Comparative evaluation of epidural bupivacaine – dexmedetomidine and bupivacaine – fentanyl on Doppler velocimetry of uterine and umbilical arteries during labor

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Summary

Objective: **uteroplacental blood flow is affected by myometrial contractions and hypotension. Epidural analgesia is frequently complicated by hypotension. The aim of the study was to compare the effect of bupivacaine- dexmedetomidine (BD) or bupivacaine – fentanyl (BF) on uterine artery pulsatitly index (UtA-PI) and umbilical artery pulsatitly index (UA-PI) during uterine contractions and relaxations.**
Methods: **this was a prospective controlled observational study performed in 130 healthy full term parturients divided into 3 groups [23 cases as control, 44 cases as (BD) epidural group and 43 cases as (BF) epidural group]. Over the study duration of 120 minutes; UtA-PI and UA-PI were measured at baseline, 30, 60, 120 minutes during uterine contractions and relaxations. Maternal hemodynamic, visual analogue scale (VAS), sedation score, side effects of epidural analgesia including nausea, vomiting, pruritis and respiratory depression were assessed.**
Results: **VAS significantly decreased after epidural compared with control group. BD group showed significant improvement in onset and duration of analgesia and sedation scores with lower incidence of nausea and pruritis compared with BF group. The BF and BD groups were associated with significant maternal hypotension and bradycadia that increase the UtA-PI during uterine contractions and relaxations compared with control group. UA-PI was increased with uterine contractions compared with during uterine relaxations in the three studied groups yet the effect of epidural and uterine contractions does significantly affect newborns apgar scores or umbilical cord pH.**
Conclusion: **bupivacaine- dexmedetomidine epidural analgesia showed better maternal satisfaction for labor pains control compared with bupivacaine – fentanyl without deleterious effect on utroplacental circulation and newborns outcome.**

Introduction

Epidural analgesia has been extensively used to provide pain relief in labor. Epidural bupivacaine is still the most widely used local anesthetic in obstetric analgesia (1). However, it's potential for motor blockade and central nervous system and cardiac toxicity by accidental intravenous injection of high dose is clinically undesirable, especially for obstetric patients (2). In addition, to minimize unwanted motor block, a trend toward the use of lower concentrations of local anesthetics combined with opioids has been used in many clinical trials with good results (3-5).

Opioids like fentanyl have been used traditionally as an adjunct for epidural administration in combination with a lower dose of local anesthetic to achieve the desired anesthetic effect (6). The addition of opioid does provide a dose sparing effect of local anesthetic and superior analgesia but there is always a possibility of an increased incidence of pruritis, urinary retention, nausea, vomiting and respiratory depression (7,8).

Clonidine and dexmedetomidine are α-2 adrenergic agonists with analgesic properties which potentiate local anesthetic effects when epidurally administered (9,10). They act on both pre and post synaptic sympathetic nerve terminal and central nervous system thereby decreasing the sympathetic outflow and nor-epinephrine release causing sedative, anti-anxiety, analgesic, sympatholytic and hemodynamic effects (11-14). Overall the experience with dexmedetomidine was quite satisfactory as compared to clonidine because of its superior sedative and anxiolytic properties during the surgical procedure under regional anaesthesia (15-18).

The most common complications occurring with epidural analgesia is maternal hypotension (19). Hypotension threatens the fetus by decreasing uterine blood flow. Modest decreases (≤ 20 %) in maternal blood pressure are of limited concern in a woman with a healthy fetus (20). The maternal blood supply to the placenta is intermittently strangulated by myometrial contractions (21). A significant reduction in the perfusion pressure of the uterine artery blood flow is seen at the maximum pressure of the uterine contraction. In diastole, when intrauterine pressure exceeds maternal diastolic pressure especially if associated with hypotension, the perfusion pressure of the uterine artery blood flow is no longer present (22).

The increase in vascular flow resistance by Doppler velocimetry as UtA-PI is positively correlated to the intrauterine pressure produced by contractions (23). Under normal circumstances the umbilical artery blood flow is not affected by uterine contractions (24,25).

The aim of the present study was to examine the effect of two pharmacological approaches of epidural analgesia (bupivacaine- dexmedetomidine and bupivacaine - fentanyl) on uteroplacental blood flow during uterine contraction and relaxation of active labor by Doppler velocimetry of uterine and umbilical arteries pulsatility indices.

Patients and methods

The study was approved by the local Clinical Research Ethics Committee of hospital and written informed consent was obtained from the patients before the onset of labor analgesia. This was a prospective comparative study performed during a 20 month period (April 2010 to November 2011) in the labor ward of Jeddah Clinic Hospital Alkanderah, Jeddah, Saudi Arabia. One hundred thirty patients had a singleton healthy full-term pregnancy; 100 patients of them who requested epidural anesthesia during labor were classified as American Society of Anesthesiologists physical status I or II. The remaining 30 women refused to receive epidural and considered as control group.

Inclusion criteria were: gestational age ≥37 weeks; with an engaged vertex presentation; intact membrane; active labor with cervical dilatation >3 cm and uterine contractions occurring at least every 5 min; normal cardiotocography (CTG) [baseline fetal heart rate (FHR) between 110 and 160 beats/minute, baseline variability >5 beats/minute, presence of accelerations, and absence of decelerations].

