COMPARISON BETWEEN FENTANYL 2 µG/mL VERSUS DEXMEDETOMIDINE 1.5 µG/mL AS ADJUVANTS WITH ISOBARIC BUPIVACAINE 0.0625% IN EPIDURAL LABOUR ANALGESIA

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ABSTRACT

BACKGROUND

Low-dose bupivacaine with opioids like fentanyl have been used traditionally as an adjunct for epidural labour analgesia, but has side effects like pruritus, urinary retention, nausea, vomiting, etc. Dexmedetomidine, an α-2 adrenergic agonist with a high placental retention, decreased sympathetic outflow and norepinephrine release thereby causing sedation, anxiolysis, analgesia, sympatholysis and maternal haemodynamic stability. Hence, this study was carried out to compare dexmedetomidine and fentanyl as adjuvants in epidural labour analgesia.

MATERIALS AND METHODS

A prospective randomised, double-blind study was conducted in 60 term parturients in active labour of ASA I and II physical status. They were randomised into 2 groups with 30 parturients in each and received 15 mL of 0.0625% Inj. Bupivacaine plus either 1.5 µg/mL Inj. Dexmedetomidine (BD group) or 2 µg/mL Inj. Fentanyl (BF group). VAS, sedation scores, modified four grade Bromage scale, haemodynamics, peripheral oxygen saturation were recorded at baseline and regular intervals. When VAS was ≥4, subsequent doses of 5 mL of the respective group drug was administered. Parturients were ambulated when Bromage scale was 0 with no postural hypotension. Duration of analgesia, labour outcome, neonatal Apgar scores and side effects were noted.

RESULTS

Demography and haemodynamic stability were similar and comparable. Duration of analgesia was significantly longer in BD group (131.83±45.760) than BF group (85.33±22.512) ($p<0.0001$). More no. of top-ups was needed in BF group (1.80±1.518) than BD group (0.17±0.461) ($p<0.0001$). Significantly reduced VAS scores was observed in BD group than BF group. Mean sedation scores ($p<0.05$) and maximum Bromage scores ($p=0.004$) were significantly higher in BD group than BF group. Ambulation was less in BD group (3 parturients) than BF group (26 parturients). Side effects were significantly more in BF group than BD group ($p=0.007$). The labour outcomes were better in BD group than BF group and Apgar scores were comparable in both the groups.

CONCLUSION

Bupivacaine-dexmedetomidine provides longer duration and better quality of analgesia for labour pain control compared to bupivacaine-fentanyl without deleterious effects on newborns and labour outcomes.

KEYWORDS

Epidural, Labour Analgesia, Bupivacaine, Dexmedetomidine, Fentanyl.

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BACKGROUND

The joy of childbirth is always accompanied with a fear of pain. 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 foetus of oxygen and nutrients.[1] The provision of effective labour analgesia is now known to decrease the inhibitory effects of endogenous maternal catecholamine on uterine contractility, attenuates maternal acidosis and improves intrapartum maternal wellbeing.

The gold standard in labour analgesia is the utilisation of epidural services,[2] which are widely used to provide pain-free labour in many parts of the world and have the advantage of providing flexibility to meet the needs of each patient.[3] The greatest advantage of implementing intermittent lumbar epidural for labour analgesia is the lack of need of volume elastomeric epidural infusion pump; making its worth role in conducting deliveries in emergency settings, primary, secondary and tertiary health centres of developing countries (India, etc.) where these facilities are not easily available, but do have the human resources to provide the intermittent top-ups.

Epidural analgesia has been extensively used to provide pain relief in labour. Bupivacaine is still the most widely used local anaesthetic in obstetric analgesia.[4] However, it is potential for motor blockade is clinically undesirable for obstetric patients. In order to minimise this, lower concentrations of local anaesthetics combined with opioids like fentanyl have been used traditionally as an adjunct for epidural administration to achieve the desired analgesic effect.[5] It provides a dose sparing effect of local anaesthetic and superior analgesia, but there is always a possibility of an increased incidence of pruritus, urinary retention, nausea, vomiting, giddiness, shivering and respiratory depression.[6] Dexmedetomidine is an α-2 adrenergic agonists with analgesic properties. They act on both pre and postsynaptic sympathetic nerve terminal and central nervous system thereby decreasing the sympathetic outflow and norepinephrine release causing sedative, anxiolysis, analgesia, sympatholysis and maternal haemodynamic stability.[7-10] The anaesthetic and the analgesic requirement get reduced to a huge extent by dexmedetomidine because of its analgesic properties and augmentation of local anaesthetic effects when epidurally administered[11,12] as they cause hyperpolarisation of nerve issues by altering transmembrane potential and ion conductance at locus coeruleus in the brainstem.[13-15] It is retained in placental tissue (0.77 maternal/foetal index) and passes less readily into the foetal circulation because of high lipophilicity and thereby has less susceptibility to cause foetal bradycardia.[16] Overall, dexmedetomidine was quite satisfactory as compared to clonidine (α-2 adrenergic agonist) because of its superior sedative and anxiolytic properties during the surgical procedure under regional anaesthesia.[17]

