal outcome.

**Key words:** Bupivacaine, dexamethasone, dexmedetomidine, fentanyl, intrathecal, morphine, labour analgesia, neonatal outcome

## INTRODUCTION

Labour pain is a stressful condition on both the mother and the foetus. The painful uterine contractions can lead to hyperventilation, with a subsequent risk of maternal and foetal hypoxaemia.[1] Moreover, the associated catecholamine surge can cause maternal hyperglycaemia, lipolysis, foetal acidosis and/or dysfunctional labour.[2] In addition, intense labour pain was reported to be associated with posttraumatic stress, postpartum depression and chronic pain.[3] Effective analgesia during labour can prevent or decrease these hazardous consequences.[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] However, its major drawback is the limited analgesia duration. Only about half of the parturients who received combined spinal-epidural



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analgesia delivered during the spinal component of analgesia.[6]

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.[5,7] These adjuvants can improve the neuraxial block characteristics while reducing the required local anaesthetic doses, thus minimising the motor component of the block.[8]

We conducted this randomised controlled trial to investigate the effectiveness and safety of intrathecal analgesia for labour using bupivacaine and dexamethasone, with morphine, fentanyl or dexmedetomidine. We hypothesised that the addition of any of these adjuvants to bupivacaine-dexamethasone would improve the intrathecal analgesia characteristics without adversely affecting the maternal or neonatal outcomes.

## METHODS

The study protocol gained the approval of the local ethics committee of the Anaesthesia Department, Faculty of Medicine, Menoufia University, Egypt in June 2017. The protocol was registered at www.pactr.org (PACTR201710002424167). The study was conducted at Menoufia university hospitals between August 2017 and January 2018. The study was conducted in a randomised, parallel groups and triple blinded manner. This study conforms to the recommendations of the declaration of Helsinki and the applicable local regulatory laws. Prior to study enrolment, informed written consent was obtained from each eligible parturient.

In the present trial, we included multiparous women, 18–45 years old, who received antenatal care, presented for vaginal delivery of uncomplicated term pregnancy of singleton fetus with engaged foetal head and cervical dilatation of at least 5 cm requiring oxytocin augmentation, and requested analgesia. Patients with 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 contraindication to neuraxial block, the occurrence of wet tap during epidural placement, allergy to any of the study drugs and need for intrapartum antiemetic or antispasmodic drugs. Parturients who were at high risk for cesarean section, unable to communicate and/or those who refused to participate were excluded.

The eligible parturients were randomly allocated into four groups, of 35 patients each, in an equal ratio using a simple randomisation table created by a computer software programme. Each participant received an intrathecal injection of 2.5 mg bupivacaine 0.5% (0.5 ml) and dexamethasone 4 mg (1 ml) plus an adjuvant (0.5 ml). The adjuvants were either morphine (100 μg) in group M, fentanyl (25 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 prepared by an anaesthetist not involved in the study.

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. In the sitting position, the epidural space was accessed at L3-4 or L4-5 interspace, followed by intrathecal injection using a 25 G spinal needle via a 'needle-through-needle' technique, then the epidural catheter was threaded and fixed. 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. After delivery, all parturients were admitted for at least 24 h for close observation.

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 5 min for the first 20 min, then every 15 min. VAS of the pain during the last uterine contraction before delivery was also recorded. The

sensory block level 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 modified Bromage score (0 = able to lift the extended leg at the hip, 1 = able to flex knee but unable to lift the extended leg, 2 = able to move the foot only and 3 = unable to move even foot) was assessed 5, 15 and 30 min after the intrathecal injection. The need for epidural activation (if VAS became ≥4 before delivery) was recorded. After epidural activation, no parameters were recorded neither in the parturient nor the offspring.

The secondary outcomes included modified Ramsay sedation score (RSS), SpO2, maternal mean arterial pressure (MAP), heart rate (HR), and maternal adverse effects (nausea, vomiting, shivering and post-delivery urine retention). FHR, Apgar score and umbilical cord gases were recorded. Hypotension in this study was defined as systolic blood pressure <90 mmHg or a >20% decrease from the baseline value, while bradycardia was HR <55 beats/min and desaturation as SpO2 <92%. All the outcomes were assessed by a blinded anaesthetist who was not involved in the study.

We planned a study of a continuous response variable from independent controls and experimental subjects with 1 control per experimental subject. In the previous study,[9] the response within each subject group was normally distributed with SD of 12. Considering the true difference in the experimental and control means as 10, we needed to study 31 experimental subject and 31 control subjects to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) of 0.9. The type I error associated with this was 0.05. We recruited 35 subjects for each group in anticipation of any dropout.