Subjects were excluded if they had pregnancy-induced hypertension (PIH) (preeclampsia), concomitant cardiovascular disease, documented coagulation abnormality or abnormal bleeding history, evidence of infection or anatomic abnormality at the proposed catheter insertion site, if they declined study participation or were unable to give informed voluntary consent, or were younger than 18 years. Subjects were also excluded from the study in cases of difficult epidural placement, inadvertent epidural puncture (wet tap), rapid progress of labor (delivery in less than 120 minutes of study period), or fetal distress mandating urgent/emergent cesarean delivery. Patients who had received opioids or presented a history of hypersensitivity to local anesthetic, fentanyl or to dexmedetomidine were excluded from the study.

All women laboring without analgesia (control group) admitted to the labor ward immediately and enrolled in the study as controls when meeting inclusion criteria. The control group received no analgesics; patient who requested analgesia during study period was excluded from the study.

Hundred women who had requested epidural analgesia for labor were randomly allocated to two groups (n = 50 each), to receive 12 ml of 0.25% bupivacaine plus either 1μg/kg dexmedetomidine diluted in 5 ml saline (BD group) or 1μg/kg fentanyl diluted in 5 ml saline (BF group). The mixed solutions for epidural analgesia were prepared under sterile conditions by the researcher anesthetist (Hasan AMA) and administered by the researcher anesthetist (Elnabtity AMA) who remained blinded to the solution prescription.

Epidural analgesia was administered in the labor ward. An intravenous infusion of 500 ml of lactated Ringer's solution was administered before the epidural injection. With the patient in a left lateral position, an epidural catheter was inserted into the L3-L4 vertebral interspace using the loss of resistance technique; 2-3 cm of catheter was introduced in the epidural space. With the patient in the supine position, a test dose of local anesthetic (3 ml of 2% lidocaine) was administered through the catheter. Maternal arterial pressure and heart rate were monitored at 5 min intervals. Once it was determined that no adverse effects such as maternal hypotension or fetal bradycardia had occurred, the study drugs were then administered. The solutions were randomly administered as 1:1 ratio for BD and BF groups.

Subject pain was assessed with a 10-cm linear visual analogue scale (VAS), where 0 represented 'no pain' and 10 represented 'most severe pain'. Pain scores were determined just before epidural placement and 5, 10, 15, 20, 30, 60, 90 and 120 min after epidural injection. When VAS was ≥ 4, a second dose of local anesthetic was required and patients were excluded from the study if the second dose of local anesthetic given within the 120 minutes of study protocol.

Sedation score (1= wide awake, 2= dozing, 3= asleep and 4= unrousable) determined at 5,10,20, 30, 60, 90 and 120 minutes after epidural injection. Motor block was assessed by means of a modified four-grade Bromage scale (0 = able to lift extended leg at hip; 1 = able to flex knee but not lift extended leg; 2 = able to move foot only; and 3 = unable to move foot) at 20 minutes after epidural injection.

The onset of analgesia was defined as the time from injection of the study medication to first reduction in pain intensity by at least 1 in VAS; and the duration of analgesia was defined as the time between the onset of analgesia and when VAS becomes ≥ 4. The occurrence of nausea and vomiting, pruritis and respiratory depression (respiratory rate <12/ min) were noted and recorded till delivery.

For hemodynamic stability; maternal mean arterial pressure (MAP), oxyhemoglobin saturation (pulse oximeter, cadiocap II, Datex, Helsinki) and maternal and fetal pulse rates were recorded every 5 minutes for first 30 minutes, every 10 minutes for second 30 minutes then every 20 minutes for second hour. The first measurement was obtained immediately before epidural dosing (baseline) between uterine contractions. Hypotension was prospectively defined as a 20% decrease in mean arterial pressure (MAP) and bradycadia as pulse rate <60/minute. Uterine artery pulsatility index (UtA-PI) and umbilical artery pulsatility index (UA-PI) during uterine relaxation and contraction were measured before (T0), 30 min (T30), 60 min (T60), 90 min (T90) and 120 min (T120) after the beginning of analgesia in the epidural groups and at the beginning of study (T0), 30 min (T30), 60 min (T60), 90 min (T90) and 120 min (T120) later in control Group. Uterine contractions were assessed with an external tocody-

namometer during labor and with manual palpation during uterine artery Doppler assessment. During uterine contractions; UtA-PI calculated during the peak of the contraction. The peak of contraction was determined visually from the tocodynamometer recording of CTG.

Ultrasound Doppler indices measurements were made in uterine arteries and umbilical artery with parturient in the recumbent position by researcher obstetrician (Selim MF) using 4 MHz convex transabdominal probe with color Doppler facility (GE Healthcare ultrasound - Logic 9, 5125134-10 Rev4). Standard Doppler indices of vascular resistance were obtained from at least three similar consecutive waveforms. Increased values indicate increased vascular resistance and correlate with decreased flow.

The uterine artery blood velocity was recorded from both uterine. The cervical canal and internal cervical os were identified in a sagittal plane. Doppler color flow mapping was used to highlight the uterine artery on the sides of the cervix and uterus at the level of the internal os. Pulsed-wave Doppler was used where uterine artery crossed the external iliac artery. When three similar, consecutive waveforms were obtained, the PI was measured and the mean UtA-PI was calculated (26).