The most common complications occurring with epidural analgesia is maternal hypotension.[18] Hypotension threatens the foetus by decreasing uterine blood flow. However, modest decreases (≤20%) in maternal blood pressure are of limited concern in a woman with a healthy foetus.[19]

Studies in labour analgesia with dexmedetomidine are limited. Hence, this study was carried out to study the effect of dexmedetomidine in comparison to fentanyl as adjuvant with low-dose bupivacaine in epidural labour analgesia.

MATERIALS AND METHODS

The study was approved by the ethical committee of Bangalore Medical College and Research Institute and a written informed consent was obtained from the parturients before the procedure. This was a hospital-based prospective, randomised, double-blind, controlled clinical study performed during a 6-month period (December 2013 to May 2014) in the labour ward of Vani Vilas Hospital attached to Bangalore Medical College and Research Institute. Keeping the power of study as 80% and confidence limit 95% to detect a 25% difference for duration of analgesia. Minimum sample size required was 15 in each group.

We enrolled 60 parturients classified as per American Society of Anesthesiologists (ASA) classes I and II for better results. The parturients were randomly allocated by sealed envelope method (www.random.org) into two groups of 30 each.

Inclusion criteria were parturients who gave informed written consent; ASA Grade I and Grade II; primigravida aged between 18 to 35 years; engaged vertex presentation with intact membrane; active labour with cervical dilatation 3-5 cm; uterine contractions occurring at least every 5 mins.; parturients in the study who later required caesarean section due to obstetric causes (continued with same epidural with lignocaine 2% and adrenaline 1:2,00,000 of required doses for caesarean section) and normal foetal cardiotocography [baseline Foetal Heart Rate (FHR) between 110 and 160 beats/minute, baseline variability >5 beats/minute, presence of accelerations and absence of decelerations].

Exclusion criteria were parturients who refused to give informed written consent; parturients with systemic disorders like pregnancy-induced hypertension (preeclampsia), concomitant cardiovascular disease, documented coagulation abnormality or abnormal bleeding history, etc.; age <18 or >35 years; evidence of infection or anatomic abnormality at the proposed catheter insertion site; inadvertent epidural puncture (wet tap) or bloody tap; failed epidural - VAS persistently >4 (other methods of analgesia were used) and parturients who had received opioids or presented a history of hypersensitivity to local anaesthetic, fentanyl or to dexmedetomidine.

After obtaining informed written consent, parturients were randomly divided into 2 groups.

Group BD: Bupivacaine – Dexmedetomidine - 30 parturients.

Group BF: Bupivacaine - Fentanyl - 30 parturients.

Each to receive 15 mL of 0.0625% isobaric Inj. Bupivacaine plus either 1.5 µg/mL Inj. Dexmedetomidine (BD group) or 2 µg/mL Inj. Fentanyl (BF group).

A routine preanaesthetic examination and investigations were done in all parturients. The mixed solutions for epidural analgesia were prepared under sterile conditions by colleagues. The parturients were trained how to use VAS scores before the start of the study. All equipment needed for resuscitation of the mother or foetus were kept ready before the institution of the block.

An intravenous infusion of 500 mL of Ringer lactate solution on flow. Monitors included Non-Invasive Blood Pressure (NIBP), pulse oximeter (oxygen saturation of haemoglobin-SpO2) and Electrocardiogram (ECG). Baseline readings were noted. The parturient was positioned in the

left lateral position. Under asepsis, after local infiltration with 2% Inj. Lignocaine, an epidural catheter was inserted into the L3-L4 or L2-L3 vertebral interspace using the loss of resistance technique. A 3-4 cm of catheter was introduced into the epidural space. With the patient in supine position and a wedge under the right hip, the study drugs were administered.

