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A comparative study of dexmedetomedine and clonidine as adjuvant to levobupivacaine for epidural anesthesia in lower abdominal and lower limb surgeries

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ABSTRACT

BACKGROUND AND AIMS: The duration and quality of analgesia is improved when a local anesthetic is combined with alpha 2 adrenergic agonist. Though, the effects of clonidine on local anesthetics have been extensively studied, there are limited studies demonstrating the effects of epidural dexmedetomidine on local anesthetics. The aim of the study is to compare the efficacy of dexmeditomedine and clonidine as adjuvant to levobupivacaine for epidural anesthesia in lower abdominal and lower limb surgeries.

MATERIAL AND METHODS: This Prospective comparative study was done to assess the efficacy and clinical profile of two α2 adrenergic agonists – clonidine and dexmedetomidine administered epidurally in combination with intrathecal 0.5%levobupivacaine. 60 adult patients ASA Class I and II undergoing lower abdomen and lower limb surgery were randomly assigned into two groups, to receive either epidural dexmedetomidine (1.5μg/kg) or clonidine (2 μg/kg) with 0.5% isobaric levobupivacaine.

RESULTS: Based on the VAS score of the patients and time taken for rescue analgesia, it was found that better post-operative analgesia was provided for longer duration by dexmedetomidine than clonidine. Though no significant differences have been observed based on the hemodynamic parameters between both the groups of the patients, dexmedetomidine has shown beteer hemodynamic stability as compared to clonidine.

CONCLUSION: It can be concluded that in patients undergoing lower abdominal and lower limb surgeries, administration of epidural anaesthesia with 0.5% of Levobupivacaine with dexmedetomidine provided better and longer post- operative analgesia as compared to clonidine.

KEY WORDS: Clonidine, dexmedetomidine, epidural, levobupivacaine.

1. INTRODUCTION

Epidural anesthesia is used both for providing anesthesia and post operative analgesia to the patient. It is hemodynamically stable and reduces perioperative stress leading to decrease in complication and improve patient outcome. By decreasing postoperative pain, it helps in early mobilization of patient which leads to decrease in the incidence of thromboembolic events [(1-5)].

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When co-administered with local anaesthetic agents, adjuvants may improve the speed of onset, the quality and / or duration of analgesia with desirable sedation. They also reduce the dose requirement of local anaesthetic. A wide range of drugs has been assessed for both neuraxial and peripheral nerve blocks. They provide potent analgesic effect by inhibiting nociceptive transmission from peripheral to central neuronal system. Large number of neuraxial adjuvants such as clonidine, dexamethasone, midazolam, ketamine, dexmeditomedine, fentanyl has shown synergistic analgesic effect with local anaesthetic drug. Alpha-2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anaesthesia [(6)]

The quality and duration of analgesia is improved when a local anaesthetic is combined with alpha-2 adrenergic agonist. Both clonidine and dexmedetomidine are alpha 2 adrenergic agonists, which have analgesic properties and potentiate local anaesthetic effects [(7-9)]. Neuraxial clonidine and dexmeditomedine improve the action of local anaesthetic drug by increasing the intensity and duration of analgesia. Alpha-2 adrenergic drugs also have sedative properties [(10-13)]. In comparison to clonidine, dexmeditomedine is more selective towards the alpha -2 adrenergic receptors hence allows the use of higher doses with less alpha-1 effect. It has been found to have better hemodynamic stability, anxiolytic, sedative, analgesic, neuroprotective and anaesthetic sparing effect. Intensity of motor blockade and post-operative sedation is increased without increasing the incidence of side effects [(14-16)].

