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Clinical Study

Comparative Effects of Single Shot Intrathecal Bupivacaine with Dexmedetomidine and Bupivacaine with Fentanyl on Labor Outcome

S. Fyneface-Ogan,[1] O. Gogo Job,[1] and C. E. Enyindah[2]

[1] *Obstetric Anesthesia Unit, Department of Anesthesia, University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria*
[2] *Department Obstetrics and Gynecology, University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria*

Correspondence should be addressed to S. Fyneface-Ogan, soglonye@yahoo.com

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Background. Effective intrapartum analgesia attenuates pain, stress, and anxiety which cause release of stress hormones as well as beta-endorphins. *Aim*. The purpose of this study was to determine the effect of adding dexmedetomidine to hyperbaric bupivacaine for neuraxial analgesia for labor. *Methods*. Ninety laboring multiparous women were allocated to have single shot intrathecal bupivacaine alone (B), bupivacaine with fentanyl (BF), or bupivacaine with dexmedetomidine (BD). Sensory and motor block characteristics; time from injection to two dermatome sensory regression, sensory regression to S1 dermatome, and motor block regression to Bromage 1 were recorded. Labor pain was assessed with a 10 cm verbal pain scale. *Results*. Peak sensory block levels in the three groups were essentially the same ($P = 0.56$). The time for sensory and motor blocks to reach T10 dermatome and Bromage 1, respectively, was faster in group BD than in the other groups ($P = 0.0001$). The time for sensory regression to S1 was significantly prolonged in the group BD ($P = 0.0001$). Motor block regression time to Bromage 1 was also prolonged in the group BD ($P = 0.0001$). Neonatal outcome was normal in all groups. *Conclusion*. Single shot intrathecal bupivacaine/dexmedetomidine significantly prolonged sensory block in laboring women.

1. Introduction

Pain during childbirth has been described by women as severe [1] and frequent; these parturients especially those in the developing countries have few or no options for labor pain relief during childbirth. Parenteral opioids and sedatives are the most frequently prescribed agents for women in labor in many poor resource settings [2]. This method of pain relief has been shown to have little or no effect on labor pain [3]. Pain relief not only provides patient's comfort, but also attenuates the release of stress hormones, whose actions can draw from the parturients' reserves as well as depriving the fetus of oxygen and nutrients [1]. The provision of effective labor analgesia is now known to decrease the inhibitory effects of endogenous maternal catecholamine on uterine contractility, attenuates maternal acidosis, and improves intrapartum maternal well-being.

Although the gold standard in labor analgesia is the utilization of epidural services [2] which are widely used to provide pain-free labor in many parts of the world and have the advantage of providing flexibility to meet the needs of each patient [4]. The use of single-shot intrathecal low dose bupivacaine for labor analgesia has been demonstrated and found to be effective [5]. The advantages of this form of technique include the rapidity of onset and reliability, with minimal hemodynamic changes and motor block. Several adjuncts have been added to intrathecal bupivacaine to prolong the duration of sensory block. Such adjuncts include the use of fentanyl [6], sufentanil [7], morpine [8], clonidine [9], and dexmedetomidine [10] just to mention but a few.

Dexmedetomidine (DMT), a new highly selective $\alpha 2$-agonist, is under evaluation as a neuraxial adjuvant as it provides stable haemodynamic conditions, good quality of intraoperative, and prolonged postoperative analgesia

with minimal side effects. Dexmedetomidine is a highly selective $\alpha 2$-adrenergic agonist which has been used for premedication and as an adjunct to general anaesthesia. It reduces opioid and inhalational anaesthetics requirements [11]. Intrathecal $\alpha 2$-receptor agonists are found to have antinociceptive action for both somatic and visceral pain [12].

The purpose of this study was to determine the effect of adding DMT to low dose hyperbaric bupivacaine for neuraxial analgesia for labor.

2. Patients and Method

Following the approval for the study from the Ethics Committee of the University of Port Harcourt Teaching Hospital, this prospective, randomized study was conducted on multiparous parturients who received antenatal care, presenting for vaginal delivery and requesting analgesia. Informed written consent was obtained from the parturients on presenting at the labor ward.