## RESULTS

Patient recruitment and flow are presented in Figure 1. One hundred-forty eligible women were included in

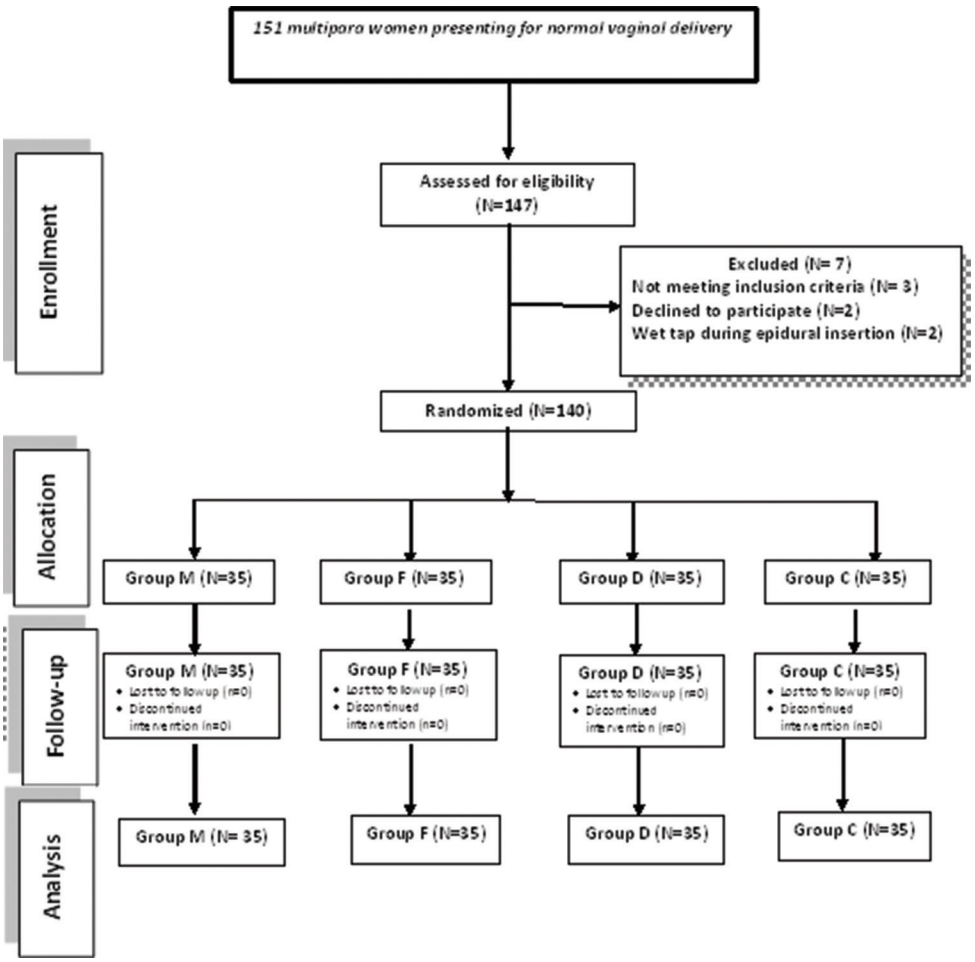


**Figure 1:** Study flowchart

the present study (35 parturients per group). One parturient in group F has undergone emergency cesarean section for persistent foetal bradycardia. There were no significant differences in age, weight, height, gestational age, cervical dilatation, duration of second stage and time to full cervical dilatation among the four groups [Table 1].

Group D showed significantly longer duration of analgesia and S1 regression time than group M ($P = 0.001$ and $P = 0.018$). In group F, these durations were significantly shorter than groups D and M ($P < 0.001$, $P = 0.023$ and $P < 0.001$, $P < 0.001$, respectively) while being significantly longer than group C ($P < 0.001$). A significantly shorter analgesia onset time was recorded in group D than group F ($P < 0.001$) and in both of them than groups M and C ($P < 0.001$). Moreover, the sensory level was significantly higher in groups D and F than groups M and C ($P < 0.001$) [Table 2].

Before the intrathecal injection, all the parturients experienced moderate pain with comparable VAS scores. Starting from 5 min after the intrathecal injection, VAS became significantly lower in groups F and D than groups M and C. Groups M and C parturients showed a comparable VAS to groups F and D at 10 min after the intrathecal injection. Subsequent VAS values till the VAS at the peak of the last uterine contraction before delivery remained comparable among groups M, D and F ($P > 0.05$) while being significantly lower than group C ($P < 0.001$) [Figure 2].

In comparison to the other groups, a significantly more proportion of group D parturients recorded a

**Table 1: Comparison of the four studied groups according to demographic data and labour progress**

| | Group M (n=35) | Group F (n=35) | Group D (n=35) | Group C (n=35) | *P* |
|---|---|---|---|---|---|
| Age (years) | 25.6±1.7 | 25.7±1.8 | 25.8±1.7 | 26.1±2.5 | 0.808 |
| Weight (kg) | 73.0±4.0 | 72.9±3.9 | 72.9±3.9 | 72.7±4.2 | 0.990 |
| Height (cm) | 164.5±1.7 | 164.6±1.8 | 164.7±2.0 | 165.1±3.0 | 0.772 |
| Gestational age (weeks) | 38.9±0.5 | 38.9±0.5 | 38.9±0.6 | 38.9±0.5 | 0.930 |
| Cervical dilatation (cm) | 5.4±0.3 | 5.4±0.3 | 5.3±0.2 | 5.4±0.3 | 0.355 |
| Time to full cervical dilatation (min) | 118.4±6.4 | 120.0±3.2 | 119.2±5.8 | 121.3±3.5 | 0.254 |
| Duration of 2nd stage (min) | 11.83±0.93 | 12.02±1.37 | 12.97±2.43 | 12.28±2.42 | 0.065 |