Levobupivacaine is being increasingly used in comparison to bupivacaine. It is long-acting local anaesthetic and an S (-) enantiomer of bupivacaine. It has emerged as a safer alternative for regional anaesthesia. Cardiac toxicity is less in levobupivacaine as compare to bupivacaine which is a racemic mixture [(17)]. Incidence of seizure also decreases with levobupivacaine to approximately 1.5-2.5 times than bupivacaine [(18)]. So, we have chosen levobupivacaine as the local anaesthetic because it is longer acting and devoid of cardiac side effects. Alpha 2-adrenergic receptor agonist have been the focus of interest for their analgesic, sedative, peri-operative sympatholytic, anaesthetic sparing, and hemodynamic stabilizing properties.

There are only few studies demonstrating the effects of dexmedetomidine when given epidural route with local anaesthetics. The aim of our study is to compare the effect of clonidine and dexmedetomidine when given as an adjuvant to levobupivacaine in epidural anaesthesia in lower abdominal and lower limb surgeries.

2. MATERIAL AND METHODS

After approval from ethical committee and informed written consent from all patients, the prospective observational study will be conducted on adult patients, aged 20-60 year of either sex, satisfying inclusion criteria at Nehru Hospital in B.R.D. Medical College, Gorakhpur.

Study Design – Prospective Observational Study.

Sample Size – 60

Sample Size Calculation

The sample size for this study is based on Acharya et al (2017), who reported the mean Parameter in the two groups as follows:

Parameter	
Group Clonidine: Mean ± SD	Group Dexmedetomidine: Mean ± SD
251.22±28.26	284.52±25.44

The sample size required in each arm of the study is calculated according to the formula given by Snedecor & Cochran (1989):

$$\text{Sample size (N)} = 1+ \frac{2(Z_{\alpha} + Z_{1-\beta})^2 \sigma^2}{\delta^2}$$

Where:

σ (Pooled SD) =26.89

δ (Difference of Means) = 33.3

Type I error (α) = 5%, Z_{α} (Value of Standard Normal Distribution for α =5%) = 1.96

Type II error (β) = 1%, Power (1 – β) = 99%, $Z_{1-\beta}$ = 2.326

Based on the formula given above, using the mentioned values, the sample size required is:

$$\text{Sample size (N)} = 1+ \frac{2(1.96 + 2.326)^2}{\frac{26.89^2}{33.3^2}} = 23.95 \approx 25$$

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Thus, assuming 90% Power and 95% Confidence interval, the minimum calculated sample size for each arm is **30** (total = 60).

Statistical analysis

- Data will be recorded and tabulated, SPSS v23 (IBM Corp.) will be used for data analysis.
- Statistical significance will be kept at $p < 0.05$

Inclusion Criteria –

1. Patient of any gender scheduled for lower abdomen and lower limb surgery.
2. Age 20- 60 year.
3. Patients with ASA physical status I and II
4. Patient giving informed consent.

Exclusion Criteria

1. Patients not willing to participate in the study.
2. Patients with ASA grade >II.
3. Those with known allergy or hypersensitivity to the study drug.
4. Patients with local infection at the site of injection.
5. Uncooperative patient
6. Patient with bleeding diathesis.
7. Patient with significant spinal deformity.
8. Patients with extremely long and short stature.
9. Obese patient.

3. OBSERVATION & RESULT

The analysis included profiling of patients on different demographic, clinical and laboratory parameters. Descriptive analysis of quantitative parameters was expressed as means and standard deviation. Categorical data were expressed as absolute number and percentage. Independent Student *t*–test was used for testing of mean difference of study parameters between two independent groups whereas Paired Student *t*–test was used for paired observation. Cross tables were generated and chi-square test was used for testing of associations. *p*- Value<0.05 was considered statistically significant. All analysis was done using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, N.Y., USA).

STATISTICAL SIGNIFICANCE:

In testing a given hypothesis, the maximum probability with which we would be willing to take risk is called Level of Significance of the Test.

For all statistical analysis, *p* –value was considered as –

p- value ≥ 0.05 – Non significant

p- value < 0.05 - Significant

p- value < 0.01 - Highly Significant

p- value < 0.001 - Very Highly Significant

The data was entered in MS Excel spreadsheet (Microsoft Corp., WA, US).