Each received 15 mL of 0.0625% isobaric Inj. Bupivacaine plus either 1.5 µg/mL Inj. Dexmedetomidine (BD group) or 2 µg/mL Inj. Fentanyl (BF group). The solutions were randomly administered as 1:1 ratio for BD and BF groups.

Parameters recorded were pain scores (visual analogue scale, onset, duration, top-ups, local anaesthetic requirement for episiotomy); sedation scores; modified Bromage scale (ambulation); maternal blood pressures; oxygen saturation of haemoglobin; maternal heart rate; labour outcome and neonatal Apgar scores following delivery and side effects (nausea, vomiting, pruritus, giddiness, shivering or respiratory depression). For the uniformity of the study, all the parameters were assessed every 5 minutes for the first 30 minutes, every 10 minutes for second 30 minutes, then every 20 minutes until delivery.

Subject pain was assessed with a 10-cm linear Visual Analogue Scale (VAS) where 0 represented no pain and 10 represented most severe pain. Onset of analgesia was defined as from the time of injection of study drugs to drop of VAS by at least 1. Duration of analgesia was defined as from the time of injection of study drugs to VAS ≥4. When VAS ≥4, 5 mL top-up of the respective group drug [0.0625% Inj. Bupivacaine plus 1.5 µg/mL Inj. Dexmedetomidine (BD group) or 2 µg/mL Inj. Fentanyl (BF group)] was administered. The no. of top-ups required was noted. Requirement of local anaesthetics for episiotomy and suturing was also noted.

Sedation score was assessed by a 4-point scale (1-wide awake; 2-dozing; 3-asleep; 4-unarousable). 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). Parturients were allowed to ambulate when Bromage scale was 0 and absence of postural hypotension. The mode of delivery whether vaginal delivery, instrumental (forceps or vacuum) or caesarean section was noted. The neonatal assessment (was done by Apgar scores at 1st and 5th mins. for haemodynamic stability; blood pressures (Systolic Blood Pressure {SBP} and Diastolic Blood Pressure {DBP}), oxygen saturation of haemoglobin (SpO2) and maternal Heart Rate (HR) were recorded. Hypotension prospectively defined as a 20% decrease in Mean Arterial Pressure (MAP) from the baseline or systolic blood pressure <90 mmHg and bradycardia as heart rate <60/minute was treated with intravenous fluids, left uterine displacement, Inj. Ephedrine 6 mg IV and Inj. Atropine 0.6 mg IV, respectively. Nausea or vomiting was treated with Inj. Ondansetron 4 mg IV.

Statistical analysis was performed with the use of SPPS 16.0 for windows. Numerical variables were presented as the mean and Standard Deviation (SD) whereas categorical data were presented using counts. The following tests were applied according to the type of variables. Student's t-test, chi-square test, Fisher's exact test. P values <0.05 were considered statistically significant.

RESULTS

We consented and enrolled 60 parturients. Demographic and labour characteristics are presented in Table 1, 2 and 3. The parturients were comparable in age, height and weight at time of entry into the study. There were 3 instrumental and 1 caesarean section (foetal distress) in BF group and all spontaneous delivery in BD group. The Apgar scores at 1st and 5th minute was not significant at 1st minute, but was significant at 5th minute (p=0.03). However, Apgar scores at 5th minute with a mean of 7.73 in BF group and 8.30 in BD group are still acceptable.

Group	BF	BD	p value
Weight (kg)	59.33±10.848	59.63±7.103	0.042
Height (cm)	157.77±5.444	154.50±6.039	0.518
Age (years)	21.50±2.649	21.27±1.780	0.021

Table 1. Demography

p<0.05 is significant.

Group	Instrumental	Caesarean	Spontaneous	Total
BF	3	1	26	30
BD	0	0	30	30
Total	**3**	**1**	**56**	**60**

Table 2. Labour Outcome

Group	BF	BD	p value
Apgar 1'	6.00±2.051	6.83±1.577	0.083
Apgar 5'	7.73±1.143	8.30±0.877	0.035