*P* – *P* value for comparing the four studied groups

**Table 2: Comparison of the four studied groups according to the intrathecal block characteristics and labour progress**

| | Group M (n=35) | Group F (n=35) | Group D (n=35) | Group C (n=35) | *P* |
|---|---|---|---|---|---|
| Duration of analgesia (min.) | 183.7±18.3 | 171.0±13.8 | 199.9±25.3 | 139.6±3.8 | <0.001* |
| Sig. bet. grps. | $P_1$=0.023*, $P_2$=0.001*, $P_3$<0.001*, $P_4$<0.001*, $P_5$<0.001*, $P_6$<0.001* | | | | |
| Analgesia onset time (min.) | 4.0±0.4 | 2.9±0.8 | 2.8±0.6 | 4.4±0.2 | <0.001* |
| Sig. bet. grps. | $P_1$<0.001*, $P_2$<0.001*, $P_3$=0.037*, $P_4$=0.925, $P_5$<0.001*, $P_6$<0.001* | | | | |
| Sensory level | | | | | |
| T8 | 18[a] (51.4%) | 20[a] (57.1%) | 21[a] (60.0%) | 13[a] (37.1%) | 0.003* |
| T9 | 17[a] (48.6%) | 15[a] (42.9%) | 14[a] (40.0%) | 14[a] (40.0%) | |
| T10 | 0[a] (0.0%) | 0[a] (0.0%) | 0[a] (0.0%) | 8[b] (22.9%) | |
| S1 sensory regression time (min.) | 182.3±7.9 | 158.2±8.0 | 188.2±7.9 | 125.3±9.5 | <0.001* |
| Significance between groups | $P_1$<0.001*, $P_2$=0.018*, $P_3$<0.001*, $P_4$<0.001*, $P_5$<0.001*, $P_6$<0.001* | | | | |
| Modified bromage scale 5 min after IT | 0.0±0.0 | 0.0±0.0 | 0.3±0.4 | 0.0±0.0 | <0.001* |
| Significance between groups | $P_1$=1.000, $P_2$<0.001*, $P_3$=1.000, $P_4$<0.001*, $P_5$=1.000, $P_6$<0.001* | | | | |
| Modified bromage scale 15 min after IT | 0.0±0.0 | 0.0±0.0 | 0.5±0.5 | 0.0±0.0 | <0.001* |
| Significance between groups | $P_1$=1.000, $P_2$<0.001*, $P_3$=1.000, $P_4$<0.001*, $P_5$=1.000, $P_6$<0.001* | | | | |
| Modified bromage scale 30 min after IT | 0.0±0.0 | 0.0±0.0 | 0.0±0.0 | 0.0±0.0 | 1.000 |
| VAS at the peak of the last contraction before delivery | 1.4±0.3 | 1.5±0.3 | 1.5±0.3 | 3.0±0.3 | <0.001* |
| Significance between groups | $P_1$=0.123, $P_2$=0.244, $P_3$<0.001*, $P_4$=0.977, $P_5$<0.001*, $P_6$<0.001* | | | | |
| Need for epidural activation before delivery | 0 (0.0%) | 3 (8.6%) | 0 (0.0%) | 9 (25.7%) | <0.001* |

Pairwise comparison between each 2 groups was done using Post Hoc Test (Tukey). *P* – *P* value for comparing the four studied groups. $P_1$ – *P* value for comparing between M group and group F. $P_2$ – *P* value for comparing between M group and group D. $P_3$ – *P* value for comparing between M group and group control. $P_4$ – *P* value for comparing between F group and group D. $P_5$ – *P* value for comparing between F group and group control. $P_6$ – *P* value for comparing between D group and group control. * – Statistically significant at $P \leq 0.05$. Common letters are not significant (i.e. Different letters are significant)

modified Bromage score of 1 at 5 and 15 min after the intrathecal injection ($P < 0.001$). Thirty minutes after the intrathecal injection, all the study parturients had modified Bromage scale of 0 ($P = 1$). None of the study parturients showed modified Bromage score of 2. Epidural activation was needed in 9 (25.7%) and 3 (8.6%) cases in groups C and F, respectively, in comparison to none (0%) in groups M and D ($P < 0.001$). The time to full cervical dilatation was comparable between the study groups ($P > 0.05$) [Table 2].

The highest sedation scores all over the labour process were recorded in group D parturients with a statistical significance at most of the time points ($P < 0.001$). At all measurement time points, the sedation scores were comparable between groups F and M ($P > 0.05$) while being significantly higher than group C ($P < 0.001$) [Figure 3]. The maternal SpO2 values were comparable and within the normal ranges in the studied groups ($P > 0.05$). Maternal MAP and HR were significantly lower in group D in comparison to groups M and C starting from 15 min after the intrathecal injection and in comparison to group F starting from 30 min after the intrathecal injection ($P < 0.05$) [Figures 4 and 5].

