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A Comparative Evaluation of Dexmedetomidine vs Clonidine used as Adjuvants with Hyperbaric Bupivacaine in Patients with Preeclampsia Undergoing LSCS

Ruchi Tandon[1], Avani Tiwari[2], Antima Singh[3]

Author's Affiliation: [1]Professor, [2]Senior Resident, Department of Anesthesia, Gandhi Medical College, Bhopal 462001, Madhya Pradesh, India, [3]Postgraduate, Deparment of Obstetrician-Gynecologists, Bhagat Phool Singh Medical College, Sonipat 131305, Haryana, India.

Abstract

Relief of operative as well as post operative pain should be the prime responsibility of an anesthesiologists. The most common treatment for post operative pain remains conventional intramuscular injection of narcoticswhich are associated with several side effects like nausea, vomiting, itching, hypotension, bradycardia,urinary retention, dysphoria,respiratory depression, early and later. Pregnancy induced hypertension is a major cause of morbidity and mortality in obstetrics, complicating 3-8% of pregnancies. Severe preeclampsia poses a dilemma for anesthesiologists, and there is some controversy about the best anaesthetic technique for caesarean delivery in such cases. Though spinal anasthesia reduces the risk of airway instrumentation in high risk patients of preeclampsia, there are still limitations about its limited duration of analgesia. In present study we intend to compare dexmedetomidine and clonidine used with hyperbaric bupivacaine for spinal anaersthesiain patients with preeclampsia undergoing LSCS.

Primary Objective: To compare the clinical efficacy of intra the caldexmedetomidine vs Clonidine on: (a) Onset and duration of sensory block (b) Onset and duration of motor block (c) Duration of analgesia (d) Side effects if any.

Secondary Objective: to compare the haemodynamic profile among patients of the two group.

Methodology: All eligible patients were randomly assigned into two groups of 50 each by chit and envelope method: Group A: SAB was given with 2ml, 0.5 % Bupivacaine(H) + 45 µg Clonidine. Group B: SAB to be given with 2ml, 0.5% Bupivacaine (H) + 5µg dexmedetomidine.

Results: Regression of sensory block was prolonged in group B as compared to group A.(p value <0.0001). There was regression of motor block in group B as compared to group A. p value<0.0001Heart rate remained stable and comparable at different time points in 2 groups. Except three patients in group A and one patient in group B, no other patient in either group developed bradycardia. Three patients in group A and in group B developed hypotension which responded to intravenous fluid therapy. Sedation score decreased to 0 within 5 hours. At no time, sedation score exceeded 2 and no patient developed signs of respiratory depression.

***Conclusion*:** Dexmedetomidine in the dose of 5µg added to 10 mg 0.5% Hyperbaric Bupivacaine in SAB for LSCS surgery in parturients with preeclampsia provides comparable onset for sensory and motor blockade but significantly prolonged duration as compared to 45µg of clonidine. Longer duration of postoperative analgesia with 5µg Dexmedetomidine makes it superior to clonidine in respect to postoperative analgesia. Both the drugs produce desirable level of intraoperative and postoperative sedation, stable hemodynamics and minimal side effects.

Keywords: Dexmedtomidine; Clonidine; preeclampsia; spinal anesthesia.

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Corresponding Author: Avani Tiwari, Senior Resident, Department of Anesthesia, Gandhi Medical College, Bhopal 462001, Madhya Pradesh, India.
E-mail: avnicvc@gmail.com
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Introduction

Relief of operative as well as post operative pain is important because it interferes with respiration, bowel movements and micturition. The most common treatment for post operative pain remains conventional intramuscular injection of one of the strongest analgesics such a morphine, pethidine, pentazocine etc. These parenteral narcotics are associated with several side effects like nausea, vomiting, itching, hypotension, bradycardia, urinary retention, dysphoria, respiratory depression, early and later.[1]

Surgical trauma is real and severe tissue damage and surgical pain is a universal phenomenon which is aggravated by associated muscle spasm and visceral distention. By rendering the patient pain free during surgery, anaesthesiologist have succeeded to a considerable extent, but once the luxury of pain free surgery is over, the patient has to face the misery of post operative pain.