The umbilical artery Doppler flow spectrum was recorded from a free-floating central part of the umbilical cord. The mean of three consecutive blood velocity waveforms were analyzed for PI (27). Women with absent or reversed diastolic umbilical artery flow were not included in the study.

The fetus was monitored by continuous CTG. The type of delivery and the neonatal Apgar scores at 1, and 5 min and umbilical cord PH were recorded. The newborns were evaluated by pediatric resident on duty.

Statistical analysis was performed with the use of SPPS 16.0 for windows (SPSS Inc., Chicago, IL, USA). Numerical variables were presented as the mean and standard deviation (SD), whereas categorical data were presented using counts and percentages. The following tests were applied according to the type of variables: Student's t-test, Mann-Whitney U-test, Chi square test, Fisher's exact probability test for categorical variables, one-way or two-way or repeated ANOVA for normally distributed variables, Pearson's correlation test were used as appropriate, and a Kruskal-Wallis test for non-parametric data. A post-hoc test was applied using the Bonferroni method for adjusting for multiple comparisons. *P* values <0.05 were considered statistically significant.

Results

We consented and enrolled 130 women. Twenty women were later excluded from the study. Hundred ten women are available for statistical analysis (23, 44 and 43 cases in control, BD, BF groups respectively) (Fig. 1). The causes of exclusion in control group were; 1 case delivered in less than 2 hours and 6 cases requested analgesia before the two hours duration of study. In the BD and BF groups the causes were as follow:

- Difficult epidural placement (one case in BD group and 2 cases in BF group).
- Inadvertent epidural puncture (one case in BD group and one cases in BF group).
- Second dose of local anesthetic is required before 2 hours of study duration (one case in BD group and 2 cases in BF group).
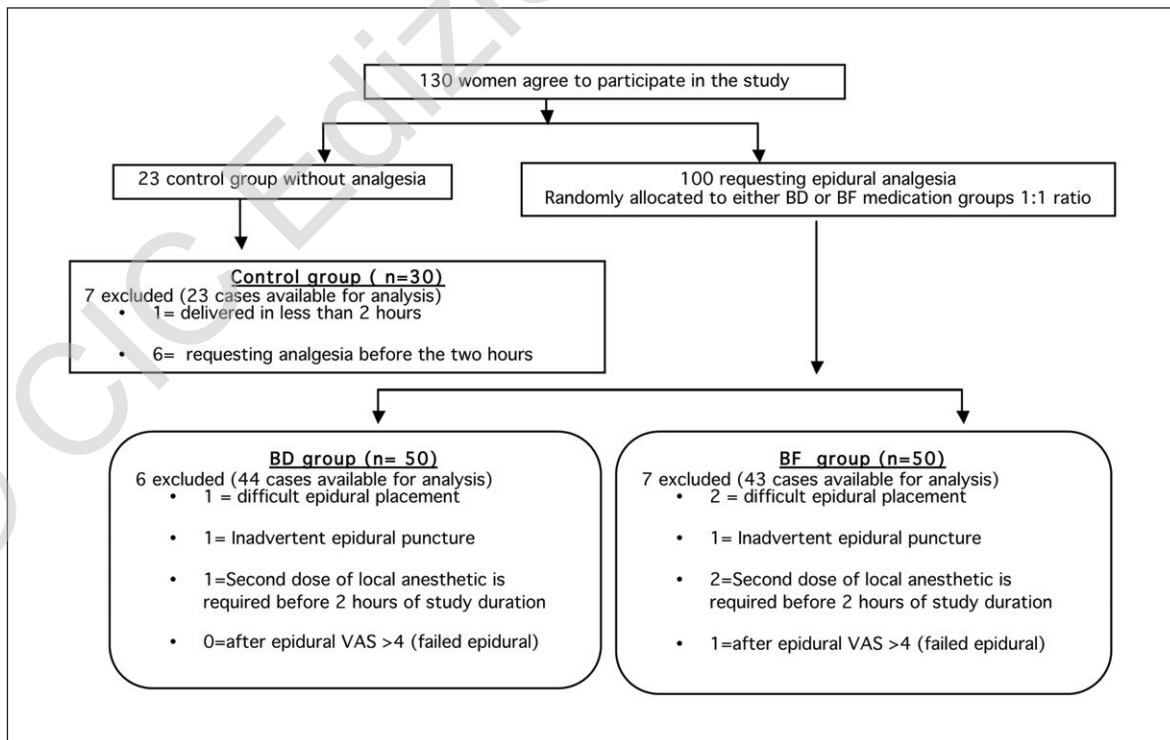

Figure 1. Flow chart of study.

- Failed epidural, after epidural was VAS >4 (one cases in BF group but none in BD group).
- Delivered before completion 2 hours of study duration (two cases in BD group and 1case in BF group).
- Emergency cesarean delivery for fetal distress (one cases in BD group but none in BF group).