In comparison with the other groups, a significantly higher number of group M parturients developed nausea, vomiting, pruritus and post-delivery urine retention ($P < 0.05$). Groups M and F showed a comparable incidence of maternal shivering which was significantly higher than groups D and C ($P = 0.001$) [Table 3]. None of the study patients developed backache, neurological deficit, respiratory depression or post-dural puncture headache.

Regarding the foetal outcomes, there was no significant difference in FHR at any time point during labour among the study groups ($P > 0.05$). FHR tracing showed bradycardia in 3 of group F parturients compared to none of the other groups. The Apgar score at 1 and 5 min, and umbilical artery pH, PCO2 and HCO3 in the 4 groups were comparable and within the normal ranges [Table 4].

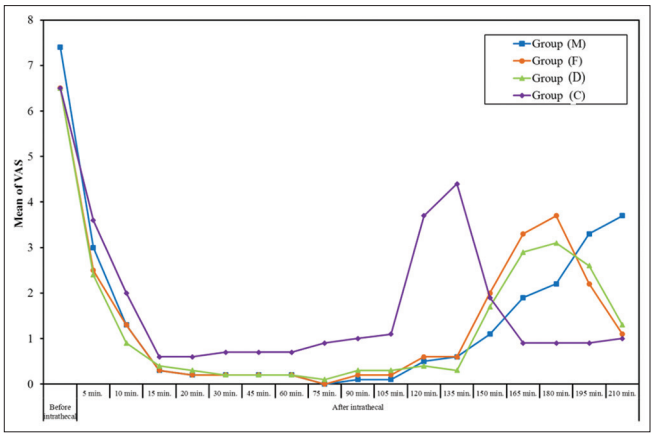


**Figure 2:** Comparison of the four studied groups according to visual analogue Scale (VAS)

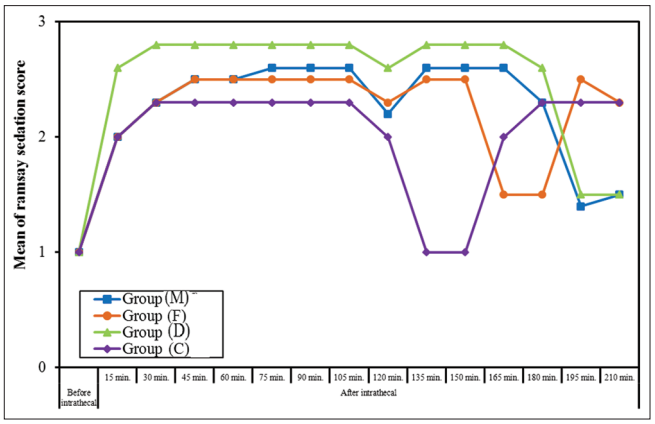


**Figure 3:** Comparison of the four studied groups according to Ramsay Sedation Score (RSS)

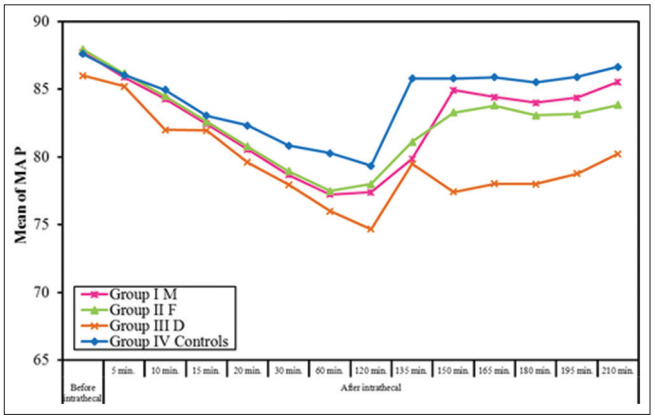


**Figure 4:** Comparison of the four studied groups according to Maternal Mean arterial pressure (MAP)

## DISCUSSION

In this study, we found that, in multiparous women undergoing vaginal delivery, there was a significantly longer analgesia duration with dexmedtomidine than morphine and with morphine than fentanyl when added to intrathecal bupivacaine-dexamethasone. Moreover, there was a significantly more rapid analgesia onset with dexmedetomidine and fentanyl than morphine. Dexmedetomidine was also associated with a better maternal sedation state and lesser incidence of side effects.

