



## INTRATHECAL DEXMEDETOMIDINE-FENTANYL FOR LABOR ANALGESIA: A COMPARATIVE PROSPECTIVE STUDY

Dr. Nitin P Chopade

Assistant Professor Dept. of Anesthesiology Amaltas Institute of Medical Sciences, Village, Bangar, Dewas Ujjain Highway, District, Dewas MP

**Article Info:** Received 02 January 2020; Accepted 30 January. 2020

**Corresponding author:** Dr. Nitin P Chopade

**Conflict of interest statement:** No conflict of interest

### ABSTRACT:

**BACKGROUND:** Women have reported the agony they experience during childbirth as being severe and frequent, and they often have few or no choices for pain management, particularly in developing nations. In many low resource settings, sedatives and parenteral opioids are the most often recommended medications for women in labor. It has been demonstrated that his approach to pain treatment has little to no impact on labor discomfort. One of the main aims of maternity care is to relieve pain during labor. Combining spinal and epidural analgesia is a well-known method for reducing labor pain with no risk to the mother or fetus. Dexmedetomidine has been used intrathecally with bupivacaine for prolonged postoperative analgesia. It is a highly selective alpha 2 adrenoreceptor agonist with analgesic effects. It is highly lipophilic and barely crosses the placenta, according to recent evaluations.

**AIM:** The study's objective was to compare the effects of intrathecal dexmedetomidine and fentanyl to those of either drug alone on mother and newborn outcomes during labor.

**MATERIAL AND METHOD:** The department of anesthesia conducted this comparative prospective observational study. All participants gave their informed and written agreement to be included in the study and to have their data used for the current research project. 100 pregnant women who were full term and admitted to the obstetric department for safe confinement made up the participants. The study was conducted in a designated labor room of the obstetrics division of a teaching hospital with tertiary care. A multipara monitor, ultrasound, anesthetic workstation, and resuscitation supplies are available in the delivery room. The pregnant moms have described the benefits and process of labor analgesia. For every patient to be included in the trial, the approval of an obstetrician was required.

**RESULTS:** 120 parturient in all met the inclusion requirements, 110 of them gave their consent and were subsequently recruited in the study after the inclusion criteria were applied. According to the exclusion criteria, ten patients were disqualified. once the predetermined sample size of 100 patients has been reached. The study of the block quality showed that Group A experienced analgesia sooner than Group B. Statistics showed that the differences were substantial. In Group A, the analgesia lasted longer as well. According to the examination of motor block, Group A has more motor block than Group B has. According to the analysis of side effects, pruritus, hypotension, bradycardia, shivering, and nausea were the most frequent side effects.

**CONCLUSION:** Contrary to dexmedetomidine or fentanyl used alone, intrathecal dexmedetomidine prolongs the duration of analgesia and reduces the prevalence of side effects. A secure and reliable technique for labor analgesia is the use of an intrathecal adjuvant walking epidural. With intrathecal dexmedetomidine, the block's intensity and duration are greater. The likelihood of a normal vaginal birth is increased with fentanyl. Dexmedetomidine should not be used as an intrathecal adjuvant for labor analgesia; fentanyl should. Compared to fentanyl, it offers an acceptable level of labor analgesia with a longer analgesic duration.

**KEYWORDS:** Analgesia, Dexmedetomidine, Fentanyl, Labor, Neonatal and labor analgesia

### Introduction:

Labor is one of the most painful physiological conditions experienced by women in their lives. Labor pain ranks second or third among all painful

conditions and consistently more than 7 on a 10-point scale.<sup>1,2</sup> Clinicians have been using techniques to lessen the severity of labor pain ever since the Middle Ages. The "etherization of labor"

by James Young Simpson, who successfully gave labor analgesia to a woman with a malformed pelvis, marked the start of the contemporary era of labor analgesia.<sup>3</sup> The mother and fetus experience a variety of negative physical and psychological effects as a result of the terrible labor pain. Hypoxemia in the mother and fetus is brought on by painful uterine contractions that result in hyperventilation and excessive catecholamine levels. The widely used method of combined spinal epidural (CSE) analgesia reduces labor pain with little harm to the mother or fetus.<sup>4</sup> The mother and fetus experience a variety of negative physical and psychological effects as a result of the terrible labor pain.