Included in the study were parturients with ASA physical status I and II, term pregnancy of singleton fetus, minimal cervical dilatation of least 5 cm, those requiring oxytocin augmentation, all vertex presentation, and uncomplicated pregnancies. Excluded from the study were patients who refused to participate, patients younger than 18 years, preexisting or pregnancy-induced hypertension, obesity, endocrine diseases, diagnosed fetal abnormalities, contraindications to regional anesthesia, previous systemic opioid administrations, allergy to study agents, unconscious parturients, and patients who are unable to communicate.

Parturients with cervical dilatation of 5 cm or more were randomly allocated into three groups using sealed envelopes. A labor ward matron, not involved in the study opened the already coded and sealed envelope for the parturients to pick from. The study solutions were prepared by an anesthesiologist not involved in the study. Resuscitation equipment such as appropriate sizes of tracheal tubes, laryngoscopes with long and short blades, oxygen source, vasopressors, anticonvulsants, antihistamines, and resuscitation bag were prepared for any possible intervention, and the parturient connected to the monitor for baseline vital signs such as pulse rate, blood pressure, and the fetal heart rate was checked and recorded. Uterine contractions and cervical dilatation were assessed by the attending obstetrician.

An intravenous cannula was inserted and 500 mL of normal saline or ringers lactate was infused as a preload volume. At an attainment of 5 cm cervical dilatation, the parturients was supported to be in either the sitting or lateral decubitus position for preparation for the administration of the local anesthetic. Aseptic cleaning with povidone iodine and draping was observed. The L_3/L_4 intervertebral space was located. Using a size 22 G hypodermic needle, the skin overlying the L_3/L_4 intervertebral space was anaesthetized with 2 mL 1% lidocaine. During the interval of uterine contractions, and using a 21 G hypodermic needle as a guide, a size 26 G whitacre spinal needle was used to inject the study agent intrathecally through the L_3/L_4 intervertebral space. Both needles were withdrawn and a light dressing placed over the puncture site. The patient was returned to supine with a 15–30° head up while ensuring a left lateral uterine displacement. Patients in whom it was difficult to access the intrathecal space after two attempts were excluded from the study. The study solutions were hyperbaric bupivacaine 2.5 mg alone (group B), hyperbaric bupivacaine 2.5 mg with dexmedetomidine 2.5 μg (group BD), and hyperbaric bupivacaine with fentanyl (group BF). The hyperbaric bupivacaine alone group was the control in this study.

Midwives conducted the obstetric management of the women during labor under the direct supervision of the attending obstetrician according to the study protocol. Routine intrapartum management of the women involved the use of intravenous dextrose saline for fluid management and cardiotocograph for monitoring of uterine contractions and fetal heart rate. Pelvic examination was performed every 2 hours to evaluate the progress of labor. If the rate of cervical dilatation is less than 1 cm/hour over a 2 hour period, poor progress of labor was diagnosed and oxytocin augmentation of labor was commenced if cephalo-pelvic disproportion was excluded.

The level of sensory block was assessed by a blinded anesthetist not involved in this study, using methylated soaked swabs on both sides of the body, and the assessor observed the maximum level of sensory block. The times from intrathecal injection to two dermatome sensory regression, sensory regression to S1 dermatome, and motor block regression to Bromage 1 were recorded. All durations were calculated in relation to the time of spinal injection. Duration of pain relief was defined as the time from spinal injection to the first request for rescue analgesics or when the VPS was 4. Motor blockade was assessed using the Bromage score [13] every 10 min after the spinal block (1 = able to raise legs above table, 2 = able to flex knees, 3 = able to move feet only, 4 = no movement in legs or feet). Pain intensity was rated by the parturient using verbal pain score (VPS) ranging from 0 = pain free up to 10 = worst pain imaginable.