Demographic and labor characteristics are presented in Tables 1 and 2. The enrolled parturient women were comparable in age, height, weight, parity, gestational age and stage of cervical dilation at time of entry into the study (Tab. 1). Obstetric outcomes, including the mode of delivery (spontaneous or instrumental vaginal delivery and cesarean delivery), were similar among groups (Tab. 2). The birth weight, Apgar scores at 1 and 5 minutes and umbilical cord pH of newborns were comparable in all groups (Tab. 2). Table 3 gives the comparison of analgesic outcomes between BD and BF groups. The mean onset of analgesic effect was significantly earlier in BD group (5.9±2.7 min) compared with BF group (9.1±1.9 min); $P<0.05$. The du-

ration of analgesia was also significantly longer in BD group (155.6±28.1min) compared with BF group (129±18.7 min); $P<0.05$. The number of parturient women with a sedation score of 2 was significantly higher ($P<0.05$) in BD group (24 cases) compared with BF group (10 cases). Bromage scores were comparable in both groups. No cases showed bromage scores and sedation scores more than 2 in both groups.

Table 4 depicts the comparisons of side effects. Epidural analgesia was associated with significant maternal hypotension and bradycardia compared to the control group. There were statistically insignificant ($P>0.05$) higher maternal hypotension and bradycardia in BD group compared with BF group. Ephedrine drugs were given for 4 cases in BD group and 2 cases in BF group as treatment for hypotension. Also, atropine drugs were given for 2 cases in BD group and 1 case in BF group as treatment for bradycardia. Non - significant difference seen in fetal heart (>160 or <100/ minute) between groups. Fetal distress that occurred did not need emergency interference

Table 1. Demographic data of studied parturient.

Variable	Control group (n=23)	BD group (n=44)	BF group (n=43)	*P* value
Age (yr)	23±6.3	25.1±5.4	24±7.1	NS
Height (cm)	164±9.5	161±8.9	163±8.3	NS
Weight (Kg)	77.5±11.3	74.7±12.7	78.1±11.3	NS
Parity	1.7±1.4	2.1±1.1	1.9±1.3	NS
Gestational age (wk)	39.1±1.2	38.9±1.3	39.2±0.9	NS
Cervical dilation at start of study (cm)	4.8±1.2	5.1±1.4	4.9±1.3	NS

Data expressed as mean (±SD).

Table 2. Obstetric outcomes.

Variable	Control group (n=23)	BD group (n=44)	BF group (n=43)	*P* value
Spontaneous delivery (n%)	20 (86.9%)	37 (84.1%)	35 (81.4%)	NS
Instrumental delivery (n%)	0 (0%)	1 (2.3%)	2 (4.7%)	NS
Cesarean delivery (n%)	3 (13.1%)	6 (13.6)	6 (13.9%)	NS
Birth weight (kg)	3.109±0.454	3.081±0.346	3.103±0.435	NS
Apgar score				NS
>7 at 1 min (n%)	23 (100%)	43 (97.7%)	41(95.3%)	
>9 at 5 min (n%)	23 (100%)	44 (100%)	43 (100%)	
Umbilical cord PH>7.2 (n%)	23 (100%)	44 (100%)	43 (100%)	NS

Data expressed as numbers and percentages.

Table 3. Analgesia outcomes.

Variable	Group BD (n=44)	Group BF (n=43)
Onset of analgesia (min)	5.9±2.7[*]	9.1±1.9
Duration of analgesia (min)	155.6±28.1[*]	129±18.7
Motor block (maximum bromage score) 0-1-2-3(n)	40-4-0-0	38-6-0-0
Sedation score of 1-2-3-4 (n)	20-24-0-0[*]	33-10-0-0

Data expressed as mean (±SD) for onset and duration of analgesia and as number for other variables.*Statistically significant ($P<0.05$).

Table 4. Anesthetic complications.

Variable	Control group N= 23	BD group N= 44	BF group N= 43
Hypotension [>20% decrease in MAP (n %)]	0/23 (0%)	12/44 (27.2%)*	8/43 (18.6%) *
Maternal Bradycardia [(heart rate<60)(n %)]	0/23 (0%)	10/44 (22.7%)*	5/43 (11.6%) *
Fetal heart (>160 or <100/ minute)	2/23 (8.6%)	5/44 (11.3%)	3/43 (6.9%)
Nausea	1/23 (4.3%)	2/44 (4.5%)	7/43 (20.5%)#
Vomiting	0/23(0%)	1/44(2.7%)	3/43 (6.9%)
Pruritis	0/23(0%)	1/44(2.7%)	5/43 (11.6%)#
Respiratory depression	0/23(0%)	0/44(0%)	0/43(0%)