Hypoxemia in the mother and fetus is brought on by hyperventilation and elevated catecholamine levels brought on by labor pain and uncomfortable uterine contractions.<sup>5,6</sup> Comforting the patient and reducing the release of stress hormones are two benefits of pain alleviation.<sup>7</sup> In addition to bringing comfort to the patient, pain medication also reduces the release of stress hormones, which can deplete the parturient's reserves and starve the fetus of oxygen and nutrition.<sup>8</sup> Today, it is understood that providing good labor analgesia might lessen the uterine contractility-inhibiting effects of endogenous mother catecholamine, lessen maternal acidosis, and enhance intrapartum maternal wellbeing.

The widely used method of combined spinal epidural (CSE) analgesia reduces labor pain with little harm to the mother or fetus.<sup>9</sup> Intrathecal opioids are increasingly popular for labor analgesia, yet there is little evidence to support their use. Fentanyl is a strong and short-acting synthetic narcotic that is a derivative of phenyl piperidine. Fentanyl is regarded as an excellent alternative for labor pain management due to its short half-life. In order to reduce motor block during labor, fentanyl and bupivacaine have been utilized widely. Nevertheless, adding opioids to local anesthetics has the drawbacks of itching and respiratory depression.

In order to reduce motor block during labor, fentanyl and bupivacaine have been utilized widely. Nevertheless, adding opioids to local anesthetics has the drawbacks of itching and respiratory depression.<sup>10</sup> Dexmedetomidine, an extremely potent and selective alpha 2 adrenergic agonist, has been used in combination with spinal bupivacaine to prolong postoperative analgesia because of its inherent analgesic qualities. Current analyses of the use of dexmedetomidine during pregnancy have demonstrated that, due to its high placental retention, it does not cross the placenta significantly.<sup>11</sup>

Dexmedetomidine has been used intravenously and epidurally in labor in numerous studies without causing any negative effects on the mother or fetus.<sup>12,13</sup> Dexmedetomidine is a highly selective alpha 2 adrenergic agonist that has inherent analgesic characteristics and has been used intrathecally to prolong postoperative analgesia.<sup>14</sup> As there is little placental transfer, the fetus should experience little to no change. Dexmedetomidine offers the benefit of lowering blood pressure because it controls catecholamine release. Dexmedetomidine occasionally causes bradycardia and hypotension in the mother, which could be harmful.<sup>15</sup> Intrathecally or intravenously administering dexmedetomidine during pregnancy is still considered off-label. Dexmedetomidine has a sympatholytic action that can lessen the stress response to surgery and an analgesic-sparing effect that considerably reduces the need for opioids.<sup>16,17</sup>

## MATERIAL AND METHODS

This comparative prospective observational study was carried out in the department of Anesthesia. All participants gave their informed and written agreement to be included in the study and to have their data used for the current research project. 100 pregnant women who were full term and admitted to the obstetric department for safe confinement made up the participants. The study was conducted in a designated labor room of the obstetrics division of a teaching hospital with tertiary care. A multipara monitor, ultrasound, anesthetic workstation, and resuscitation supplies are available in the delivery room. The pregnant moms have described the benefits and process of labor analgesia. For every patient to be included in the trial, the approval of an obstetrician was required. After discussing the effects of the medications used for labor analgesia, the patient provided written and informed consent to participate in the observational study.

### The inclusion criteria were as follows:

- Prebooked patients who had given consent for labor analgesia
- Age: 20–40 years
- Body mass index <35 kg.m<sup>-2</sup>
- American Society of Anesthesiology Classification Status I or II.

### The exclusion criteria were as follows:

- Any condition that contraindicates the administration of central neuraxial blockade (such as coagulopathy or hypovolemic shock)
- Gestational age <36 weeks

- Obstetric complications such as preeclampsia, pregnancy-induced hypertension, gestational diabetes, or cephalopelvic disproportion
- Patients in the second stage of labor or on oxytocin infusion

All participants who met the inclusion criteria were randomized into two groups (A and B) using computer-generated randomization. Under aseptic precautions, labor analgesia was administered through a combined spinal–epidural technique using an 18G Tuohy needle and a 27G spinal needle in the left lateral position. The drugs and volumes administered were as follows:

- Group A: Bupivacaine 2.5 mg (0.5 mL diluted to 2 mL) + 20 µg dexmedetomidine in 1 mL saline intrathecally (total volume: 3 mL)
- Group B: Bupivacaine 2.5 mg (0.5 mL diluted to 2 mL) + fentanyl (15 µg) in 1 mL saline intrathecally (total volume: 3 mL).