**Table 3: Comparison of the four studied groups according to maternal side effects**

| Side effect | Group M (n=35) | Group F (n=31) | Group D (n=35) | Group C (n=26) | *P* |
|---|---|---|---|---|---|
| Maternal Nausea and Vomiting | 14[a] (40.0%) | 10[ab] (32.3%) | 3[c] (8.6%) | 3[bc] (11.5%) | 0.005* |
| Maternal pruritus | 13[a] (37.1%) | 8[a] (25.8%) | 0[b] (0%) | 0[b] (0%) | <0.001* |
| Maternal shivering | 2[a] (5.7%) | 2[a] (6.5%) | 1[a] (2.9%) | 2[a] (7.7%) | 0.915 |
| Post-delivery urine retention | 8[a] (22.9%) | 3[ab] (9.7%) | 0[b] (0%) | 0[b] (0%) | 0.001* |

*P* – *P* value for comparing the studied groups. * – Statistically significant at *P*≤0.05. Common letters are not significant (i.e. Different letters are significant)

**Table 4: Comparison of the four studied groups according to Neonatal parameters**

| | Group M (n=35) | Group F (n=31) | Group D (n=35) | Group C (n=26) | *P* |
|---|---|---|---|---|---|
| APGAR 1 | 7.8±0.4 | 7.74±0.4 | 7.7±0.5 | 7.6±0.6 | 0.459 |
| APGAR 5 | 8.7±0.4 | 8.7±0.5 | 8.7±0.5 | 8.6±0.6 | 0.633 |
| Umbilical pH immediately after delivery | 7.3±0.06 | 7.3±0.0 | 7.3±0.04 | 7.3±0.1 | 0.131 |
| Umbilical $PCO_2$ immediately after delivery | 44.7±0.4 | 44.7±0.4 | 44.6±0.2 | 44.5±0.2 | 0.235 |
| Umbilical $HCO_3$ immediately after delivery | 21.1±0.8 | 21.3±0.8 | 21.4±1.1 | 21.0±1.5 | 0.304 |
| Neonatal HR 5 min after delivery | 138.5±10.3 | 140.7±10.6 | 144.3±9.9 | 141.6±9.7 | 0.130 |
| Neonatal HR 15 min after delivery | 139.6±9.2 | 140.9±9.0 | 142.5±8.7 | 142.6±8.0 | 0.466 |
| Neonatal HR 30 min after delivery | 140.5±8.3 | 142.0±8.7 | 144.5±7 | 143.3±5.8 | 0.172 |

Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey). Statistically significant at *P*≤0.05, HR - Heart rate

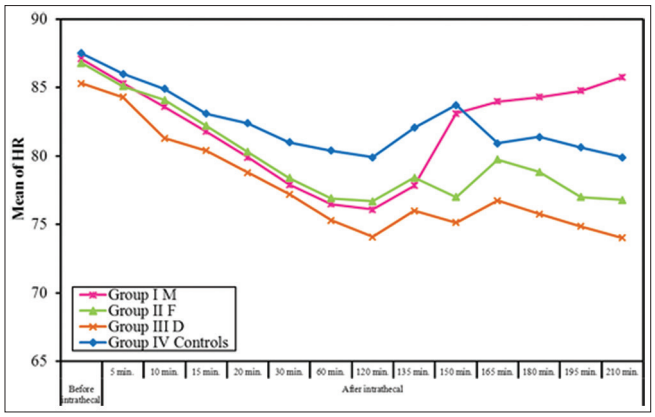


**Figure 5:** Comparison of the four studied groups according to Maternal heart rate (HR)

To date, the use of intrathecal narcotics or local anaesthetics in labour is limited by their short duration of action. Recently, a growing body of evidence has suggested a beneficial role of different adjuvants in the analgesic efficacy of intrathecal anaesthesia.[5,10] Neuraxial opioids provide equipotent analgesia to that of systemically administered opioids with smaller doses and concentrations; thus, it carries less risk of serious side effects.[11,12] On the other hand, intrathecal α2 agonists, e.g., dexmedetomidine, have antinociceptive action for both somatic and visceral pain. They depress the release of C-fiber transmitters and substance P by hyperpolarising the post-synaptic dorsal horn neurons.[12] Reportedly, intrathecal dexamethasone decreases intraspinal prostaglandin, glutamate and substance P production and exerts local actions on nerve fibres leading to analgesic and block prolonging effects.[13,14]

In concordance with the previous reports,[15-19] our results showed that, in comparison to the other groups, there were a significantly more rapid analgesia onset with fentanyl and dexmedetomidine and significantly longer analgesia duration with dexmedetomidine and morphine. Fentanyl also facilitated significantly longer analgesia duration than placebo. The hydrophilic nature of morphine together with the lipophilic nature of fentanyl and dexmedetomidine may have contributed to these findings. Notably, we found longer analgesia durations than that reported by Hess *et al.*[10] and Yeh *et al.*[20] (89 and 90 min, respectively) who used fentanyl (12.5 μg) with bupivacaine (2 mg) and fentanyl (25 μg) with bupivacaine (2.5 mg), respectively. This may be attributed to the added dexamethasone in our study. However, analgesia duration of about 3 h has been reported in the absence of dexamethasone.[21] Dexmedetomidine 5 μg as an adjuvant to intrathecal bupivacaine was recommended in quite lengthy procedures to facilitate excellent analgesia quality with minimal side effects.[22] Comparable analgesia durations have been reported in other studies with different adjuvants but they were associated with a higher incidence of clinically significant side effects like motor block[23] and hypotension.[24] In the current study, the longer analgesia durations were not associated with major maternal or neonatal adverse effects. Furthermore, the peak sensory level was highest with dexmedetomidine followed by fentanyl, morphine and placebo, respectively. Hence, these additives allowed a higher sensory level with such low bupivacaine dose.

