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Original Research Article

A Comparative Study between Dexmedetomidine and Fentanyl as Adjuvant with Epidural Levobupivacaine in Abdominal Hysterectomy

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Abstract

Background: Objective of this study was to compare epidural dexmedetomidine or fentanyl with levobupivacaine in terms of onset of sensory block, peak height of sensory block, duration of analgesia, Onset, and duration of motor block, intra operative haemodynamic stability, surgeon's satisfaction regarding operating condition by VAS scale and untoward side effects

Methods: After the approval of the Institutional Ethics Committee this randomized, parallel group, double-blind controlled study was carried out under the Department of Anaesthesiology of a tertiary care centre in north India.

Results: Dexmedetomidine (50µg) is better adjuvant that fentanyl (50µg) in terms early onset of sensory and motor block. Dexmedetomidine provides longer duration of sensory and motor block than fentanyl. Both are comparable regarding maximum level of sensory block. Regarding haemodynamic parameter (Mean BP, Heart rate) and adverse effect (bradycardia, hypotension, nausea & vomiting, pruritus) dexmedetomidine is better alternative than fentanyl, though it cause more decrease of heartrate. Dexmedetomidine provides more satisfaction among surgeon than fentanyl.

Conclusions: Therefore, epidural dexmedetomidine is a feasible, safe, and more reliable adjuvant with levobupivacaine (0.5%) to provide smooth anaesthesia and analgesia with higher satisfaction to surgeon than epidural fentanyl in abdominal hysterectomy.

Keywords: Dexmedetomidine, Fentanyl, Adjuvant, Epidural Levobupivacaine, Abdominal Hysterectomy

Introduction

Regional anaesthesia is a popular method of anaesthesia for gynaecological surgery than general anaesthesia as it has so many advantages. Spinal, epidural anaesthesia are common options for gynaecological surgeries. Spinal anaesthesia is advocated because of its reliability and simplicity, but suffers the limitation of a single injection technique, longer discharge times, and a higher incidence of side effects than the other two techniques [1] (epidural and general anaesthesia). Epidural anaesthesia for gynaecological surgery is widely accepted for its greater advantages over general anaesthesia in terms of avoidance of laryngoscopic surge, better perioperative pain management and greater patient satisfaction. [2] Epidural anaesthesia also attenuates neuroendocrine response to surgery if given well ahead of surgical stimulus. [3] Many beneficial aspects of epidural anaesthesia have been reported, including better suppression of surgical stress, [4] positive effect on postoperative nitrogen balance. [5] It can be used to extend analgesia into postoperative period, where their use has been shown to provide better analgesia than can be achieved with parenteral analgesic.

Many local anaesthetic agents have been used for epidural anaesthesia. Bupivacaine is a well established long acting local anaesthetic which like all amide anaesthetic has been associated with cardiac toxicity when used in high concentration or when accidentally administered intravascularly. Levobupivacaine, the the s-enantiomer of 1-butyl-N-2, piperidine-2-carboxamide is a local anaesthetics with a chemical structure related to mepivacaine and bupivacaine. A number of studies suggest that levobupivacaine is associated with less central nervous system toxicity and cardiactoxicity with less motor block potency but anaesthesia and analgesic property is comparable with 6dimethyiphenyl bupivacaine. [6]

Gynaecological surgeries are sometimes associated with significant blood loss and there is greater incidence of hypotension. Epidural anaesthesia provides more stable cardiovascular haemodynamics, reduces blood loss, better peripheral vascular circulation [7,8] though it itself may cause hypotension. It is a major concern specially in aged patient population. In this scenario sedative drugs, either inhalational or intravenous, may potentiate the incidence of respiratory depression as well as hypotension. To avoid this and to have stable haemodynamics and postoperative analgesia, an effort has been made to administer various adjuvant in the epidural route along with local anaesthetics.