The syringes were disguised, and the medical staff—who are unaware of the composition—performed the drug administration and following patient monitoring. On the patient's request, epidural top-up was given in both groups through the catheter. The medication was bupivacaine 0.125%.

hepatic information Blood pressure, pulse rate, oxygen saturation, and respiration rate were all non-invasively measured. The doctor displayed the fetal heart rate, cervical dilation, and stage and progress of labor. When the patient was experiencing active labor, the administration of intrathecal analgesia should have started. The period of time prior to the intrathecal medication injection was referred to as the baseline. When a VAS less than 3 was recorded after intrathecal injection, analgesia had begun. After that, VAS was measured once per minute for 10 minutes, then every 10 minutes until it achieved a value of 3. The period from the intrathecal injection until the VAS reached more than 3 and required

further analgesia through the epidural catheter was used to define the duration of analgesia.

Following the intrathecal injection, the mother's heart rate and non-invasive blood pressure were monitored every five minutes. Hypotension, defined as a 20% or greater drop in blood pressure from baseline, and bradycardia, defined as a heart rate under 60, were both treated right away with intravenous fluids, ephedrine, or atropine, as necessary. A cardiotocograph was used to detect and treat fetal bradycardia, which was initially managed by giving the mother oxygen while positioning her on her side to prevent aortocaval compression. There were also reported adverse effects include itching, nausea, and respiratory depression. pruritus was treated with i.v. diphenhydramine 50 mg and 10 mg oral loratadine and nausea and vomiting were treated with ondansetron 4 mg. Modes of delivery were recorded. Neonatal outcomes like; neonatal Apgar score and umbilical cord blood pH were recorded.

#### STATISTICAL ANALYSIS

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM, Chicago, IL). Data are presented as mean ±SD or numbers as appropriate. Patient characteristics (age, weight, height, parity, and gestational age), onset and duration of analgesia, and pH of the umbilical artery were analyzed using the independent two-sample t-test. Other parameters were studied using the Chi-square test or Fisher's exact test as appropriate.

#### RESULT:

A total of 120 parturient fulfilled the inclusion criteria, of whom 110 patients provided consent and were subsequently enrolled in the study after applying the inclusion criteria. Ten patients were excluded based on the exclusion criteria. After reaching the preselected sample size of 100 patients. The demographic and baseline variables are shown in Table 1 and were statistically similar

**Table 1: Demographic and baseline parameters among participants**

Parameters	Mean±SD	
	Group A (n=50)	Group B (n=50)
Age (years)	23.80±2.76	24.66±1.86
Weight (kg)	61.27±5.52	55.05±6.86
Height (cm)	152.85±3.18	153.50±3.93
Heart rate (bpm)	106.12±5.12	102.80±6.51
SBP (mmHg)	113.38±3.33	112.29±6.32
DBP (mmHg)	70.18±5.81	71.12±6.73
MAP (mmHg)	81.22±3.52	83.10±6.42
SpO <sub>2</sub> (%)	94.31±0.64	92.33±0.69
VAS score	7.87±0.86	6.72±1.02

**Table 2: Mode of delivery among participants**

Mode of delivery	Group A (N=50)	Group B (N=50)
Normal (n=65)	30	35
Instrumental vaginal delivery (n=8)	5	3
Cesarean delivery (n=27)	15	12

A total of 100 patients reported sufficient analgesia (Group A: 50; Group B: 50), and 65 patients delivered vaginally (Group A: 30; Group B: 35), indicating an overall success rate of 61.66%; however, the success rate was significantly higher in Group B. The rates of forceps-assisted vaginal delivery and cesarean delivery were higher in Group A.

**Table 3: Quality of block among the participants**

Parameter	Mean±SD	
	Group A (N=50)	Group B (N=50)
Onset time (s)	57.22±15.20	85.50±23.30
Duration of analgesia (min)(VAS score <3)	117.11±21.17	102.21±15.81
Degree of the motor block as on the Bromage Scale	3.10±0.88	3.77±0.83
Top-up required in first 6 h	6.20±1.33	10.32±3.34

The analysis of the quality of the block revealed an earlier onset of analgesia in Group A than in Group B. The differences were statistically significant. The duration of analgesia was also higher in Group A. The analysis of motor block reveals a higher degree of motor block in Group A than that in Group B.