*P<0.05 when compared BD and BF group with control group; # *P*<0.05 when compared BF group with BD and control groups.
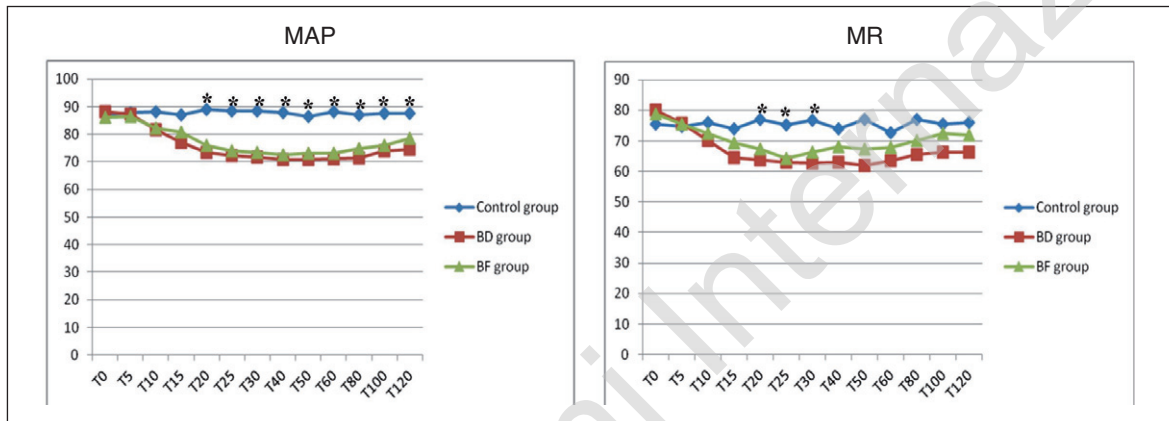

Figure 2. Maternal mean arterial pressure (MAP) and Heart Rate (HR) during study period for the three studied groups. Each data point represents the mean . * Statistically significant (p<0.05)

as FHR became reassuring within short time (< 1 min). The incidences of nausea, vomiting and pruritus were highest in BF group and lowest in control group. The nausea and pruritus were significantly higher in BF group compared with BD and control group. Incidence of respiratory depression was nil in all three groups.

MAP was comparable in all three groups at baseline (T0). From T0 to T120 there were no significant changes in MAP in control group, where as it decreased significantly at T20 in both epidural groups compared with control group (*p*<0.05). MAP showed non significant decrease in BD group compared with BF group (Fig. 2). Maternal heart rates (HR) were comparable at start of study (0T) in all groups. The epidural groups started to show decrese in HR than control group from T10 till end of study period that were statistically significant at T20, T25 and T30 and non significant in other times. HR showed non significant decrease in BD group compared with BF group (Fig. 2). There were no changes in oxyhemoglobin saturation (SpO$_2$) at any time in all enrolled women. No women with SpO$_2$ less than 94% throughout the study period.

The mean VAS scores decreased significantly at T5 and T10 in BD group compared with control and BF groups. By T20, although both BD and BF groups had a significant lower VAS scores compared with control group, the VAS scores between BD and BF groups were not significantly different (Fig. 3).
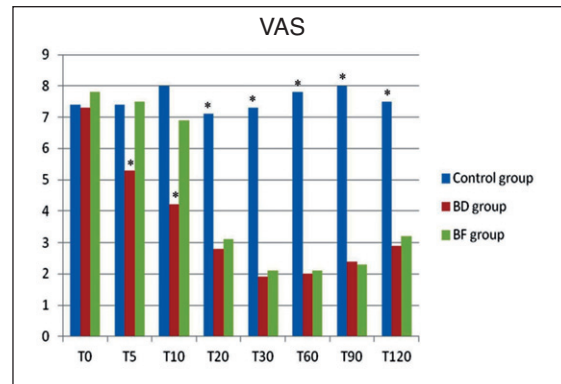

Figure 3. Visual analog scale (VAS) pain scores over study period in the three studied groups. Each data expressed as Mean. * Statistically significant (P<0.05)

Table 5 shows the uterine and umbilical arteries pulsatility indices during uterine contractions and relaxations at different time periods at baseline, 30, 60 and 120 minutes. Uterine contractions significantly increase UtA-PI when compared with PI during relaxations in all three groups (*P*<0.05). Also the epidural analgesia groups (BD and BF groups) showed significantly increases UtA-PI when compared with control group during uterine relaxations and contractions. Umbilical artery Doppler pulsatility indices

Table 5. PI of uterine and umbilical arteries during uterine contractions and relaxations.

Variable	During Uterine relaxation			During Uterine contraction		
	Control group N= 23	BD group N= 44	BF group N= 43	Control group N= 23	BD group N= 44	BF group N= 43
UtA-PI						
Baseline	0.67±0.09	0.66±0.18	0.64±0.22	1.12±0.09[#]	1.02±0.19[#]	1.10±0.07[*#]
At 30 min	0.64±0.12	0.81±0.15[*]	0.78±0.26[*]	1.01±0.17[#]	1.36±0.18[*#]	1.23±0.12[*#]
At 60 min	0.66±0.19	0.78±0.21[*]	0.76±0.20[*]	0.99±0.07[#]	1.24±0.19[*#]	1.14±0.15[*#]
At 120 min	0.70±0.17	0.76±0.22[*]	0.74±0.24[*]	1.01±0.06[#]	1.20±0.21[*#]	1.09±0.19[*#]
UA-PI						
Baseline	0.81±0.19	0.79±0.21	0.81±0.18	0.99±0.23[#]	0.96±0.18[#]	0.97±0.21[#]
At 30 min	0.77±0.16	0.82±0.21	0.81±0.22	0.97±0.21[#]	1.04±0.27[#]	0.99±0.31[#]
At 60 min	0.79±0.14	0.80±0.09	0.82±0.17	0.98±0.25[#]	1.01±0.18[#]	0.98±0.27[#]
At 120 min	0.80±0.11	0.81±0.23	0.82±0.21	0.97±0.19[#]	0.96±0.17[#]	0.97±0.25[#]