Table 3. Neonatal Outcome

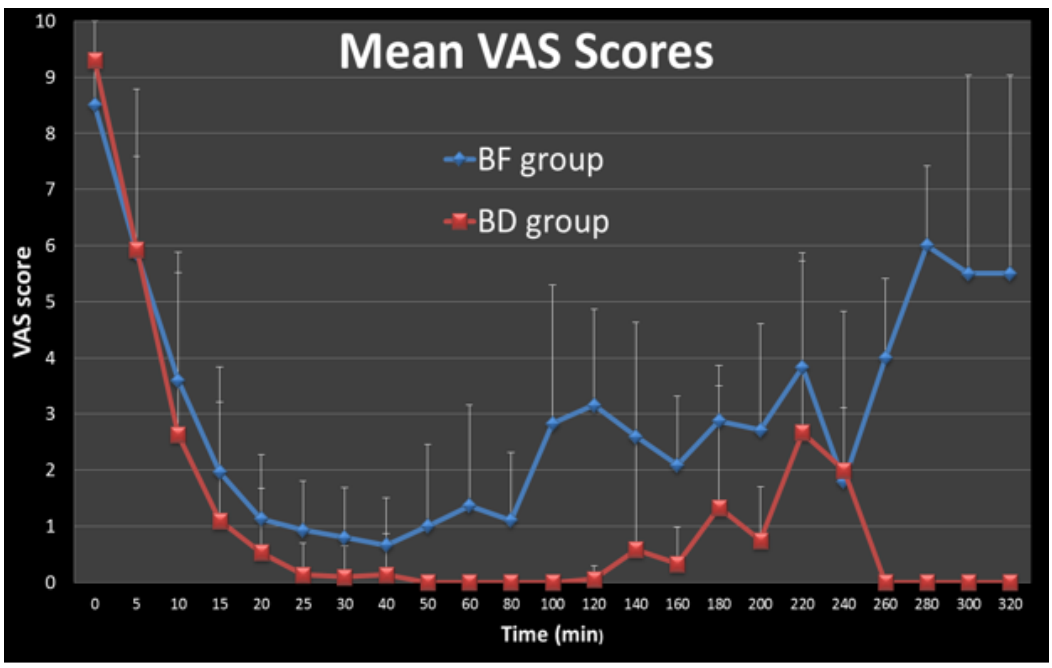
p<0.05 is significant

Table 4 gives the comparison of analgesic outcomes between the two groups. The onset of analgesia was found to be 6±2 mins. in BF group and 5.3±1.2 mins. in BD group, which were almost similar and not significant. The duration of analgesia was statistically significant (p<0.0001) and longer in BD group (131.8±45.7 mins.) compared to BF group (85±22.5 mins.). The number of top-ups required in BF group was more (1.8±1.4) in comparison to BD group (0.17±0.4), which was also significant (p<0.0001). In BF group, 29 parturients required local anaesthetic for episiotomy followed by suturing after delivery whereas 28 parturients of the 30 in BD group did not require local anaesthetic at all for episiotomy as well as suturing (p<0.0001) and 1 delivered without episiotomy. VAS scores was significantly reduced (p<0.05) in BD group from 20th minute onwards till the end of delivery in comparison to BF group (Graph 1).

Group	BF	BD	p value
Onset (mins.)	6.00±2.034	5.33±1.269	0.133
Duration of analgesia (mins.)	85.33±22.512	131.83±45.760	<0.0001
Number of top ups	1.80±1.518	0.17±0.461	<0.0001
Episiotomy/suturing without local anaesthetic (number)	1	28	<0.0001

Table 4. Analgesic Outcomes

p<0.05 is significant.