**Table 4: Incidence of maternal and fetal side effects in both the groups**

Parameter	Mean±SD	
	Group A (N=50)	Group B (N=50)
Pruritus	0	21
Hypotension	5	3
Bradycardia	4	2
Nausea	1	3
Vomiting	0	1

Pruritus was shown to be the most frequent side effect (although it was only noticed in Group B), followed by hypotension, bradycardia, shivering, and nausea, according to the analysis of negative effects. There were no abnormalities in the umbilical artery and uterine blood flow, according to fetal ultrasonography and Doppler study. With a lower pulsatility index, Group A saw less variation in heart rate. Both procedures were safe, as shown by the study of fetal data, and all neonates in both groups were confirmed to be safe and healthy after 6 weeks of birth.

#### DISCUSSION

Myths and disputes have always surrounded labor pain relief. Hence, providing efficient and secure analgesia during childbirth has continued to be difficult. Over time, labor analgesia has changed to reduce motor blockage, allow for walking epidurals, and prevent labor from being prolonged. Together with local anesthetics, lipophilic opioids like

fentanyl have been utilized for labor analgesia widely intrathecally and epidurally. Dexmedetomidine is a selective alpha 2 adrenoreceptor agonist that has been used as an adjuvant in spinal and epidural anesthesia. It offers a number of benefits over local anesthetics alone, including a longer duration of analgesia and no negative neurological effects.<sup>18,19</sup> However, in order to successfully perform a normal vaginal delivery, the severity of the block must be balanced during labor analgesia to prevent any motor block. Adjuvants have long been utilized in spinal anesthesia in clinical practice, and they are increasingly becoming more common in labor spinal analgesia.

Niu et al 2013<sup>14</sup> in their meta-analysis showed that intrathecal dexmedetomidine prolonged the duration of spinal anesthesia and improved postoperative analgesia and did not increase the incidence of hypotension and adverse events. Wong et al.2004<sup>20</sup>

investigated the efficacy of various doses of fentanyl as an adjuvant for labor spinal analgesia; they concluded that 15 µg was a safe and effective dose of fentanyl. This forms the basis of using a 15 µg dose of fentanyl in the current study. **Ezz Gehan et al.2017**<sup>21</sup> used 20 µg dexmedetomidine intrathecally, which formed the basis of the dexmedetomidine dose in this study. Dexmedetomidine has high placental retention (0.77 maternal/fetal index) and does not cross the placenta significantly. Being highly lipophilic like fentanyl it is retained in placental tissue. Studies show that dexmedetomidine has high placental retention and increases the frequency and amplitude of uterine contractions directly and in a dose-dependent fashion suggesting advantages for use as an analgesic adjunct during labor.<sup>22</sup> **Fyनेface-Ogan et al.2012**<sup>23</sup> compared 2.5 µg dexmedetomidine intrathecally along with 2.5 mg hyperbaric bupivacaine versus bupivacaine and fentanyl intrathecally in labor and has shown that dexmedetomidine along with bupivacaine intrathecally significantly prolonged sensory block in laboring women.

Dexmedetomidine has been shown in studies to have significant placental retention and to directly and dose-dependently increase the frequency and amplitude of uterine contractions, suggesting potential benefits for usage as an auxiliary analgesic during labor.<sup>11</sup> Dexmedetomidine was therefore expected to produce great analgesia and have no motor block after intrathecal delivery, making it an appropriate medication for labor analgesia. Its intrathecal usage in labor, however, continues to be against the rules. There were no expected negative effects on the infant due to the 10 g dose used in this study, which was lower than prior intravenous doses utilized during pregnancy. Dexmedetomidine inhibits the firing of nociceptive neurons triggered by peripheral A and C fibers by acting on receptors in the substantia gelatinosa of the dorsal horn of the spinal cord. Moreover, it prevents the release of substance P, a nociceptive neurotransmitter.<sup>24</sup>

**Al-Mustafa et al 2009**<sup>25</sup> and **Hala et al 2011**<sup>26</sup> observed dose-dependent prolongation of the duration of action of analgesia with reduced analgesic requirement when intrathecal dexmedetomidine dosages increased (5, 10, and 15 µg). Similar to our findings **Mahdy et al 2011**<sup>27</sup> found that after intrathecal dexmedetomidine and fentanyl injection, there were no adverse effects on mothers or babies in any group. **Palanisamy et al 2009**<sup>28</sup> used i.v. dexmedetomidine successfully as an adjunct to opioid-based PCA and general anesthesia

for the respective provider of labor analgesia and cesarean delivery anesthesia in a parturient with a tethered spinal cord, with favorable maternal and neonatal outcomes.