Data expressed as mean (±SD), [*]$P<0.05$ when compared control with either epidural groups; [#]$P<0.05$ when compared between contraction and relaxation in the same group.

showed non significant changes in all three studied groups if compared during uterine relaxations or during uterine contractions. A significant increase in UA-PI was seen when compared in the same group during uterine contraction compared with during relaxation but epidural analgesia groups did not showed significant changes in UA-PI compared with control group both during uterine contractions and relaxations. Pearson's correlation test showed that UtA-PI during contractions and relaxations with or without epidural analgesia not significantly correlated with UA-PI and newborns outcomes.

Discussion

This study appears to be the first study to use dexmedetomidine as adjuvant drug with bupivacaine in obstetric epidural analgesia. It also, compares two pharmacological approaches of epidural analgesia (bupivacaine-dexmedetomidine and bupivacaine - fentanyl) with parturients without epidural during uterine contractions and relaxations.
In the present study, overall the maternal satisfaction for labor pains control was better after epidural than non-epidural. Comparative VAS scores suggested that dexmedetomidine was as effective as fentanyl for labor pains control. The BD group showed visible superiority over BF group in some characteristics like the onset and duration of analgesia and sedation score. BD group showed less nausea and pruritis than BF group. A slight decrease in heart rate and mean arterial pressure was observed in BD group compared to BF group. The other side effects of both groups were quite favorable as none of the patient in either groups had deep sedation or respiratory depression which correlates very well with other studies (1,9,10,15,28,29). The requirement of vasopressors for maintenance of stable hemodynamic parameters did not reveal any significant differences between the epidural groups. UtA-PI was higher during uterine contractions than during uterine relaxations that can be explained by

strangulation of blood flow by myometrial contractions. During epidural analgesia there was increased in UtA-PI compared with baseline before epidural administration that can be explained by maternal hypotensive effect of epidural analgesia. A significant increase in UtA-PI by combined effects of myometrial contraction and hypotension of epidural had no effect on uteroplacental blood flow as UA-PI did not showed significant increase that affect fetal and neonatal outcomes. The results of the present study demonstrated that Apgar scores at 1 and 5 min in all the neonates were more than 7 and umbilical cord pH was >7.2.
The α-2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anaesthesia (28). Dexmedetomidine is a highly selective α-2 adrenergic agonist with an affinity of eight times greater than clonidine (16). Clonidine has been used successfully over the last decade for the said purpose and the introduction of dexmedetomidine has further widened the scope of α-2 agonists in regional anaesthesia (29). Bajwa et al. (10), conclude that dexmedetomidine is a better adjuvant than clonidine in epidural anesthesia as far as patient comfort, stable cardio-respiratory parameters, intra-operative and post-operative analgesia is concerned. Epidural administration of dexmedetomidine has not been well studied in labor analgesia but there are some studies of clonidine (15,30-33). Clonidine can be considered a useful adjunct in labor analgesia with bupivacaine as it provides longer and better analgesia with local anesthetic sparing effect without any significant side effects, but large scale studies are indicated before strong recommendation for its routine use in epidural labor analgesia (15). Epidural clonidine does not induce hemodynamic instability (28,31,32). A study of orthopedic surgery concluded that, Dexmedetomidine seems to be a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable hemodynamics, early onset, and establishment of sensory anesthesia, prolonged post-operative analgesia and much better sedation levels (9).
Chen et al. (34) suggested an increased UtA-PI during

continuous epidural infusion with bupivacaine and this increase is further enhanced during uterine contraction that is consistent with our results. However, Chen et al. (34) did not compare these indices with control group throughout the study also they used continuous epidural regimen. Takeuchi et al. have reported that both the resistance index (RI) and PI of the arterial uterine blood flow velocity waveform were significantly increased during uterine contraction than during relaxation. However, they did not compare these indices with those under epidural analgesia (35).

Previous reports of the effects of epidural anesthesia on the Doppler velocimetry of umbilical and uterine arteries during normal term labor have been controversial. Lindblad et al. found no significant changes in resistance in the umbilical vein or fetal aorta associated with uncomplicated epidural anesthesia (36). Hughes et al. concluded that effective epidural anesthesia did not have a significant impact on Doppler flow characteristics of either the maternal or fetal umbilical vasculature, despite lowered maternal blood pressure and heart rate (37). Morrow et al. also concluded that epidural anesthesia had neither a beneficial nor detrimental effect on uterine or umbilical blood velocity in uncomplicated pregnancy (38). Giles et al. reported a significant decrease in umbilical arterial and maternal S/D ratios after administration of epidural anesthesia in their small series of eight non-laboring patients with intact amniotic membranes (39). On the contrary, Stephen et al. reported an increase in PI of the uterine arteries after epidural anesthesia with lidocaine, epinephrine, and fentanyl but there was no change in the umbilical PI (40).