Motor function impairment can result in higher instrumental delivery and cesarean section rates. α2 agonists, via binding to motor neurons in the dorsal horn, can potentially induce motor block.[25] However, our study revealed that the potentiated motor block observed with dexmedetomidine regressed completely within 30 min. This indicates that dexmedetomidine should not have affected the maternal expulsive efforts. This coincides with Salgado *et al*.[15] results. This finding can be explained by the low dexmedetomidine dose and the low net concentration of bupivacaine component of the intrathecal cocktail. In consistency with other studies,[26,27] we found that there was no statistically significant difference among the study groups as regards cervical dilatation rate; however, there was a decrease in the durations of the first and second stages of labour in all groups. Thus, this shortening was mostly related to the use of intrathecal analgesia and not related to the drugs used. This could be explained by the preserved motor power and the coordinated action of uterine contractions on the cervix as these contractions became more regular after analgesia which subsequently decreases the circulating catecholamines. This is analogous to the finding reported by Wong *et al*.[28]

It has been reported that although neuraxial analgesia may be associated with some short-term maternal side effects, it does not exacerbate foetal acidosis and may partially protect the foetus from foetal hypoxia. Furthermore, neuraxial analgesia was found to be associated with better neonatal Apgar scores and improvement in acid-base balance compared to systemic analgesia and even in comparison to no analgesia.[29] In concordance with other studies,[22,30] our results revealed comparable FHR trends between the studied groups.

However, it was reported that the rapid onset of intrathecal analgesia causes a rapid decrease in plasma epinephrine and ß-endorphine but not of norepinephrine and oxytocin. This, in turn, increases the uterine tone which increases the uterine vascular resistance and subsequently reduces foetal oxygenation, leading to nonreassuring FHR tracings.[31-33] Then, it was reported that the incidence of foetal bradycardia was significantly increased in parturients receiving an intrathecal opioid compared with any nonintrathecal opioid neuraxial technique. However, the risk of cesarean delivery because of FHR abnormalities was not greater with intrathecal opioids.[34-37]

The three cases of foetal bradycardia reported in our study were associated with uterine hypertonia in the absence of maternal hypotension. The FHR improved in 2 cases after left uterine displacement, increasing the FiO2 and temporary cessation of oxytocin infusion. The third case has shown 2 attacks of foetal bradycardia; the first one (4 min after the intrathecal injection) was relieved with the previously mentioned manoeuvres, while the second attack (47 min later) was persistent (6 min) even after IV nitroglycerine 250 μg. Hence, the obstetrician decided to convert to an emergency cesarean section which was followed by good neonatal outcome. Similar findings were reported by other investigators[34,36] who reported 2 parturients who have undergone emergency cesarean section for persistent foetal bradycardia after intrathecal fentanyl which was also associated with uterine hypertonia in the absence of maternal hypotension. We have no clear explanation for the occurrence of these events with fentanyl but not with dexmedetomidine despite the comparable analgesia onset time with both of them. Louber *et al*.[37] suggested that factors (other than sudden pain relief, imbalance in catecholamines and uterine hypertonia) associated with intrathecal opioids may play a role in the development of FHR abnormalities. Our findings may support this suggestion.

The most significant reported side effects of intrathecal α2 agonists are bradycardia and hypotension due to α2 inhibition of sympathetic preganglionic activity in the spinal medulla.[38] Our results highlighted that although dexmedetomidine adjuvant was associated with a statistically significant lower maternal MAP and HR in comparison to the other groups, the difference was clinically insignificant and did not indicate any intervention as per the study protocol. This is analogous to the findings reported by Mohamed *et al*.[38] and Belhadj *et al*.[39] This finding has been further confirmed by the normal and comparable Apgar scores (at 1 and 5 min) and umbilical cord blood pH and base excess in all the neonates in the current study. This is similar to the findings reported by Fyneface-Ogan *et al*.[9] and Qi *et al*.[40] These findings confirm the safety of dexmedetomidine as an adjuvant despite its statistically significant haemodynamic compromise.

In consistency with the findings of Safari *et al*.,[41] parturients who received dexmedetomidine were more sedated than those of the other groups. This could be due to dexmedetomidine's both anxiolytic and analgesic effects. Its sedative effects could be

mediated by interacting with its receptors in locus coeruleus through circulation of cerebrospinal fluid.[41]

We found, as did other investigators,[18,42,43] higher incidences of pruritis, nausea, vomiting and urine retention with morphine than fentanyl. However, we here report lower incidences for most of these side effects. This may be attributed to the lower doses of these adjuvants together with a possible beneficial effect of dexamethasone.

A limitation of our study is the limited number of parturients. In addition, all our parturients were multiparous; therefore, the results should not be generalised to primipara women. The intrathecal fentanyl associated FHR changes is a point for further research.