Table 1: Distribution of patients in between groups

		N	%
Group C	Clonidine	30	50.0
Group D	Dexmedetomidine	30	50.0

Table 1 shows the distribution of patients in between groups. Total 60 patients were enrolled in this study, in which 30 (50%) in group C (Clonidine group) and 30 (50%) in group D (Dexmedetomidine group) were included.

Table 2: Comparisons of mean Height (cm), Weight (kg) in between group C and group D

	Group C (n=30)		Group D (n=30)		t-Value	p-Value
	Mean	±SD	Mean	±SD		
Height(cm)	157.63	8.49	157.27	6.67	0.19	0.853
Weight(kg)	60.90	4.35	60.30	5.23	0.48	0.631

Table 2 shows the comparisons of mean Height (cm), Weight (kg) in between group C and group D. The mean height (cm), weight (kg) was 157.63±8.49 and 60.90±4.35 in group C and 157.27±6.67 and 60.30±5.23in group D. The mean height (cm), weight (kg) was comparable in between group C group D.

Table 3: Comparisons of mean duration of surgery (hrs) in between group C and group D

	Group C (n=30)	Group D (n=30)	t-Value	p-Value

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	Mean	±SD	Mean	±SD		
Duration of Surgery (hr)	1.35	0.42	1.36	0.46	-0.105	0.916

Table 3 show the comparisons of mean duration of surgery (hrs) in between group C and group D. The mean duration of surgery (hrs) was 1.35±0.42 in group C and 1.36±0.46 in group D. The mean duration of surgery (hrs) was comparable between groups.

Table 4: Comparisons of mean time of onset of sensory block, in between group C and group D

	Group C (n=30)		Group D (n=30)		t- Value	p-Value
	Mean	±SD	Mean	±SD		
Time of onset of sensory block	11.33	1.37	9.63	0.93	5.619	<0.001*

*=*Significant (p<0.001)*

Table 4 show the comparisons of mean time of onset of sensory block in between group C and group D. The mean Time of onset of sensory block was 11.33±1.37 in group C and 9.63±0.93 in group D. The mean time of onset of sensory block was significantly lower in group D as compared to group C.

Table 5: Comparisons of mean time to achieve maximum sensory block in between group C and group D.

	Group C (n=30)		Group D (n=30)		t-Value	p-Value
	Mean	±SD	Mean	±SD		
Time to achieve maximum sensory block	15.80	1.00	12.63	1.16	11.346	<0.001*

*=*Significant (p<0.001)*

Table 5 show the comparisons of mean time to achieve maximum sensory block in between group C and group D. The mean time to achieve maximum sensory block was 15.80±1.00 in group C and 12.63±1.16 in group D. The mean time to achieve maximum sensory block was significantly lower in group D as compared to group C.

Table 6: Comparisons of mean onset of motor blockade in between group C and group D

	Group C (n=30)		Group D (n=30)		t-Value	p-Value
	Mean	±SD	Mean	±SD		
Onset of complete motor blockade (bromage 3)	22.03	1.79	18.80	1.88	6.816	<0.001*

*=*Significant (p<0.001)*

Table 6 show the comparisons of mean onset of complete motor blockade (bromage 3) in between group C and group D. The mean onset of motor blockade was 22.03±1.79 in group C and 18.80±1.88 in group D. The mean onset of motor blockade was significantly lower in group D as compared to group C.

Table 7: Comparisons of mean duration of motor blockade in between group C and group D

	Group C (n=30)		Group D (n=30)		t- Value	p-Value
	Mean	±SD	Mean	±SD		
Duration of motor blockade	223	11.04	251.17	12.30	-9.336	0.001*

*=*Significant (p<0.001)*

Table 7 show the comparisons of mean duration of motor blockade in between group C and group D. The mean duration of motor blockade was 223.00±11.04in group C and 251.17±12.30 in group D. The mean duration of motor blockade was significantly more in group D as compared to group C.