Fratelli et al. reported that UtA-PI measured during contraction was significantly increased 30 min after administration of bolus ropivacaine 0.1% in women laboring with epidural analgesia when compared with PI measured in women laboring without analgesia. This increase in uterine arterial impedance, however, was not associated with neonatal acidosis or low Apgar scores at birth. But the increase in UtA-PI did not persist 90 min after the beginning of analgesia, when the action of ropivacaine would be diminished (41). It has been suggested that maternal hypotension related to epidural analgesia is associated with an increase in the Doppler indices for the uterine arteries (11-13). The increased impedance measured during uterine contraction might be related to an insufficient increase in preload because of epidural anesthesia-induced sympathetic block and vasodilation (41,42).

The current and Fratelli et al.(41) studies did not demonstrate a relationship between UtA-PI during contraction in the epidural groups and maternal mean arterial pressure. Reduced uterine blood flow induced by epidural analgesia was not associated with significant decrease in placental blood flow, neonatal acidosis or low Apgar scores at birth.

Conclusion

Epidural analgesia is an effective method for providing pain relief during child birth. Using dexmedetomidine gave better parturients satisfactions than fentanyl as adjuvant drug to local anesthetic for its earlier onset and

longer duration of analgesia and fewer side effects as nausea and pruritis. Combined effects of hypotension and uterine contractions during epidural analgesia can increase the resistance of blood flow through uterine artery without deleterious effect on newborns compared with normal labor outcomes. More studies are recommended to support the use of dexmedetomidine as adjuvant drug during obstetric epidural analgesia as this is a new finding and it seems there are no previous reports regarding use of this drug in the labor.

References

1. Nakamura G, Ganem EM, Rugolo LM, Castiglia YM. Effects on mother and fetus of epidural and combined spinal-epidural techniques for labor analgesia. Rev Assoc Med Bras 2009;55(4):405-9.

2. Wang LZ, Chang XY, Liu X, Hu XX, Tang BL. Comparison of bupivacaine, ropivacaine and levobupivacaine with sufentanil for patient-controlled epidural analgesia during labor. A randomized clinical trial. Chin Med J (Engl) 2010; 20: 123(2):178-83.

3. Fischer C, Blanié P, Jaouën E, Vayssière C, Kaloul I, Coltat JC. Ropivacaine, 0.1%, plus sufentanil 0.5 microg/ml, versus bupivacaine 0.1%, plus sufentanil 0.5 microg/ml, using patient-controlled epidural analgesia for labor: a double-blind comparison. Anesthesiology 2000; 92: 1588-1593.

4. Owen MD, Thomas JA, Smith T, Harris LC, D'Angelo R. Ropivacaine 0.075% and bupivacaine 0.075% with fentanyl 2 microg/ml are equivalent for labor epidural analgesia. Anesth Analg 2002; 94: 179-183.

5. Fernández-Guisasola J, Serrano ML, Cobo B, Muñoz L, Plaza A, Trigo C et al. A comparison of 0.0625% bupivacaine with fentanyl and 0.1% ropivacaine with fentanyl for continuous epidural labor analgesia. Anesth Analg 2001; 92: 1261-1265.

6. Benzon HT, Wong HY, Belavic AM, Jr, Goodman I, Mitchell D, Lefheit T et al. A randomized double-blind comparison of epidural fentanyl infusion versus patient controlled analgesia with morphine for postthoracotomy pain. Anesth Analg 1993;76:316-22.

7. Salomaki TE, Laitinen JO, Nuutinen LS. A randomized doubleblind comparison of epidural versus intravenous fentanyl infusion for analgesia after thoracotomy. Anesthesiology 1991;75:790-5.

8. Lorenzini C, Moreira LB, Ferreira MB. Efficacy of ropivacaine compared with ropivacaine plus sufentanil for postoperative analgesia after major knee surgery. Anaesthesia 2002;57:424-8.

9. Bajwa SJ, Arora V, Kaur J, Singh A, Parmar SS. Comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries. Saudi J Anaesth 2011;5(4):365-70.

10. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S et al. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. Indian J Anaesth 2011;55:116-21.

11. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs 2000;59:263-70.