Different drugs have been tried as adjuvant to local anaesthetic. Local anaesthetic with opioids demonstrate significant synergy, They provide excellent analgesia and prolongs the time of regression of sensory block. [9]

Since the introduction of epidural opioids into clinical practice of anaesthesia in 1979, it has gained widespread popularity and acceptance. Epidural administration of combination of opioids and levobupivacaine for postsurgical pain relief has resulted in better pain scores. Several authors have suggested that this combination may produce a synergistic effect, while reducing the incidence of side effects. [10,11]

Since hydrophilic opioids such as morphine, remain in the cerebrospinal fluid for long duration and may be responsible for undesirable side effects like delayed onset of peak analgesic effect and late respiratory depression, highly lipophilic opioids such as fentanyl have been used to reduce the side effects of extradural opioid administration. [12,13] Fentanyl, a potent opioid receptor agonist is largely used to provide analgesia for acute pain and to enhance the quality to epidural block for perioperative analgesia. [14]

α2 adrenargic agonist has both analgesic and sedative effect when administered in epidural route along with local anaesthetics. [15,16] The incidence of vomiting, prurtitus and respiratory depression is less frequent as compared with that seen after epidural opioid. Both dexmedetomidine and clonidine are α2 agonist used widely in clinical practice. Clonidine also have sedative and analgesic property. [17] It has Aδ and C fidres and intensifies local anaesthetic conduction block and also prolongs analgesia. [18] Dexmedetomidine, a denantiomer of medetomidine, has analgesic property and augmentation of local anaesthetic effect causing hyperpolarisation of nerve tissues by altering transmembrane potential and ion conduction at locus coeruleus in brainstem. The drug has sedative, hypnotic and analgesic effect [19] with limited respiratory depression with special property of easy arousability without cloudiness of mind and better haemodynamic control. Decreased oxygen demand due to enhanced sympathoadrenal stability [4] makes it very useful in the perioperative period as well.

With this previous review, this study was conducted to compare dexmedetomidine with fentanyl with epidural levobupivacaine in respect of perioperative anaesthesia and analgesia.

Aims and Objectives

Objective of this study was to compare epidural dexmedetomidine or fentanyl with levobupivacaine in terms of onset of sensory block, peak height of sensory block, duration of analgesia, Onset, and duration of motor block, intra operative haemodynamic stability, surgeon's satisfaction regarding operating condition by VAS scale and untoward side effects

Materials & Methods

After the approval of the Institutional Ethics Committee this randomized, parallel group, double-blind controlled study was carried out under the Department of Anaesthesiology of a tertiary care centre in north India from March 2015 to June 2016.

Inclusion Criteria

- ASA grade: I and II
- Age: 40 to 60 years
- Sex: Female
- Type of surgery: Elective gynaecological surgeries (Abdominal hysterectomy)

Exclusion Criteria

- Local infection in the lumbar region
- Known hypersensitivity to amide local anaesthetic
- Bleeding diathesis
- Spinal deformity
- Diabetes
- Preexisting neurological, cardiac, renal, metabolic, psychiatric disorder.

Written informed consent was obtained. Patients thus enlisted for the study were randomly allocated into two groups, group-A and group-B using a computer generated randomization chart.

Group-A (n=30): received 15 ml of 0.5% Levobupivacaine hydrochloride plus 50 µg dexmedetomidine

Group-B (n=30): received 15 ml of 0.5% Levobupivacaine hydrochloride plus 50 µg Fentanyl citrate.

Sample Size

60(30 in each group). For the purpose of sample size calculation the duration of analgesia was taken as primary outcome measure. It was estimated that n=27 subjects (recruitment target being 30 subjects per group) would be required per group in order to detect the difference of 30 minutes in the duration of analgesia between two groups with 80% power and 5% probability of type 1 error. This calculation assumes a standard deviation

of 45 minutes for the duration of analgesia parameters.

Statistical Methods

Data were entered in MS excel data base and were analyzed with the help of statistical package for social science (SPSS software version 16.0 for Windows, SPSS Inc.

Chicago). Numerical variables would be compared between groups by Student's unpaired ttest if normally distributed or by Mann-Witney U-test if otherwise. Categorical variables would be compared between groups by Chi-square test or Fisher's exact test as appropriate. Analysis would be two tailed and $p<0.05$ would be considered statistically significant.

Results

There was no statistically significant difference in age distribution among the study groups as (P value = 0.472). There was no statistically significant difference (p=0.517) between the Group-A and group-B in respect to the body weight.

There was no statistically significant difference (p=0.282) among the study groups (Gr. B) and the control group (Gr. A) in respect to the height. There was no statistically significant difference (p=0.222) among the Group-A and Group-B in respect to the duration of surgery in minutes. There was no statistical significance between the two groups with regard to ASA grading (P value = 0.800).