Therefore, it is suggested that with the prolonged duration of analgesia shown by intrathecal dexmedetomidine and fentanyl, along with a lack of side effects (such as sedation, respiratory depression, hypotension in the mother, and neonatal depression), could be considered an appealing alternative for labor analgesia. The findings of this study will be important in low-resource economies where there is a lack of equipment, accessories, and knowledge necessary to implement an epidural analgesia service.<sup>29</sup> Intrathecal bupivacaine/dexmedetomidine may be the only medication given as a single shot to multiparous women in labor due to the prolonged time of analgesia it displayed in our study. Dexmedetomidine may have additional benefits for women going through labor and delivery because it does not have any negative side effects including drowsiness, respiratory depression, maternal hypotension, or newborn depression. Although this study advances our understanding of dexmedetomidine, more research may be required to fully understand how this drug works to relieve labor pain. Yet, this trial demonstrated that intrathecal low-dose dexmedetomidine administered in a single shot had significant potential to reduce discomfort during labor and delivery. In primiparous women in labor and childbirth, a greater dose of intrathecal DMT may be required in order to achieve a more potent and longer block.

#### CONCLUSION:

Contrary to dexmedetomidine or fentanyl used alone, intrathecal dexmedetomidine prolongs the duration of analgesia and reduces the prevalence of side effects. A secure and reliable technique for labor analgesia is the use of an intrathecal adjuvant walking epidural. With intrathecal dexmedetomidine, the block's intensity and duration are greater. The likelihood of a normal vaginal birth is increased with fentanyl. Dexmedetomidine should not be used as an intrathecal adjuvant for labor analgesia; fentanyl should. Compared to fentanyl, it offers an acceptable level of labor analgesia with a longer analgesic duration. It keeps hemodynamic stability while having no negative effects on the mother or the baby.