Pregnancy induced hypertension is a major cause of morbidity and mortality in obstetrics, complicating 6-8% of pregnancies.[2] Severe preeclampsia poses a dilemma for anaesthesiologists, and there is some controversy about the best anaesthetic technique for caesarean delivery in such cases. Because of the risks related to airway edema, difficulty with the airway or failed intubation, hypertensive response to direct laryngoscopy, and aspiration pneuminitis, general anesthesia is associated with more untoward outcomes in this particular group of patients. Spinal anaesthesia has the advantage of simplicity of technique, rapid onset of action and reliability in producing uniform sensory and motor bloackade. Its main disadvantage relates to its limited duration of action and hence, lack of long lasting post operative analgesia. To overcome this problem, administration of local anaesthetics in combination with different adjuvants is ana excellent technique which not only relives postoperative pain but also refines the quality of sensory and motor blockade of subarachnoid block and hence, acts as synergistic to local anaesthetics with lower local anaesthetic requirement, decreased side effect and excellent post operative analgesia.

Spinal anaesthesia has the advantage of simplicity of technique, rapid onset of action and reliability in producing uniform sensory and motor blockade. Its main disadvantage relates to its limited duration of action and hence, lack of long lasting post operative analgesia. To overcome this problem, administration of local anaesthetics in combination with different adjuvants is an excellent technique which not only relives postoperative pain but also refines the quality of sensory and motor blockade of subarachnoid block.[1]

Materials and Method

After approval from Institutional Ethics Committee, written informed consent was obtained from all patients. Patients with preeclampsia were drawn frpm those scheduled for operations requiring subarachnoid block for LSCS. 100 ASA I and II patients are randomized into groups using envelope method.

Inclusion Criteria

Full term parturients with Pre-eclampsia scheduled for LSCS.

- Systolic BP >140mm and < 160 mmHg, Diastolic BP > 90mm and < 110 mmHg.
- Proteinuria < 5 gm in 24 hour urine sample or ½+ on dipstick urine test.

Exclusive Criteria

- Patients with severe preeclampsia.
- Height < 147 cm and > 170 cm.
- Weight > 90 kg.
- Patients with local infection, abscess.
- Patients with known local anaesthetic hypersensitivity.
- Patients with coagulopathies.
- Opioid dependence.
- ASA III, IV patients.
- Patients refusal, spinal deformity and any other contraindications to spinal anaesthesia.

All eligible patients were randomly assigned into two groups of 50 each by chit and envelope method: **Group A:** SAB was given with 2ml, 0.5 % Bupivacaine(H) + 45 µg; **Group B:** SAB to be given with 2ml, 0.5% Bupivacaine (H) + 5µg dexmedetomidine.

After Pre-anaesthetic assessment of the patient, patients were explained about the procedure, consents were taken. Inside the OT multi-para monitoring was done. A venous access was secured using 16 or 18G cannula and the patient was preloaded with ringer lactate (15-20 ml/kg) before the induction of spinal anaesthesia. SAB will bw performed at L3-4 or L4-5 intervertebral space with the patient in sitting and lateral decubitus position under complete asepsis a disposable 25G spinal Quincke needle. Our study was doubly blinded, both the observer and the patient were not informed abouth the drug combinations. Total

volume of drug injected was 2.3 ml in each group. The onset of sensory block was recorded using Hollmen scale. (Time zero to Hollmen scale to reach T6 level) The onset of motor block was evaluated using the bromage scale.[3] (Time zero to bromage scale grade 4). If hypotension occurs (systolic blood pressure lower than 20% of baseline value), it was treated with 5 mg boluses of intravenous ephedrine. Injection atropine 0.6 mg intravenous was administered if bradycardia (HR<50 beats per minute) occurs. Oxygen was administered through simple facemask at 5 L/min. Side effects such as hypotension (SBP < 20% of the initial value), bradycardia (HR<50 bpm), nausea, vomiting, dry mouth, pruritus and shivering will be recorded.

Results

The present study included 100 patients. Patients characteristics in terms of age and weight were comparable in both the groups (p > 0.05).

Consort Diagram

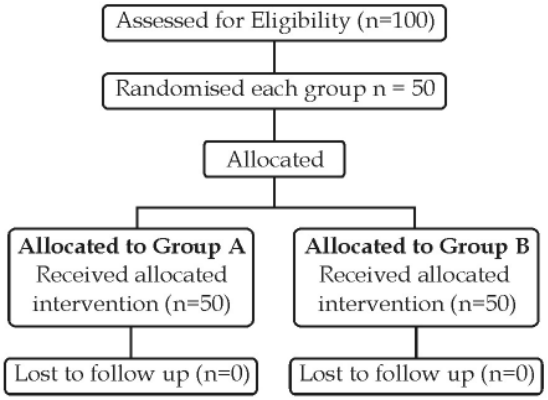


Table 1: Showing Comparison of Sensory Characteristics of Subarachnoid Block Between two Groups.