Table 1: Distribution of Onset of Sensory Block and Onset of Motor Block

Duration of Sensory Block (min)	**Group A (N=30)**	**Group B (N=30)**
Minimum time	8	8
Maximum time	13	15
Mean	10.10	11.40
Std. Dev	1.373	1.886
Distribution of Onset of Sensory Block between Two Groups		
Duration of Motor Block (min)	**Group A (N=30)**	**Group B (N=30)**
Minimum time	14	16
Maximum time	22	25
Mean	17.53	21.37
Std. Dev	1.995	2.470
Distribution of Onset of Motor Block in Two Groups		

There was statistically significant difference (p=0.003) between the Group-A and Group-B in respect to the time for onset of sensory block. Patients in Group-A had early onset of sensory block than Group-B. Patients in the group-B had significantly earlier onset of motor block than Group-A (p=0.000).

There was no statistically significant difference in distribution of block height achieved in different patients between Group-A and Group B (P value=0.441 for T4 level, 0.292 for T5 level and 0.759for T6 level).

Table 2: Distribution of Duration of Sensory Block Onset of Motor Block and Analgesia

Duration (min)	**Group A (N=30)**	**Group B (N=30)**
Mean	157.33	138
Std. Dev	15.468	10.296
Distribution of Duration of Sensory Block (Two Segment Regression) between Two groups		
Duration (min)	**Group A (N=30)**	**Group B (N=30)**

Mean	250.37	213.97
Standard deviation	21.281	25.187
Distribution of Duration of Motor Block Between Two Groups		
Duration (min)	**Group A (N=30)**	**Group B (N=30)**
Mean	355.87	302.40
Std. Dev	18.846	37.736
Distribution of Duration of Analgesia (MIN) between Two Groups		

There was statistically significant difference (p=0.000) among the Group-A and Group-B in respect to the duration of sensory block. There was statistically significant difference (p=0.0000) among the Group-A and Group-B in respect to the duration of motor block.

There was a statistically significant difference (p=0.000) between the Group-A and Group-B in respect to the duration of analgesia. This was assessed on the basis of VAS score in the post-operative period (When VAS score≥4) or patient demand for analgesics in the post-operative period. Thus duration of analgesia was longer in Group-B (252.38 min) as compared to Group-A (231.25).

There was no statistically significant difference (p value >0.05) between the patients of Group-A and Group-B as per as mean arterial pressure (MAP) was concerned at any time in the study period.

Table 3: Comparison of Heart Rate between Two Groups

Time	Group-A (MEAN±SD)	Group-B (MEAN±SD)	Significance (p VALUE)
0 MIN	82.30±5.87	83.43±5.57	.446
5 MIN	80.60±6.86	83.67±4.79	.049
10 MIN	78.73±6.04	84.07±4.67	.000
15 MIN	77.80±6.16	86.80±4.83	.000
20 MIN	76.97±5.91	88.17±6.85	.000
25 MIN	78.37±6.99	89.80±7.09	.000
30 MIN	82.33±5.56	90.73±6.09	.000
45MIN	84.80±4.72	91.83±5.92	.000
60MIN	87.37±5.55	91.33±6.24	.014
75MIN	89.80±4.72	93.10±7.16	.039
90MIN	92.04±6.04	96.54±6.29	.011
105MIN	91.93±8.04	95.67±10.02	.492

Regarding the base line value no significant difference was noted between the two groups (p>0.05). Thereafter there was decline of heart rate from baseline value in group A after 10 min of administration of administration of epidural levobupivacaine and dexmedetomidine, which was statistically significant(p<0.05). It was continued upto 90 minutes. Thereafter heart rate become comparable between the two groups.

There was significant difference between group A (2.33) and group B (1.8) with regard to mean surgeon's satisfaction score (p value=0.000).

There was no significant statistical difference between the two groups with regard to side effects (p value > 0.05).

Discussion

The mean time of motor block were less in group A (17.53±1.99 minutes) than Group B (21.37±2.47 minutes). Appropriate statistical test shows, there was significant difference (p<0.05) in the time of onset of motor block between the two groups. Bajwa et al. [20] evaluated the addition of

dexmedetomidine or fentanyl to epidural ropivacaine in patient undergoing lower limb orthopaedic surgeries and they found that the onset of sensory analgesia and the establishment of the complete motor blockade was significantly earlier in the dexmedetomidine group. Gupta K, et al. [21] in their study with single shot epidural anaesthesia found that onset of complete motor block was 19.27± 4.7 minutes in group D (levobupivacaine + dexmedetomidine) and 22.78±5.5 minutes in group F (levobupivacaine+ fenanyl).