Table 8: Comparisons of mean VAS score in between group C and group D at pre-operative, Intra-operative and post-operative

	Group C (n=30)		Group D (n=30)		t-value	p-Value
	Mean	±SD	Mean	±SD		
30 min	0.00	0.00	0.00	0.00	-	-
1hr	0.43	0.50	0.50	0.51	-0.510	0.612
2hr	1.37	0.49	1.53	0.51	-1.294	0.201
3hr	2.50	0.51	2.50	0.51	0.000	1.000
4hr	2.53	0.51	2.40	0.50	1.027	0.309
8hr	2.33	0.48	2.40	0.50	-0.528	0.599
12hr	4.43	0.94	4.27	1.05	0.650	0.518
24hr	2.87	0.73	2.73	0.78	0.681	0.498

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Table 8 shows the comparisons of mean VAS score in between group C and group D at pre-operative, Intra-operative and post-operative. The mean VAS score was comparable in between groups.

Table 9: Comparisons of mean Time for rescue analgesia (min) in between group C and group D

	Group C (n=30)		Group D (n=30)		t	p-Value
	Mean	±SD	Mean	±SD		
Time for rescue Analgesia (min)	416.33	21.45	446.00	6.21	-11.67	<0.001*

*=*Significant (p<0.001)*

Table 9 show the comparisons of mean Time for rescue analgesia (min) in between group C and group D. The mean time for rescue analgesia (min) was 416.33±21.45 in group C and 446.00±6.21 min in group D. The mean time for rescue analgesia was significantly more in group D as compared to group C.

4. DISCUSSION

Surgical procedures of the lower limb and lower abdomen are facilitated by both general and regional anaesthesia. Epidural anaesthesia provides many advantages over general anaesthesia including maintaining patient's awareness, produces adequate analgesia, reduces intraoperative bleeding, reduces post- operative pain, produces early mobilization, decreases incidence of deep venous thrombosis and enhances rehabilitation. Additionally, perioperative epidural analgesia confers physiologic benefits, which potentially decreases perioperative complications and improves post- operative outcomes. However, it is associated hemodynamic fluctuations due to usage of large volume of local anaesthetic drug [(1-3)].

In recent years, levobupivacaine has gained more popularity in regional anaesthesia. Levobupivacaine is a pure S (-) enantiomer of bupivacaine. The enantio-selective properties of levobupivacaine exhibit affinity and inhibitory forces in lower cardiac sodium channels as well as the blockade effect of CNS solitary tract nucleus. It has advantages in pharmacokinetic profile and lack of side effects on CVS and CNS as compared to bupivacaine [(23)].

Many drugs are used as adjuvants to local anaesthetic agents to improve the quality of the block and decrease the dose of levobupivacaine. The drugs that can be used as adjuvants include opioids, alpha 2 agonists (dexmedetomedine,clonidine) ketamine, etc. Alpha 2 agonists are being extensively used as an adjuvant as it has no opioid related side effects like nausea, respiratory depression, urinary retention and pruritis. Epidural administration of these drugs is associated with sedation, analgesia, anxiolysis, hypnosis and sympatholysis. The faster onset of action of local anaesthetics, rapid establishment of both motor and sensory blockade, prolonged duration of analgesia in the post- operative period, dose sparing action of local anaesthetics and stable cardiovascular parameters makes these agents a very effective adjuvant in regional anaesthesia[(24,25)].

Our study is to compare the efficacy of dexmedetomidine and clonidine as adjuvants to levobupivacaine for epidural anaesthesia in lower limb and lower abdominal surgeries.