## CONCLUSION

Based on the results of this study, in comparison to fentanyl or morphine, dexmedetomidine seems to be a safe and efficacious adjuvant to intrathecal bupivacaine-dexamethasone 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 and/or in whom epidural insertion has failed or not available as in low resource settings.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Dilesh PK, Eapen S, Kiran S, Chopra V. A comparison of intrathecal dexmedetomidine verses intrathecal fentanyl with epidural bupivacaine for combined spinal epidural labor analgesia. J Obstet Anaesth Crit Care 2014;4:69-74.
2. Panni MK, Segal S. Local anesthetic requirements are greater in dystocia than in normal labor. Anesthesiology 2003;98:957-63.
3. Jung H, Kwak KH. Neuraxial analgesia: A review of its effects on the outcome and duration of labor. Korean J Anesthesiol 2013;65:379-84
4. Attanasio L, Kozhimannil KB, Jou J, McPherson ME, Camann W. Women's experiences with neuraxial labor analgesia in the listening to mothers II survey: A content analysis of open-ended responses. Anaesth Analg 2015;121:974.
5. AbdElBarr T, Elshalakany NA, Shafik YM. Single dose spinal analgesia: Is it a good alternative to epidural analgesia in controlling labour pain? Egy J Anaesth 2014;30:241-6.
6. Missant C, Teunkens A, Vandermeersch E, Van de Velde M. Intrathecal clonidine prolongs labour analgesia but worsens fetal outcome: A pilot study. Can J Anaesth 2004;51:696.
7. Aguilar-Montiel M, Carrillo-Torres O. Remifentanil and dexmedetomidine as an alternative to regional analgesia in obstetrics. Rev Med Hosp Gen Mex 2017;80:67-70.
8. Swain A, Nag DS, Sahu S, Samaddar DP. Adjuvants to local anesthetics: Current understanding and future trends. World J Clin Cases 2017;5:307.
9. Fyneface-Ogan S, Gogo Job O, Enyindah CE. Comparative effects of single shot intrathecal bupivacaine with dexmedetomidine and bupivacaine with fentanyl on labor outcome. ISRN Anesthesiol 2012. doi.org/10.5402/2012/816984.
10. Hess PE, Vasudevan A, Snowman C, Pratt SD. Small dose bupivacaine-fentanyl spinal analgesia combined with morphine for labor. Anaesth Analg 2003;97:247-52.
11. Carvalho B. Respiratory depression after neuraxial opioids in the obstetric setting. Anaesth Analg 2008;107:956-61.
12. Cascio M, Pygon B, Bernett C, Ramanathan S. Labour analgesia with intrathecal fentanyl decreases maternal stress. Can J Anaesth 1997;44:605-9.
13. Kim JE, Kim NY, Lee HS, Kil HK. Effects of intrathecal dexmedetomidine on low-dose bupivacaine spinal anesthesia in elderly patients undergoing transurethral prostatectomy. Biol Pharm Bull 2013;36:959-65.
14. Bani-Hashem N, Hassan-Nasab B, Pour EA, Maleh PA, Nabavi A, Jabbari A. Addition of intrathecal Dexamethasone to Bupivacaine for spinal anesthesia in orthopedic surgery. Saudi J Anaesth 2011;5:382.
15. Salgado PF, Sabbag AT, Silva PC, Brienze SL, Dalto HP, Módolo NS, *et al.* Synergistic effect between dexmedetomidine and 0.75% ropivacaine in epidural anesthesia. Rev Assoc Med Bras (1992) 2008;54:110-5.
16. Harada Y, Nishioka K, Kitahata LM, Kishikawa K, Collins JG. Visceral antinociceptive effects of spinal clonidine combined with morphine, [D-Pen sup 2, D-Pen sup 5] enkephalin, or U50, 488H. Anaesthesiology 1995;83:344-52.
17. Lee BB, Kee WN, Hung VY, Wong EL. Combined spinal–epidural analgesia in labour: Comparison of two doses of intrathecal bupivacaine with fentanyl. BJA 1999;83:868-71.
18. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, *et al.* Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand 2006;50:222-7.
19. Mohamed T, Susheela I, Balakrishnan BP, Kaniyil S. Dexmedetomidine as adjuvant to lower doses of intrathecal bupivacaine for lower limb orthopedic surgeries. Anesth Essays Res 2017;11:681.
20. Yeh HM, Chen LK, Shyu MK, Lin CJ, Sun WZ, Wang MJ, *et al.* The addition of morphine prolongs fentanyl-bupivacaine spinal analgesia for the relief of labor pain. Anesth Analg 2001;92:665-8.
21. Pace MC, Aurilio C, Bulletti C, Iannotti M, Passavanti MB, Palagiano A. Subarachnoid analgesia in advanced labor: A comparison of subarachnoid analgesia and pudendal block in advanced labor: Analgesic quality and obstetric outcome. Ann N Y Acad Sci 2004;1034:356-63.
22. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, *et al.* Effect of dexmedetomidine