Highest level of sensory block was achieved in both the groups was up to T4 dermatome and lowest level was up to T6 dermatome. Among the patient of group A 47% found to have a height of sensory block up to T4 dermatome, 30% up to T5, 23% up to T6 and in the patient of group B 37% up to T4,43% upto T5, 20% upto T6 dermatome. There was no significant difference between the two groups according to block height. Soliman R et al [22] also concluded that both the group in his study were comparable according to maximum sensory block height, also supported our study.

The duration of sensory block was calculated by counting time required to two segment regression of sensory block after surgery under epidural anaesthesia. The mean duration of sensory block was more (157.33±15.46 minutes) in group A than in group B (138±10.29 minutes). Gupta S et al. [21] in their study with single shot epidural anaesthesia found that two segment regression time was more for levobupivacine and dexmedetomidine than levobupivacine and fentanyl, which was stasistically significant ($p<0.05$), also supported our study.

The mean duration of motor block (250.37± 21.28 minutes) was more in group A in than group B (213.97±25.18 minutes). Gupta S et al. [21] in their study with single shot epidural anaesthesia found that mean duration of motor block was more in group LD (213.97±25.18 minutes) than group L (199±12.95 minutes) also supported our study.

Duration of analgesia was assessed from onset of sensory block to first request for resque analgesic or vas score >4(0=no pain and 10= worst possible pain). The mean duration of analgesia was 355.87±18.84 minutes in group A, in group B 302.40±37.73 minutes. The difference between two groups were statistically significant in respect to duration of analgesia. Hanoura SE et al. [23] in their study also found that time for first analgesic dose was more in DBF group in (321±19 mins) than in BF group (174±15.7 mins).

In the present study the baseline values of mean BP were similar in both the groups. Reduction of mean BP from their baseline values were noted following epidural dexmedetomidine as well as epidural fentanyl. We have noticed episode of hypotension in the intraoperative period in some patients of both the groups which was also statistically insignificant. Intra operative mean BP remain stable after 30-45 minutes. Gupta K et al.84 found no statistically significant episode of hypotension either in dexmedetomidine or fentanyl groups which also supported our study. [24]

Decrease in the intraoperative heart rate is known clinical effect of opioids but dexmedetomidine has similar chronotropic action in a exaggerated manner. They are α2 agonist, decrease heart rate due to postsynaptic activation of α2 adrenoreceptors in the central nervous system, resulting in decreased sympathetic activity. In the present study baseline heartrate was similar in both the groups. But decrease in the heart rate was more prominent in the dexmedetomidine group than fentanyl which was aiso statiscally significant($p<0.05$). Intraoperative heartrate become stable in both the group around 75-90 minutes. Soliman R et al. [22] also found stastically significant difference in intraoperative heartrate in

both the group ($p<0.05$) which also supported our study.

There was no statistical difference ($p=0.126$) between the two groups with regard to number of patients suffer from the episodes of hypotension. Bajwa et al. found no difference in the incidence of bradycardia or hypotension in the two groups.

Surgeon's satisfaction score ($p=.000$) were significantly higher in group A, which proved clearly that dexmedetomidine was superior adjuvant than fentanyl to provide satisfactory sensory-motor block when administered with 0.05% levobupivacaine in epidueal anaesthesia.

Five patients in group A and eight patient in group B had incidence of nausea and vomiting. Four patients in group B complaint about pruritus, while none in group A. Three patients in either group had shivering. Two patient in group A and one patient in group B had headache. There was no incidence of respiratory depression and urinary retention in any group. The side effects such as nausea and vomiting, pruritis, were lower in the dexmedetomidine group compared to fentanyl group and a similar result was shown by Gupta et al.[21]

Conclusion

Dexmedetomidine(50µg) is better adjuvant that fentanyl (50µg) in terms early onset of sensory and motor block. Dexmedetomidine provides longer duration of sensory and motor block than fentanyl. Both are comparable regarding maximum level of sensory block. Regarding haemodynamic parameter (Mean BP, Heart rate) and adverse effect (bradycardia, hypotension, nausea & vomiting, pruritus) dexmedetomidine is better alternative than fentanyl, though it cause more decrease of heartrate. Dexmedetomidine provides more satisfaction among surgeon than fentanyl. Therefore, epidural dexmedetomidine is a feasible, safe and more reliable adjuvant with levobupivacaine (0.5%) to provide smooth anaesthesia and analgesia with higher satisfaction to surgeon than epidural fentanyl in abdominal hysterectomy.

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