Pain at the peak of a contraction was assessed with a 10 cm VPS immediately before spinal analgesia, every 5 min for 30 min and then every 15 min until request for further analgesic. The parturient rated the pain score during the last contraction experienced and after delivery. A repeat dose of the study solution was administered if the labor prolonged and the anesthetic wore off before delivery. Maternal blood pressure, heart rate, and oxygen saturation were measured and recorded at the same intervals using the multiparameter monitor (DASH 3000/4000), USA. Hypotension in this study was defined as systolic blood pressure <90 mmHg or a <20% decrease from baseline, while bradycardia was heart rate <50 beats/min and desaturation as SpO_2 <90%. Hypotension was treated with intravenous ephedrine and bradycardia with intravenous atropine, while desaturation was treated with oxygen by facemask as required.

Tracing analysis included baseline fetal heart rate, number of accelerations per 20 min, long-term variability, decelerations (early, late, and variable), and number of uterine contractions per 20 min. The requirements for oxytocin augmentation, an instrumented (forceps/vacuum) or caesarean

delivery, neonatal Apgar scores, and umbilical venous blood pH were also recorded.

All parturients postpartum were on admission for at least 48 hours for close observation, and with specific instructions for strict bed rest, adequate fluid intakes, and analgesics in the events of a postdural puncture headache and also to report to the investigator if headache developed at home upon discharge.

2.1. Statistical Analysis. Statistical analysis was done by SPSS version 15.0 for analyzing the collected data. Data was expressed as either mean and standard deviation or numbers and percentages. Continuous covariates in the demographic data of patients were analyzed using analysis of variance (ANOVA). For categorical covariates (ASA class, hypotension, bradycardia, use of ephedrine, use of additive analgesia, sedation scores, and Apgar scores) the comparison was studied using chi-squared test or the Fisher's exact test as appropriate, with the P value reported at the 95% confidence interval. The level of significance used was $P = 0.05$. To calculate the sample size, a power analysis of ([alpha] = 0.05 and [beta] = 0.90) showed that 30 patients per study group were needed to detect an increase of 30 min difference between the median duration of spinal sensory block between the groups.

3. Results

A total of ninety (90) laboring women were accepted and participated throughout the study. None of them requested for additional analgesia.

The demographic data is shown in Table 1. The three groups, group B (hyperbaric bupivacaine alone), group BF (hyperbaric and fentanyl mixture), and group BD (hyperbaric bupivacaine and dexmedetomidine) were comparable in terms of demographic variables, gestational age, level of parity, and ASA class.

Table 2 shows the block onset and regression times of the intrathecal agents. The peak sensory block levels in the three groups were essentially the same. Although a higher dermatomal level was observed in the groups BF and BD there was no statistical difference between them ($P = 0.56$). The time for sensory block to reach T10 dermatome was different in the three groups. The Group BD attained the T10 sensory block at a shorter time. The difference between the three groups was statistically significant ($P < 0.0001$). The time difference for motor block to reach Bromage 1 was also significant statistically between the three groups ($P < 0.0001$). It was faster in group BD than group BF and B. None of the patients in all the groups had Bromage score of 2. However, both the time for sensory regression to S1 segment and time for motor block regression to Bromage were statistically significant ($P < 0.0001$).

Table 3 shows the labor characteristics and neonatal outcome. The mean duration of the first stage of labor was essentially the same in the three groups ($P = 0.57$). The second stage of labor was also essentially the same in all the groups ($P = 0.56$). All the babies delivered in this study had Apgar scores ≥7 and ≥8 in the first and fifth minutes, respectively. The mean umbilical venous blood pH in each of the groups was within reference values (7.20–7.40). The difference between the groups was not statistically significant ($P = 0.75$). The mean birth weight of the babies delivered was normal in the three groups; there was no statistical difference between the three groups ($P = 0.62$).

Table 4 shows the adverse events observed and recorded during the study. One of the adverse events common to the three groups was hypotension. Two (6.67%) women in group B, 1 (3.33%) woman in group BF and 3 (10.0%) women in group BD, had mild hypotension that was corrected with fluid administration. Mild bradycardia was also observed in all the groups. One (3.33%) woman in group B, 2 (6.67%) women in group BF, and 1 (3.33%) woman in group BD had mild bradycardia that was transient. Postdural puncture headache occurred in some women in groups B and BF but adequate bed rest and rapid fluid administration were able to bring it under control.

All the patients could move their legs easily and reported normal sensation with minimal numbness and were able to micturate spontaneously throughout the period of study. No patient was allowed to walk during the study period due to the need for continuous maternal and fetal monitoring for safety reasons.