12. Jaakola ML, Salonen M, Lehtinen R, Scheinin H. The analgesic action of dexmedetomidine: A novel alpha2-adrenoceptor agonist–in healthy volunteers. Pain 1991;46:281-5.
13. Talke P, Richardson CA, Scheinin M, Fisher DM. Post-operative pharmacokinetics and sympatholytic effects of dexmedetomidine. Anesth Analg 1997;85:1136-42.
14. Kelly JG, McIlroy PJ. Chemistry. In: Dundee JW, Clarke RS, McCaughey W, Editors. Clinical anaesthetic pharmacology. Edinburgh: Churchill Livingstone; 1991. p. 3-14.
15. Syal K, Dogra R, Ohri A, Chauhan G, Goel A. Epidural labour analgesia using bupivacaine and clonidine. J Anaesthesiol Clin Pharmacol 2011;27(1):87-90.
16. Sudheesh K, Harsoor S. Dexmedetomidine in anaesthesia practice: A wonder drug? Indian J Anaesth 2011;55(6):556-62.
17. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care 2000;4:302-8.
18. Bloor BC, Abdul-Rasool I, Temp J, Jenkins S, Valcke C, Ward DS. The effects of medetomidine, an alpha2-adrenergic agonist, on ventilatory drive in the dog. Acta Vet Scand Suppl 1989;85:65-70.
19. Gerhardt MA, Gunka VB, Miller RJ. Hemodynamic Stability During Labor and Delivery With Continuous Epidural Infusion. J Am Osteopath Assoc 2006; 106(12):692-8.
20. Vincent RD Jr, Chestnut DH. Epidural analgesia during labor [review]. Am Fam Physician 1998;58:1785-92.
21. Li H, Gudmundsson S, Olofsson P. Uterine artery blood flow velocity waveforms during uterine contractions. Ultrasound Obstet Gynecol 2003;22(6):578-85.
22. Mihu D, Diculescu D, Costin N, Mihu CM, Blaga L, Ciortea R, Măluţan A. Applications of Doppler ultrasound during labor. Med Ultrason 2011;13(2):141-9.
23. Janbu T, Nesheim BI. Uterine artery blood velocities during contractions in pregnancy and labour related to intrauterine pressure. Br J Obstet Gynaecol 1987; 94: 1150-1155.
24. Janbu T, Koss KS, Nesheim BI, Wesche J. Blood velocities in the uterine artery in humans during labour. Acta Physiol Scand 1985; 124: 153-161.
25. Brar HS, Platt LD, DeVore GR, Horenstein J, Medearis AL. Qualitative assessment of maternal uterine and fetal umbilical artery blood flow and resistance in laboring patients by Doppler velocimetry. Am J Obstet Gynecol 1988; 158: 952-956.
26. Hofstaetter C, Dubiel M, Gudmundsson S, Marsal K. Uterine artery color Doppler assisted velocimetry and perinatal outcome. Acta Obstet Gynecol Scand 1996;75:612-19.
27. Gosling RG, Dunbar G, King DH, Newman DL, Side CD, Woodcock JP et al. The quantitative analysis of occlusive peripheral arterial disease by a non-intrusive ultrasonic technique. Angiology 1971;22:52-5.
28. Eisenach JC, De Kock M, Klimscha W. Alpha (2)-adrenergic agonists for regional anesthesia. A clinical review of clonidine (1984-1995). Anesthesiology 1996;85:655-74.
29. Paris A, Tonner PH. Dexmedetomidine in anaesthesia. Curr Opin Anaesthesiol 2005;18:412-8.
30. Hawkins JL. Epidural analgesia for labor and delivery. N Engl J Med 2010;362:1503-10.
31. Claes B, Soetens M, Van Zundert A, Datta S. Clonidine added to bupivacaine-epinephrine sufentanil improves epidural analgesia during childbirth. Reg Anesth Pain Med 1998; 23: 540-7.
32. Kizilarsalaran S, Kivaki B, Onul U, Sagiroglu E. Epidural fentanyl - bupivacaine compared with clonidine - bupivacaine for analgesia in labour. Eur J Anaesth 2001; 17 (11): 692-7.
33. Parker RK et al. Epidural clonidine added to a bupivacaine infusion increases analgesic duration in labor without adverse maternal or fetal effects. J Anesth 2007; 21(2): 142-7.
34. Chen LK, Lin CJ, Huang CH, Wang MH, Lin PL, Lee CN, Sun WZ. The effects of continuous epidural analgesia on Doppler velocimetry of uterine arteries during different periods of labour analgesia. Br J Anaesth. 2006;96(2):226-30. Epub 2005 Dec 23.
35. Takeuchi Y. Changes of arterial uterine blood flow velocity waveform during uterine contraction and relaxation in labour. Acta Obstet Gynaecol Jpn 1990; 42:79-85.
36. Lindblad A, Marsal K, Vernersson E, Renck H. Foetal circulation during epidural analgesia for cesarean section. Br Med J 1984; 288: 1329-30.
37. Hughes AB, Devoe LD, Wakefield ML, Metheny WP. The effects of epidural anaesthesia on the Doppler velocimetry of umbilical and uterine arteries in normal term labour. Obstet Gynecol 1990; 75: 809-12.
38. Morrow RJ, Rolbin SH, Knox Ritchie JW, Haley S. Epidural anaesthesia and blood flow velocity in mother and foetus. Can J Anaesth 1989; 36: 519-22.
39. Giles WB, Lah FX, Trudinger BJ. The effect of epidural anaesthesia for caesarean section on maternal uterine and foetal umbilical artery blood flow velocity waveforms. Br J Obstet Gynaecol 1987; 94: 55-9.
40. Stephen H, Phyllis G, Terri M et al. Uterine and umbilical blood flow velocity during epidural anaesthesia for caesarean section. Can J Anaesth 1994; 40: 1057-62.
41. Fratelli N, Prefumo F, Andrico S, Lorandi A, Recupero D, Tomasoni G, Frusca T. Effects of epidural analgesia on uterine artery Doppler in labor. Br J Anaesth 2011; 106(2):221-4.
42. Manninen T, Aantaa R, Salonen M, Pirhonen J, Palo P. A comparison of the hemodynamic effects of paracervical block and epidural anesthesia for labor analgesia. Acta Anaesthesiol Scand 2000; 44: 441-5.