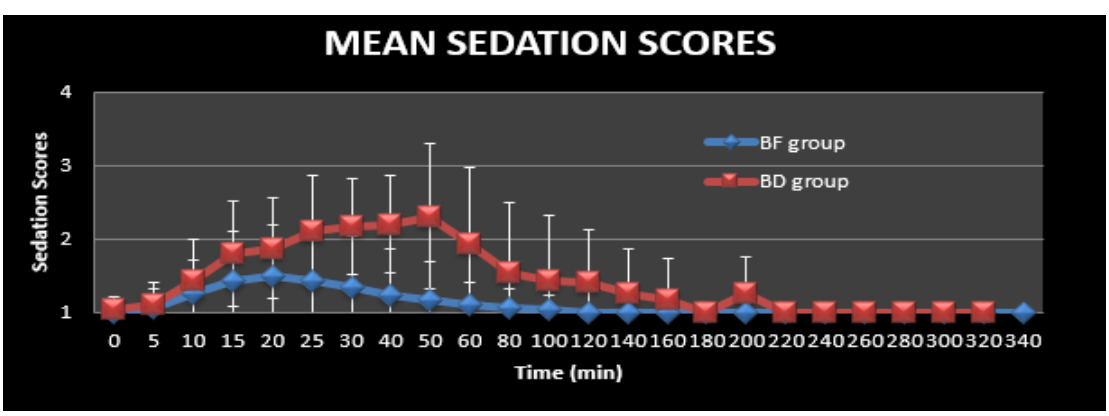
Graph 1. VAS Scores

Bromage scores (Table 5) with 1 and more were significantly (p=0.004) more in BD group (13 parturients), which made them inability to ambulate as compared to BF group (2 parturients). Out of 30 parturients in each group, 26 parturients could ambulate in BF group and only 3 parturients in BD group, which was one of the drawback in BD group (p<0.0001). The sedation scores as depicted in Graph 2 were significantly (p<0.05) higher between the 15th and 120th minutes in BD group than BF group.

Group	BF (Number)	BD (Number)	p value
Bromage Scores (0-1-2-3)	28-2-0-0	17-12-1-0	0.004
Ambulation	26	3	<0.0001

Table 5. Bromage Score and Ambulation

p<0.05 is significant



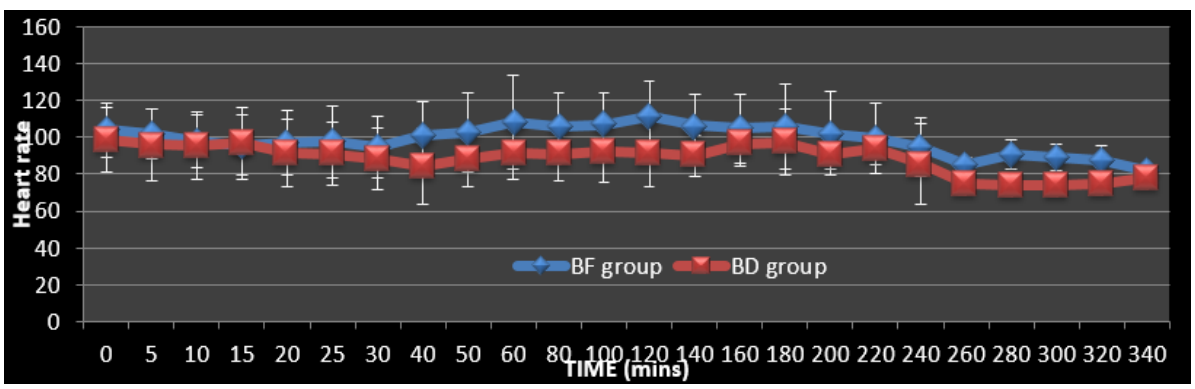
Graph 2. Sedation Scores

Table 6 depicts the comparison of side effects. The incidences of nausea and vomiting (6 parturients), giddiness (2 parturients) and headache (1 parturient) was significantly higher (p=0.03) in BF group than BD group and 1 parturient from each group had shivering. Incidence of pruritus or respiratory depression was absent in both the groups.

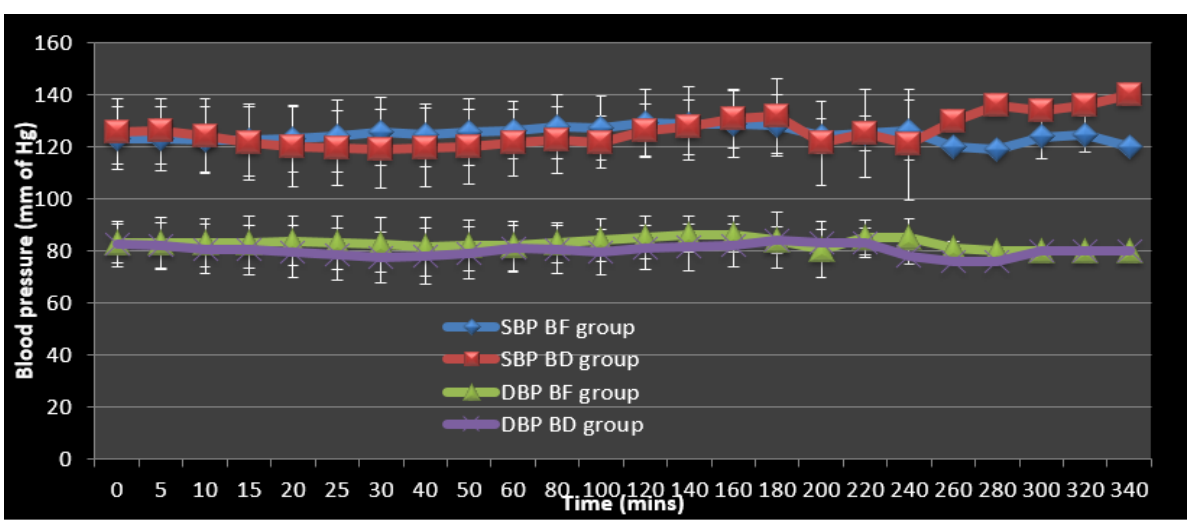
Group	Nil	Nausea/Vomiting	Giddiness	Shivering	Headache	Total
BF	20	6	2	1	1	30
BD	29	0	0	1	0	30
Total	49	6	2	2	1	60