Hypotension was mild to moderate in both groups except one patient in group B, who had a blood pressure less than 80 mmHg and received a rapid intravenous fluid treatment. There was an episode each (1.33%) of nausea and vomiting in group B and group BF, respectively, but the difference was irrelevant.

4. Discussion

The result of our study has shown that a single shot intrathecal low dose bupivacaine/dexmedetomidine significantly prolonged the duration of analgesia in laboring women. This finding adds to the existing literature which investigated the efficacy of intrathecal opioids [14], local anesthetic, and $\alpha 2$-adrenergic agonist, particularly clonidine [15, 16] in laboring parturients.

The parturients who had bupivacaine/dexmedetomidine had a prolonged lower pain scores than those who had either bupivacaine/fentanyl or bupivacaine alone. The analgesic effect of DMT could be due to synergism with the local anaesthetic. Although the mechanism of action of DMT is unknown, it has been suggested to act by binding to the presynaptic C-fibres and postsynaptic horn neurons [17]. On the hand, fentanyl which lipophilic and a μ-receptor agonist exerts its effect intrathecally, by combining with opioid receptors in the dorsal horn of the spinal cord that could have a supraspinal spread and action. Our study supports clinical evidence suggesting that $\alpha 2$-adrenergic agonist enhances analgesia from bupivacaine [18]. Gautier et al. [19] reported that spinal clonidine 30 μg/sufentanil 2.5 μg produced 140 minutes of labor analgesia, significantly less than the 268 minutes of labor analgesia observed in our study.

Table 1: Demographic data.

Demographic data	Group B $n = 30$	Group BF $n = 30$	Group BD $n = 30$	P value
Age (years)	27.8 ± 3.99	27.2 ± 4.01	26.13 ± 3.89	0.27
Height (cm)	166.7 ± 2.58	165.4 ± 2.55	165.8 ± 2.27	0.12
Weight (kg)	72.2 ± 8.60	70.5 ± 7.09	69.8 ± 9.73	0.82
Gestational age (weeks)	39.1 ± 0.68	39.3 ± 0.80	39.2 ± 0.66	0.53
Parity	2.3 ± 1.08	2.1 ± 0.89	2.0 ± 0.87	0.48
ASA I, II	25, 5	27, 3	24, 6	

Values are expressed as means ± SD or numbers.

Table 2: Block onset and regression times.

Characteristics	Group B $n = 30$	Group BF $n = 30$	Group BD $n = 30$	P value
Peak sensory block level	T11 (T7–T10)	T10 (T8–T10)	T10 (T9–T11)	0.56
Time for sensory block to reach T10 dermatome (min)	8.39 ± 1.63	7.2 ± 0.71	5.5 ± 0.57	<0.0001
Time for motor block to reach Bromage 1 (min)	15.3 ± 1.18	10.8 ± 4.02	9.4 ± 0.63	<0.0001
Time for sensory regression to S1 segment (min)	107.9 ± 22.11	122.9 ± 10.42	268.9 ± 15.84	<0.0001
Time for motor block regression to Bromage 0 (min)	98.7 ± 1.70	103.2 ± 3.33	221.1 ± 1.37	<0.0001

Values are expressed as means ± SD or numbers.

Table 3: Labor characteristics and neonatal outcome.

Variables	Group B $n = 30$	Group BF $n = 30$	Group BD $n = 30$	P value
Cervical os dilatation	5	5	5	
Duration of first stage of labor	234.1 ± 37.17	234.9 ± 44.35	251.8 ± 39.22	0.47
Duration of second stage of labor	36.0 ± 11.97	40.8 ± 8.07	37.8 ± 9.32	0.66
Apgar scores				
1 min				
≥7	30 (100)	30 (100)	30 (100)	
5 mins				
≥9	30 (100)	30 (100)	30 (100)	
Umbilical vein pH	7.20 ± 0.07	7.19 ± 0.06	7.25 ± 0.07	0.52
Birth weight (grammes)	3010 ± 343.83	2905 ± 326.13	2855 ± 403.77	0.13
Additional analgesia for episiotomy repair				
Needed	13 (43.33)	8 (26.67)	4 (13.33)	
Not needed	2 (6.67)	4 (13.33)	9 (30.0)	

Values are expressed as means ± SD or numbers (percentage).