Variables	Group A	Group B	P value
Highest sensory level achieved(range)	T_6-T_8	T_6-T_8	0.1713
Onset of sensory block(min) at L1	01.4± 00.45	01.50± 00.40	0.2466
Onset of sensory block (min) at T10	03.32 ± 01.17	03.59± 00.68	0.1703
Onset of sensory block(min) at highest sensory level	10.45± 01.91	10.99± 01.69	0.1364
Time to reach peak of sensory block(min) till L1	02.71± 00.84	02.9± 00.47	0.3591
Time to reach peak of sensory block(min) till T10	04.64±01.36	04.81±00.93	0.4555
Time to reach highest sensory level	14.69±01.36	16.26±0.72	0.1218
Time for 2 segment regression (min)	120.9±24.61	147.04±32.09	<0.0001
Time for complete regression (min)	264.8±38.87	325.76±38.49	<0.0001

Chi-square

Table 2: Showing Comparison of motor Characteristics of Subarachnoid Block Between two Groups

Variables	Group A	Group B	P value
Time to achieve grade I motor block (min)	03.72±00.78	03.75±00.88	0.8582
Time to achieve grade II motor block (min)	05.95±01.13	05.92±01.15	0.8964
Time to achieve grade III motor block(min)	10.91±01.85	10.88±01.72	0.9335
Regression of motor block to previous grade	147.18±24.94	161.38±24.05	<0.0001
Time to complete regression of motor block	194.72±22.57	213.44±22.27	<0.0001

Chi-square

Table 3: Showing Comparison of Sensory Characteristics of Subarachnoid Block Between two Groups.

Variables		Group A	Group B	P Value
Highest Sensory level achieved (Range)		T_6-T_8	T_6-T_8	0.1713
Onset of sensory block (min)	At L1dermatome	01.4+ 00.45	01.4+ 00.45	0.2466
	At T10dermatome	03.32+ 01.17	03.59+ 00.68	0.1703
	At highest sensory level	10.45+ 01.91	10.99+ 01.69	0.1364
Time to reach peak of sensory block (min)	At L1dermatome	02.71+ 00.84	02.9+ 00.47	0.3591
	At T10dermatome	04.64+ 01.36	04.81+ 00.93	0.4555
	Highest Sensory level	14.69+ 01.36	16.26+ 0.72	0.4555
Time for regression of sensory block (min)	2 Segment regression	120.9+ 24.61	147.04+ 32.09	<0.0001
	Complete regression	264.8+ 38.87	325.76+ 38.49	<0.0001

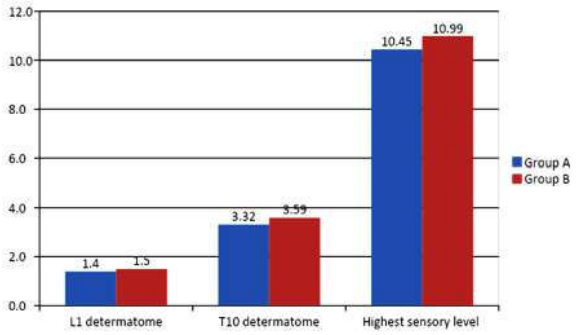
Values given in Mean + SD.

Inference

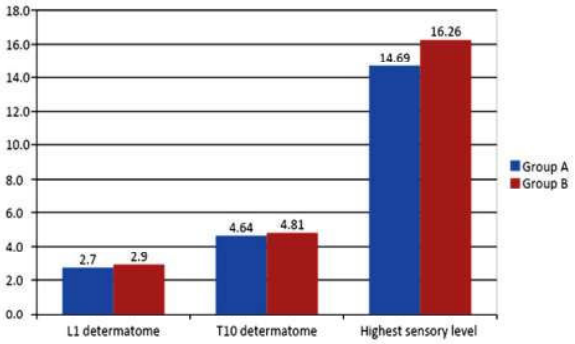
There was no statistically significant difference in mean time for onset, peak of sensory block in two groups. There was statistically significant difference in two segment and complete regression of sensory block. Regression of sensory block was prolonged in group b as compared to group A, (P<0.001).