added to spinal bupivacaine for urological procedures. Saudi Med J 2009;30:365-70.
23. Campbell DC, Banner R, Crone LA, Gore-Hickman W, Yip RW. Addition of epinephrine to intrathecal bupivacaine and sufentanil for ambulatory labor analgesia. Anesthesiol 1997;86:525-31.
24. D'Angelo R, Evans E, Dean LA, Gaver R, Eisenach JC. Spinal clonidine prolongs labor analgesia from spinal sufentanil and bupivacaine. Anesth Analg 1999;88:573-6.
25. Anabah T, Olufolabi A, Boyd J, George R. Low-dose spinal anaesthesia provides effective labour analgesia and does not limit ambulation. South Afr J Anaesth Analg 2015;21:19-22.
26. Miro M, Guasch E, Gilsanz F. Comparison of epidural analgesia with combined spinal-epidural analgesia for labor: A retrospective study of 6497 cases. Int J obst Anaesth 2008;17:15-9.
27. Anim-Somuah M, Smyth RM, Jones L. Epidural versus non-epidural or no analgesia in labour. Cochrane Database Syst Rev 2011:CD000331. doi: 10.1002/14651858.CD000331.pub3.
28. Wong CA, Scavone BM, Peaceman AM, McCarthy RJ, Sullivan JT, Diaz NT, *et al.* The risk of cesarean delivery with neuraxial analgesia given early versus late in labor. NEJM 2005;352:655-65.
29. Reynolds F. The effects of maternal labour analgesia on the fetus. Best Pract Res Clin Obstet Gynaecol 2010;24:289-302.
30. Owen MD, Özsaraç Ö, Şahin Ş, Uçkunkaya N, Kaplan N, Mağunaci I. Low-dose clonidine and neostigmine prolong the duration of intrathecal bupivacaine–fentanyl for labor analgesia. Anaesthesiology 2000;92:361-.
31. Hattler J, Klimek M, Rossaint R, Heesen M. The effect of combined spinal–epidural versus epidural analgesia in laboring women on nonreassuring fetal heart rate tracings: Systematic review and meta-analysis. Anaesth Analg 2016;123:955-64.
32. Abrão KC, Francisco RP, Miyadahira S, Cicarelli DD, Zugaib M. Elevation of uterine basal tone and fetal heart rate abnormalities after labor analgesia: A randomized controlled trial. Obst Gynecol 2009;113:41-7.
33. Al-Kazwini H, Sandven I, Dahl V, Rosseland LA. Prolonging the duration of single-shot intrathecal labour analgesia with morphine: A systematic review. Scand J Pain 2016;13:36-42.
34. Clarke VT, Smiley RM, Finster M. Uterine hyperactivity after intrathecal injection of fentanyl for analgesia during labor: A cause of fetal bradycardia? Anesthesiology 1994;81:1083.
35. Chatrath V, Khetarpal R, Sharma S, Kumari P. Fentanyl versus tramadol with levobupivacaine for combined spinal-epidural analgesia in labor. Saudi J Anaesth 2015;9:263.
36. Côrtes CA, Sanchez CA, Oliveira AS, Sanchez FM. Labor analgesia: A comparative study between combined spinal-epidural anaesthesia versus continuous epidural anesthesia. Rev Bras Anestesiol 2007;57:39-51.
37. Loubert C, Hinova A, Fernando R. Update on modern neuraxial analgesia in labour: A review of the literature of the last 5 years. Anaesthesia 2011;66:191-212.
38. Mohamed AA, Fares KM, Mohamed SA. Efficacy of intrathecally administered dexmedetomidine versus dexmedetomidine with fentanyl in patients undergoing major abdominal cancer surgery. Pain Physician 2012;15:339-48.
39. Belhadj MA, Draief A, Ouezini R, Dhahri S, Jebali A, Lamine K, *et al.* 30 microg intrathecal clonidine prolongs labour analgesia, but increases the incidence of hypotension and abnormal foetal heart rate patterns. Ann Fr Anaesth Reanim 2007;26:916-20.
40. Qi X, Chen D, Li G, Huang X, Li Y, Wang X, *et al.* Comparison of intrathecal dexmedetomidine with morphine as adjuvants in cesarean sections. Biol Pharm Bull 2016;39:1455-60.
41. Safari F, Aminnejad R, Mohajerani SA, Farivar F, Mottaghi K, Safdari H. Intrathecal dexmedetomidine and fentanyl as adjuvant to bupivacaine on duration of spinal block in addicted patients. Anaesth Pain Med 2016;6:e26714
42. Weigl W, Bieryło A, Wielgus M, Krzemień-Wiczyńska Ś, Kołacz M, Dąbrowski MJ. Perioperative analgesia after intrathecal fentanyl and morphine or morphine alone for cesarean section: A randomized controlled study. Medicine (Baltimore) 2017;96:e8892.
43. Wu JL, Hsu MS, Hsu TC, Chen LH, Yang WJ, Tsai YC. The efficacy of intrathecal coadministration of morphine and bupivacaine for labor analgesia. Acta Anaesthesiol Sin 1997;35:209-16.