Table 4: Adverse events.

Events	Group B $n = 30$	Group BF $n = 30$	Group BD $n = 30$
Hypotension	2 (6.67)	1 (3.33)	—
Bradycardia	1 (3.33)	2 (6.67)	1 (3.33)
Nausea	1 (3.33)	—	—
Vomiting	—	1 (3.33)	—
Shivering	1 (3.33)	—	—

Values are expressed as number (percentage).

Intravenous DMT has been used in obstetrics in the past but has contended with regulatory and other challenges. The restriction imposed on the use of DMT is necessary as reckless administration could have posed difficult challenges to both mother and child [20]. DMT, if used within the reference dose maintains psychomotor function, could preserve maternal effort and enhance participation in the laboring process [21]. In our study, a very low dose of intrathecal DMT/bupivacaine was used. The choice for this dose was informed on the principle of striking a balance between preservation of maternal expulsive effort and achieving the maximal duration of analgesia. Six (20%) women in group BD who required additional analgesia for the second stage of labor rejected the offer for the repair of episiotomies. The rejection of a second intrathecal DMT injection could be due to the inconveniences of pain of injection which could add to the existing stress of labor. However, all the women in groups BF and B requested for and received additional analgesia before the commencement of second stage of labor and for the repair of episiotomy.

Higher doses of local anaesthetics administered neuraxially in women undergoing the birthing process can impair motor function [22]. The impairment of such motor function can result in higher instrumental delivery and caesarean section rates. The motor block observed in our study had regressed completely before the commencement of the second stage of labor. Probably this explains why the maternal expulsive effort was also preserved.

Studies have demonstrated the safety of intrathecal DMT [5, 23] in humans. However it has been shown that DMT in relatively high doses can lead to hypotension when administered either neuraxially or intravenously. Prolonged sensory block can be achieved by intrathecal 5 μg and 10 μg dexmedetomidine with no significant effect on blood pressure or heart rate [24, 25]. A lower dose (2.5 mcg) of DMT was used in our study and the parturients remained hemodynamically stable. It is well known that intrathecal administration of local anesthetics reduce blood pressure by decreasing sympathetic outflow. However, alpha-2 agonist, when coadministered with bupivacaine intrathecally, did not show a further decrease in blood pressure presumably because the blockade produced by bupivacaine is nearly maximum [26]. This may explain the observation that 150 μg clonidine added to a high dose of bupivacaine (15 mg or more) did not decrease blood pressure compared with bupivacaine alone [27] but when added to a small dose of bupivacaine (5 mg) [24] or used alone as sole analgesic [28] resulted in a greater reduction in blood pressure in comparison to bupivacaine alone or saline, respectively.

By virtue of its effect on spinal α-2 receptors, dexmedetomidine mediates its analgesic effects. Dexmedetomidine has been found to prolong analgesia when used as an adjuvant to local anesthetics for subarachnoid, epidural, and caudal epidural blocks. However, there is no proper consensus regarding the dose of drug to be used for neuraxial blocks. Doses varying from 3 to 15 mcg have been used as adjuvant to bupivacaine for spinal anesthesia. There has been dose-dependent prolongation of analgesia.

The Apgar scores and the umbilical venous blood pH did not show significant differences between the groups in this study. Baseline fetal heart rates also did not change after injection in any group, and maternal blood pressure was unchanged. No differences in muscle strength were found in any group following the intrathecal administration of the agents, although anesthetic levels to cold were documented in all patients in the different groups. The maximum sensory level reached was also essentially the same in the three groups.

The outcome of this study will be of relevance in low resource economies where the availability of equipment, accessories, and expertise for instituting epidural analgesia service is scarce [29]. With the prolonged period of analgesia demonstrated by intrathecal bupivacaine/dexmedetomidine in our study, it has the potential of being the only agent used as single shot in multiparous women in labor. The lack of adverse effects such as sedation, respiratory depression, hypotension in the mother, and neonatal depression could be additional advantages of the dexmedetomidine in women in labor and delivery.