Fig. 3: Showing Comparision of Sensory Characteristics of Subarachnoid Block Between Two Groups:

Bar diagram 3A: Onset of sensory blockade



Bar diagram 3B: Time to reach peak of sensory blockade



Bar diagram 3C: Time for regression of sensory blockade

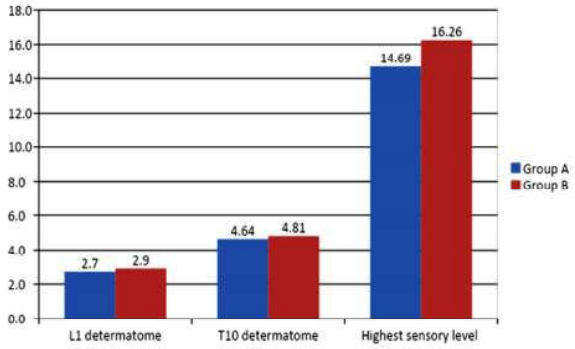
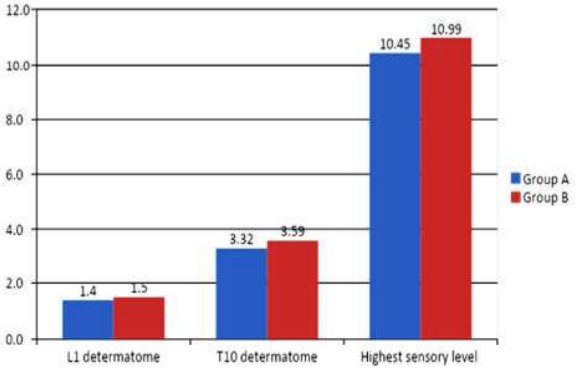


Table 4: Showing Comparison of Motor Characteristicsof Subarachnoid Block Between Two Groups

Variables	Group A (Mean+SD)	Group B (Mean + SD)	P Value
Time to acheive grade I motor block (min)	03.72 +00.78	03.75 +00.88	0.8582
Time to acheive grade II motor block (min)	05.95 +01.13	05.92 +01.15	0.8964
Time to acheive grade III motor block (min)	10.91 +01.85	10.88 +01.72	0.9335
Time to acheive grade IV motor block (min)	147.18 +24.94	161.38 +24.05	<0.0001
Time to complete regression of motor block	194.72 +22.57	213.44 +22.27	<0.0001

Fig.1: Showing Comparision of Sensory Characteristics of Subarachnoid Block between two Groups

Bar diagram: Onset of sensory blockade in two groups



Bar diagram: Regression of motor blockade in two groups

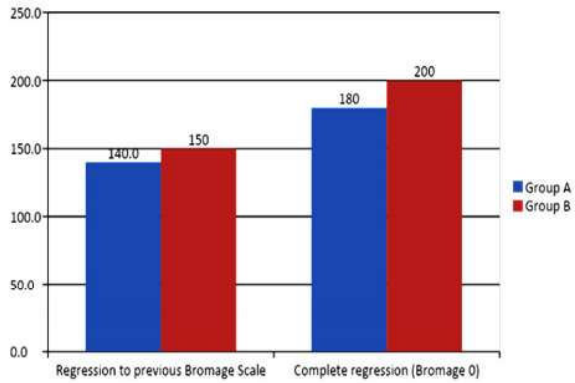


Fig. 2: Showing Statistical Analysis of Pulse Rate (Per/Min) Between Two Groups

Line diagram

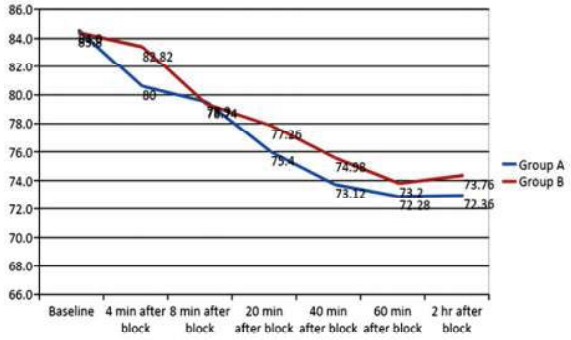


Fig. 4: Line diagram: Showing Statistical Analysis of SpO2 between two groups

Line Diagram: Changes in SpO2 between two groups.