#### REFERENCES:

1. Beigi NM, Broumandfar K, Bahadoran P, Abedi HA. Women's experience of pain during

- childbirth. *Iran J Nurs Midwifery Res* 2010;15:77-82.
2. Labor S, Maguire S. The pain of labor. *Rev Pain* 2008;2:15-9.
  3. Cohen J. Doctor James Young Simpson, Rabbi Abraham De Sola, and Genesis,. *Obstet Gynecol* 1996;88:895-8.
  4. Collis RE, Davies DW, Aveling W. Randomised comparison of combined spinal-epidural and standard epidural analgesia in labor. *Lancet* 1995;345:1413-6.
  5. Mohamed AA and Salem RA. Intrathecal dexmedetomidine fentanyl for labor analgesia: a randomized comparative study..*J Anaesthesiol Clin Sci*. 2015; 4:1.
  6. Dilesh PK, Eapen S, Kiran S, Chopra V. A comparison of intrathecal dexmedetomidine versus intrathecal fentanyl with epidural bupivacaine for combined spinal epidural labor analgesia. *J Obstet Anaesth Crit Care* 2014;4:69-74.
  7. Onah HE, Obi SN, Oguanuo TC, Ezike HA, Ogbuokiri CM and Ezugworie JO. Pain perception among parturient in Enugu, South-eastern Nigeria. *J Obstet Gynaecol*. 2007; 27:585-8.
  8. H. E. Onah, S. N. Obi, T. C. Oguanuo, H. A. Ezike, C. M. Ogbuokiri, and J. O. Ezugworie, "Pain perception among parturient in Enugu, South-Eastern Nigeria," *Journal of Obstetrics and Gynaecology*, 2007;27(6):585–588.
  9. Collis RE, Davies DW, Aveling W. Randomised comparison of combined spinal-epidural and standard epidural analgesia in labor. *Lancet* 1995;345:1413-6
  10. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. *J Anaesthesiol Clin Pharmacol* 2011;27:339-43.
  11. Nair AS, Sriprakash K. Dexmedetomidine in pregnancy: Review of literature and possible use. *J Obstet Anaesth Crit Care* 2013;3:3-6.
  12. Abu-Halaweh SA, Al Oweidi AK, Abu-Malooh H, Zabalawi M, Alkazaleh F, Abu-Ali H, et al. Intravenous dexmedetomidine infusion for labor analgesia in patients with preeclampsia. *Eur J Anaesthesiol* 2009;26:86-7.
  13. Palanisamy A, Klickovich RJ, Ramsay M, Ouyang DW, Tsen LC. Intravenous dexmedetomidine as an adjunct for labor analgesia and cesarean delivery anesthesia in a parturient with a tethered spinal cord. *Int J Obstet Anesth* 2009;18:258-61.
  14. Niu XY, Ding XB, Guo T, Chen MH, Fu SK, Li Q. Effects of intravenous and intrathecal dexmedetomidine in spinal anesthesia: A meta-analysis. *CNS Neurosci Ther* 2013;19:897-904.
  15. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. *J Anaesthesiol Clin Pharmacol* 2011;27:339-43.
  16. Venn RM, Hell J, and Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. *Crit Care*. 2000; 4:302-8.
  17. Taghinia AH, Shapiro FE, and Slavin SA. Dexmedetomidine in aesthetic facial surgery: improving anesthetic safety and efficacy. *Plast Reconstr Surg*. 2008; 121:269-76
  18. Grewal A. Dexmedetomidine: New avenues. *J Anaesthesiol Clin Pharmacol* 2011;27:297-302.
  19. Mahendru V, Tewari A, Katyal S, Grewal A, Singh MR, Katyal R. A comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double-blind controlled study. *J Anaesthesiol Clin Pharmacol* 2013;29:496-502
  20. Wong CA, Scavone BM, Slavenas JP, Vidovich MI, Peaceman AM, Ganchiff JN, et al. Efficacy and side effect profile of varying doses of intrathecal fentanyl added to bupivacaine for labor analgesia. *Int J Obstet Anesth* 2004;13:19-24.
  21. Ezz Gehan F, Fathi Heba M, Abd Eldayem Hussein M. Effect of intrathecal dexmedetomidine on the quality of combined spinal epidural analgesia and obstetric outcome during vaginal delivery. *Res Opin Anesth Intensive Care* 2017;4:23-9.
  22. Karaman S, Evren V, Firat V, Cankayali I. The effects of dexmedetomidine on spontaneous contractions of isolated gravid rat myometrium. *Adv* 2006;23:238-43.
  23. Fyneyface-Ogan S, Job OG, Enyindah CE. Comparative effects of single shot intrathecal bupivacaine with dexmedetomidine and bupivacaine with fentanyl on labor outcome. *ISRN Anesthesiol* 2012.
  24. Candiotti KA, Bergese SD, Bokesch PM, Feldman MA, Wisemandle W, Bekker AY, et al. Monitored anesthesia care with dexmedetomidine: A prospective, randomized,

- double-blind, multicenter trial. *Anesth Analg* 2010;110:47- 56.
25. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, Al-Edwan GM, and Ramsay MA. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. *Saudi Med J*. 2009; 30:365-70.
26. Hala EA, Shafie MA and Youssef H. Dose-related prolongation of hyperbaric bupivacaine spinal anesthesia by dexmedetomidine. *Ain Shams J Anesthesiol*. 2011; 4:83- 95.
27. Mahdy WR and Abdullah SI. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics and neonatal outcome in uncomplicated cesarean delivery: A randomized double-blind placebo-controlled study. *Menoufiya Medical Journal*. 2011; 24:221-32.
28. Palanisamy A, Klickovich RJ, Ramsay M, Ouyang DW and Tsen LC. Intravenous dexmedetomidine as an adjunct for labor analgesia and cesarean delivery anesthesia in a parturient with a tethered spinal cord. *Int J Obstet Anesth*. 2009; 18:258-61.
29. C. O. Imarengiaye, "Trends in pain relief in labor: implications for obstetric analgesia service in Nigeria," *Nigerian Postgraduate Medical Journal*, 2005;12(3) 193–202, 2005