Table 6. Side Effects

There was no significant (p>0.05) maternal hypotension, bradycardia or changes in oxygen saturation of haemoglobin (SpO2) in both the groups at any point of time in all the parturients. Stable haemodynamics were maintained in both the groups. (Graph 3, 4).



Graph 3. Maternal Heart Rate



Graph 4. Maternal Blood Pressure (Systolic and Diastolic Blood Pressure)

DISCUSSION

This study compares two pharmacological approaches of epidural analgesia (bupivacaine-dexmedetomidine and bupivacaine-fentanyl) in parturients. Our study with dexmedetomidine as adjuvant has showed superiority in characteristics like duration and quality of analgesia, sedation scores, absent episiotomy pain, no deleterious effects on labour and neonatal outcome and no side effects.

Parturients receiving dexmedetomidine were unable to ambulate in comparison to fentanyl. This could be due to the action on alpha motor neurons, which prolonged motor blockade. None required vasopressors or atropine for maintenance of stable haemodynamic parameters in both the groups.

Comparative VAS scores suggested that dexmedetomidine was more effective than fentanyl for labour pain control. The BD group showed visible superiority over BF group in some characteristics like duration of analgesia, sedation score, labour outcome and episiotomy pain. BD group parturients showed no incidence of nausea, vomiting or giddiness in comparison with BF group pointing out that side effects were more common in BF group. Majority of the BD group were unable to ambulate in comparison to BF group, which was one drawback in the BD group. Labour outcomes was also better in the BD group compared to BF group. The results of the present study did not demonstrate any gross changes in Apgar scores at 1st and 5th min. in all the neonates. None required vasopressors or atropine for maintenance of stable haemodynamic parameters in both the groups.

Tomar et al found that epidural fentanyl 2 µg/mL is better than 1 µg/mL when combined with bupivacaine in

intermittent bolus technique as it leads to faster onset, longer duration of analgesia, higher maternal satisfaction, lesser drug requirement of local anaesthetic with comparable side effect profile.[20] Hence, our study has chosen an optimum dose 2 µg/mL of fentanyl as well. Bajwa et al in lower limb orthopaedic surgeries have shown dexmedetomidine to be a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable haemodynamics, early onset of sensory anaesthesia, prolonged postoperative analgesia, lower consumption of postoperative local anaesthetics for epidural analgesia and much better sedation levels.[21]

Selim et al concluded that bupivacaine-dexmedetomidine epidural analgesia showed better maternal satisfaction for labour pain control compared with bupivacaine-fentanyl without deleterious effect on uteroplacental circulation and newborns outcome.[22] Fyneface et al proved to have normal neonatal outcomes and single shot intrathecal bupivacaine-dexmedetomidine significantly prolonged sensory and motor block in labouring women.[23]

Bajwa et al epidural study on hysterectomies had shown dexmedetomidine (1.5 µg/kg) as a better adjuvant than clonidine (2 µg/kg) for patient comfort, stable cardiorespiratory parameters, intraoperative and postoperative analgesia.[24] Dilesh et al has shown that 10 µg dexmedetomidine intrathecally provides a longer duration of analgesia with lesser incidence of pruritus compared to 20 µg fentanyl intrathecally for combined epidural labour analgesia with comparable neonatal side effects.[25]

CONCLUSION

Epidural analgesia is an effective method for providing pain relief during childbirth. Our study with lower doses of dexmedetomidine as adjuvant in comparison to other studies yielded similar results and gave parturients better satisfaction than fentanyl. This is shown by the VAS scores yielding better quality of analgesia with longer duration and fewer side effects without deleterious effect on newborns and labour outcomes.

More studies are recommended with lower doses of dexmedetomidine as adjuvant drug for the study of duration of analgesia and to probably achieve an early ambulation.

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