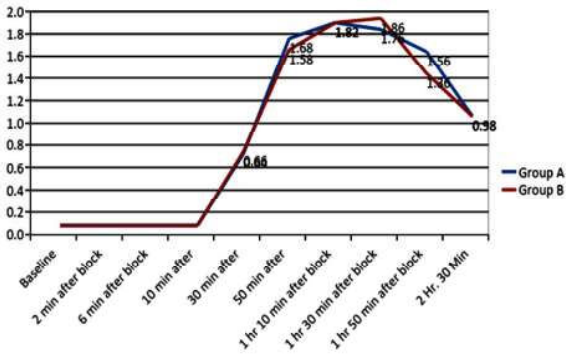


Fig. 5: Showing Distribution of Sedation Score Between Two Groups.

Line Diagram: Sedation score between two groups

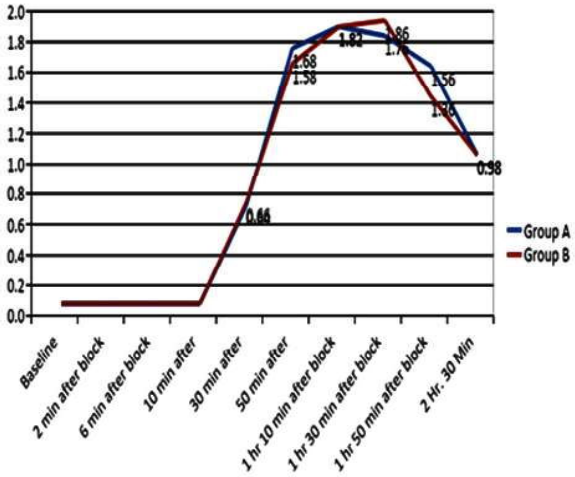


Fig. 6: Showing Statistical Analysis of Visual Analogue Scale Between Two Groups

Bar Diagram: Visual Analogue scale and time of first rescue analgesic required in two groups

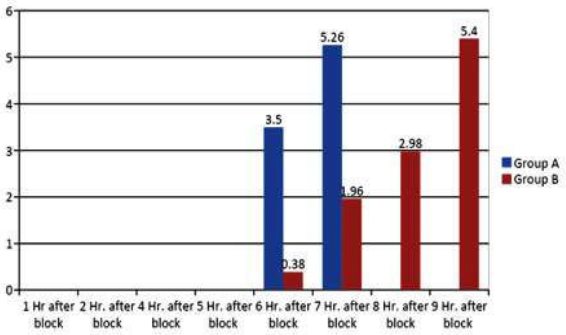


Table 3: Showing Complications in Two Groups

Complications	Group A No. of patients (%)	Group B No. of patients (%)
Hypotension	3 06%	3 06%
Bradycardia	3 06%	1 02%
Nausea-vomiting	4 08%	6 12%
Headache	0 00%	0 00%
Respiratory depression	0 00%	0 00%
Neurological complication	0 00%	0 00%

Discussion

Dexmedetomidine hydrochloride, a newer agent within the class of α2 adrenoceptor agonist, delivers clinically effective sedation within analgesic property for use in intensive care unit setting. Additionally, it has an ability to eliminate or reduce the need for other analgesic medications. There is no evidence of repiratory depression with dexmedetomidine. Because of its selective α2 receptor activity, use of dexmedetomidine has modest and predictable haemodynamic effects, making it a popular sedative and analgesic drug in ICU.[4,5,6]

Dexmedetomidine is now being used outside the ICU in variety of clinical settings, including sedation and adjunct analgesia in the operating room and for post operative analgesia.[4,5]

Though clonidine, an older member of α2 adrenoceptor family, has well established record of efficacy and safety as an adjuvant to local anesthetic in subarachnoid block,[9,15,16], dexmedetomidine

is yet to be established for this purpose. We decided to study the efficacy and safety profile of Dexmedetomidine versus clonidine in combination with local anaesthetic in subarachnoid block in pts. Of preeclampsia undergoing LSCS.