Although this study adds to the current knowledge on dexmedetomidine, further studies to investigate the effects of intrathecal dexmedetomidine for labor pain relief may be needed. However this study showed that single shot intrathecal low dose dexmedetomidine has great potential in pain relief during labor and delivery. A higher dose of intrathecal DMT which could produce a more intense and prolonged block may be needed in primiparous women in labor and childbirth. Again this still needs further evaluation.

References

[1] H. E. Onah, S. N. Obi, T. C. Oguanuo, H. A. Ezike, C. M. Ogbuokiri, and J. O. Ezugworie, "Pain perception among parturients in Enugu, South-Eastern Nigeria," *Journal of Obstetrics and Gynaecology*, vol. 27, no. 6, pp. 585–588, 2007.

[2] S. Fyneface-Ogan, C. N. Mato, and S. E. Anya, "Epidural anesthesia: views and outcomes of women in labor in a Nigerian hospital," *Annals of African Medicine*, vol. 8, no. 4, pp. 250–256, 2009.

[3] F. Reynolds and J. A. Crowhurst, "Opioids in labour—no analgesic effect," *The Lancet*, vol. 349, no. 9044, pp. 4–5, 1997.

[4] A. H. Lebovits, P. Zenetos, D. K. O'Neill et al., "Satisfaction with epidural and intravenous patient-controlled analgesia," *Pain Medicine*, vol. 2, no. 4, pp. 280–286, 2001.

[5] O. Adeyemi, R. Vernon, and O. Medge, "A spinal labour analgesia protocol for Ghana," in *Proceedings of the 4th All Africa Anaesthesia Congress*, pp. 67–68, 2009.

[6] J. Bogra, N. Arora, and P. Srivastava, "Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for cesarean section," *BMC Anesthesiology*, vol. 5, article 5, 2005.

[7] N. Vyas, D. K. Sahu, and R. Parampill, "Comparative study of intrathecal sufentanil bupivacaine versus intrathecal bupivacaine in patients undergoing elective cesarean section," *Journal of Anaesthesiology Clinical Pharmacology*, vol. 26, no. 4, pp. 488–492, 2010.

[8] A. Lehavi, P. Abecasis, A. Weissman, A. Winterstern, and Y. S. Katz, "Subarachnoid block with hyperbaric bupivacaine and morphine may shorten PACU stay after cesarean delivery,"

Journal of Perianesthesia Nursing, vol. 25, no. 6, pp. 371–379, 2010.

[9] I. Labbene, H. Gharsallah, A. Abderrahman et al., "Effects of 15 mcg intrathecal clonidine added to bupivacaine and sufentanil for labor analgesia," *La Tunisie Medicale*, vol. 89, no. 11, pp. 853–859, 2011.

[10] R. Gupta, R. Verma, J. Bogra, M. Kohli, R. Raman, and J. K. Kushwaha, "A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine," *Journal of Anaesthesiology Clinical Pharmacology*, vol. 27, no. 3, pp. 339–343, 2011.

[11] E. Martin, G. Ramsay, J. Mantz, and S. T. J. Sum-Ping, "The role of the α2-adrenoceptor agonist dexmedetomidine in postsurgical sedation in the intensive care unit," *Journal of Intensive Care Medicine*, vol. 18, no. 1, pp. 29–41, 2003.

[12] E. A. Kalso, R. Poyhia, and P. H. Rosenberg, "Spinal antinociception by dexmedetomidine, a highly selective α2-adrenergic agonist," *Pharmacology and Toxicology*, vol. 68, no. 2, pp. 140–143, 1991.

[13] P. R. Bromage, *Epidural Analgesia*, WB Saunders, Philadelphia, Pa, USA, 1978.

[14] C. A. Wong, B. M. Scavone, J. P. Slavenas et al., "Efficacy and side effect profile of varying doses of intrathecal fentanyl added to bupivacaine for labor analgesia," *International Journal of Obstetric Anesthesia*, vol. 13, no. 1, pp. 19–24, 2004.