Present study showed that the supplementation of 10 mg of spinal Bupivacaine with 45 µg clonidine or 5µg dexmedetomidine did not show any significant difference in the time for onset and peak of sensory blockade. But addition of 5 µg dexmedetomidine showed significantly prolonged two segment regression and total duration of sensory blockade. Dexmedetomidine also showed longer postoperative analgesia period of 9 hours as compared to 7 hours in clonidine group. Findings of our study are similar to the findings reported by G.E Kanazi et al.[8] Rampalsingh et al[15] concluded that there was no singinficant difference in onset of sensory and motor block. Rampal Singh et al also concluded that total duration of sensory and motor block was prolonged with Dexmedetomidine as compared to clonidine. Solanki S L et al concluded that addition of dexmedtomidine to intrathecal Bupivacaine produces longer post operative analgesia than clonidine.

The mechanism by which intrathecal α2 adrenoceptor agonists prolonged the motor and sensory block is not well understood. It is not a result of altered systemic absorption, as the plasma level of Bupivacaine is not altered after the addition of intrathecal clonidine to Bupivacaine. It may be an additive or synergistic effect secondary to the different mechanism of action of local anesthetic and α2 receptor agonist.

The local anaesthetic acts by blocking the Na+ channels, whereas α2 receptor agonist acts by binding to presynaptic C fibers and post synaptic dorsal horn neurons. Intrathecal α2 adrenoceptor agonists produce analgesia by depressing the release of C fiber transmitters and by hyperpolarisation of post synaptic dorsal horn neurons.[6,7,13,14,18] These α2 adrenergic receptors are located on the superficial laminae of spinal cord and brain stem nuclei implicated in pain, so analgesia can be produced at peripheral, spinal and brain stem sites.[12] Intrathecal α2 receptor agonist have been found to have antinociceptive effect for both somatic and visceral pain.

α2 adrenergic agonists are known to cause bradycardia. Mechanism of bradycardia ia presynaptic feedback inhibition of norepinephrine release and possible vagomimetic effect on nucleus tractus solitaries by α2 agonist.[12] In the present study, 1 patient in the dexmedetomidine group and 3 patients in the clonidine group, presented with bradycardia.Use of low doses of Dexmedetomidine and clonidine in the present study may be responsible for low incidence of bradycardia.

In this study, addition of dexmedetomidine did not cause significant fall in the blood pressure intraoperatively and postoperatively. 3 patients in the dexmedetomidine group and 3 patients in the clonidine group developed hypotension which responded to intravenous fluid therapy and is statistically not significant. Intrathecal local anaesthetics block the sympathetic outflow and reduce the blood pressure. Sympathetic block is near maximum with the doses of local anaesthetic used for spinal anaesthesia. The addition of low dose of α2 agonist to high dose of local anaesthetics does not further affect the near maximal sympatholysis.[6]

Intrathecally administered α2 adrenoceptor agonists have a dose dependent sedative effect.[8, 10, 11, 16, 17] The dose of Dexmedetomidine and clonidine selected in this study did not produce excessive sedation, as at no time, sedation score exceeded two and no patient developed respiratory depression or fall in SPO2. In fact, the sedation produced by Dexmedetomidine and Clonidine was found to be desirable as all the patients remained calm and quite in intraoperative and postoperative period.

The only side effect noted was nausea and vomiting but it was not clinically and statistically significant and its incidence was comparable in both the groups.

Conclusion

Addition of 45µg of clonidine or 5µg Dexmedetomidine as an adjuvant to 0.5% hyperbaric bupivacaine in subarachnoid block provides comparable time for onset and peak of sensory and motor block but significantly prolonged, duration of motor blockade, duration of postoperative analgesia with Dexmedetomidine as compared to clonidine. Both the drugs as an adjuvant to bupivacaine in subarachnoid block produced effective and safe level of sedation the intraoperative and postoperative period extending upto 5 hours. Stable haemodynamics establishes the safety of both drugs in the doses used in presnt study. There was no steep fall in BP/HR. BP was maintained throughout surgery and postoperatively too.

In conclusion, Dexmedetomidine in the dose of 5µg added to 10 mg 0.5% Hyperbaric Bupivacaine in SAB for LSCS surgery in parturients with preeclampsia provides comparable onset for sensory

and motor blockade but significantly prolonged duration as compared to 45µg of clonidine.Longer duration of postoperative analgesia with 5µg Dexmedetomidine makes it superior to clonidine in respect to postoperative analgesia.Both the drugs produce desirable level of intraoperative and postoperative sedation, stable haemodynamics and minimal side effects.

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