[15] B. S. Sethi, M. Samuel, and D. Sreevastava, "Efficacy of analgesic effects of low dose intrathecal clonidine as adjuvant to bupivacaine," *Indian Journal of Anaesthesia*, vol. 51, pp. 415–419, 2007.

[16] M. D. Owen, O. Özsaraç, S. Şahin, N. Uçkunkaya, N. Kaplan, and I. Mağunaci, "Low-dose clonidine and neostigmine prolong the duration of intrathecal bupivacaine-fentanyl for labor analgesia," *Anesthesiology*, vol. 92, no. 2, pp. 361–366, 2000.

[17] Y. Harada, K. Nishioka, L. M. Kitahata, K. Kishikawa, and J. G. Collins, "Visceral antinociceptive effects of spinal clonidine combined with morphine, [D-Pen2, D-Pen5] enkephalin, or U50,488H," *Anesthesiology*, vol. 83, no. 2, pp. 344–352, 1995.

[18] F. Bonnet, V. B. Buisson, Y. Francois, P. Catoire, and M. Saada, "Effects of oral and subarachnoid clonidine on spinal anesthesia with bupivacaine," *Regional Anesthesia*, vol. 15, no. 4, pp. 211–214, 1990.

[19] P. E. Gautier, M. de Kock, L. Fanard, A. van Steenberge, and J. L. Hody, "Intrathecal clonidine combined with sufentanil for labor analgesia," *Anesthesiology*, vol. 88, no. 3, pp. 651–656, 1998.

[20] J. E. Mattingly, J. D'Alessio, and J. Ramanathan, "Effects of obstetric analgesics and anesthetics on the neonate: a review," *Pediatric Drugs*, vol. 5, no. 9, pp. 615–627, 2003.

[21] R. Gertler, H. C. Brown, D. H. Mitchell, and E. N. Silvius, "Dexmedetomidine: a novel sedative-analgesic agent," *Proceedings (Baylor University Medical Center)*, vol. 14, pp. 13–21, 2001.

[22] C. Olofsson, A. Ekblom, G. Ekman-Ordeberg, and L. Irestedt, "Obstetric outcome following epidural analgesia with bupivacaine-adrenaline 0.25% or bupivacaine 0.125% with sufentanilva prospective randomized controlled study in 1000 parturients," *Acta Anaesthesiologica Scandinavica*, vol. 42, no. 3, pp. 284–292, 1998.

[23] K. Fukushima, Y. Nishimi, K. Mori, and J. Takeda, "Effect of epidurally administered dexmedetomidine on sympathetic activity and postoperative pain in man," *Anesthesia and Analgesia*, vol. 82, article S121, 1996.

[24] S. M. Al-Ghanem, I. M. Massad, M. M. Al-Mustafa et al., "Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures: a double blind controlled study," *American Journal of Applied Sciences*, vol. 6, no. 5, pp. 882–887, 2009.

[25] A. A. Weinbroum and R. Ben-Abraham, "Dextromethorphan and dexmedetomidine: new agents for the control of perioperative pain," *European Journal of Surgery*, vol. 167, no. 8, pp. 563–569, 2001.

[26] W. Klimscha, A. Chiari, P. Krafft et al., "Hemodynamic and analgesic effects of clonidine added repetitively to continuous epidural and spinal blocks," *Anesthesia and Analgesia*, vol. 80, no. 2, pp. 322–327, 1995.

[27] S. Strebel, J. A. Gurzeler, M. C. Schneider, A. Aeschbach, and C. H. Kindler, "Small-dose intrathecal clonidine and isobaric bupivacaine for orthopedic surgery: a dose-response study," *Anesthesia and Analgesia*, vol. 99, no. 4, pp. 1231–1238, 2004.

[28] K. S. Filos, L. C. Goudas, O. Patroni, and V. Polyzou, "Hemodynamic and analgesic profile after intrathecal clonidine in humans: a dose-response study," *Anesthesiology*, vol. 81, no. 3, pp. 591–601, 1994.

[29] C. O. Imarengiaye, "Trends in pain relief in labour: implications for obstetric analgesia service in Nigeria," *Nigerian Postgraduate Medical Journal*, vol. 12, no. 3, pp. 193–202, 2005.