In this study, it was observed that the mean time of onset of sensory block for the patients belonging to Group C was 11.3 minutes while for those patients belonging to Group D was 9.63 minutes. The mean time taken for maximum sensory blockade was observed to be 15.8 minutes for patients belonging to Group C and 12.63 minutes for patients belonging to Group D. Hence patients who received Dexmedetomidine group had significant faster onset and maximum sensory block as compared to the patients who received clonidine (<0.001). These results were in correlation with the similar study conducted by Karthik G S et al., in patients undergoing lower limb surgeries [(31)]. Sukhminder Jit Singh Bajwa et al., conducted a similar study using ropivacaine as the local anaesthetic agent and clonidine and dexmedetomidine as adjuvants and observed that the patients receiving dexmedetomidine had faster onset of sensory block as compared to clonidine [(32)]. Similar results were observed in a study conducted by Plabon Hazarika et al., in patients who underwent elective lower abdominal gynaecological surgeries [(35)]. Our results were in congruence with a study conducted by Shilpi Agarwal et al., in patients who underwent infraumbilical surgeries [(38)].

The mean time taken for onset of motor blockade in patients belonging to Group C was 22.03 minutes and patients belonging to Group D were 18.8 seconds. The mean duration of motor blockade was 223 minutes in Group C while it was 251 minutes in Group D which was statistically significant (<0.001). Thus, the duration of block was significantly higher in patients who received dexmedetomidine as compared to those who received clonidine. Our studies were in congruence with a study conducted by Aditya Kumar Kejriwal et al., who did a similar study in patients undergoing laparoscopic cholecystectomy under thoracic epidural anaesthesia[(34)].

The Pulse rate, SBP and DBP were on a decreasing trend for the initial two hours in both the groups. All the patients were preloaded with fluid in order to prevent sudden fall in the blood pressure. No significant difference has been observed in the pulse rate of the patients belonging to both the groups in the peri-operative period. The mean blood pressure was found to be significantly lower in patients who received clonidine than those patients who received dexmedetomidine. It has been observed that the perioperative vitals were stable in patients who received dexmedetomidine than those patients who received clonidine. Similar results were observed in a study conducted by Agarwal S et al who did a study in patients who underwent infraumbilical surgeries [(38)]. Similar

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results were also found in a study conducted by Shailesh et al. Our results were however incongruent with the study conducted by Shruti Kabi et al. and Sarvesh B et al [33, 36].

The VAS scores of the patients belonging to both the groups were compared at various time intervals intra-operatively and post operatively. Rescue analgesia was provided when VAS score was >4. However no significant difference was found in the VAS scores of the patients belonging to both the groups. In a study conducted by Salgado et al., similar results were obtained. In a study conducted by Shruti Kabi et al., VAS scores were comparable in both the groups.

The mean time taken for rescue analgesia was 416.33 minutes in patients who received Clonidine while it was 446.00 minutes in patients who received dexmedetomidine . Hence the duration of post- operative analgesia was significantly higher in Group D. In a similar study conducted by Bajwa S et al., it has been observed that dexmedetomidine provides smooth and prolonged post-operative analgesia than clonidine [32]. Prolonged post-operative analgesia was found with dexmedetomidine in a study conducted by Karthik GS et al. However, it has been observed that the perioperative vitals were more stable and duration of post- operative analgesia was found to be significantly better in the group of patients who received dexmedetomidine as compared to patients who received clonidine.

LIMITATIONS:

1) Patients with extreme heights were not included in the study; hence results of our study would not be applicable for those patients.
2) Since sample size of our study was small, results would not be applicable for the generalized population.
3) It was conducted on patients of lower limb surgeries and lower abdominal surgeries, because the perception of postoperative pain will certainly differ depending on the level of surgery.
4) Side effects and sedation scores have not been observed for in patients belonging to both the groups.

5. REFERENCES

1. Nimmo SM. Benefit and outcome after epidural analgesia. ContinEducAnaesthCrit Care Pain 2004;4:44-7.
2. Park WY, Thompson JS, Lee KK. Effect of epidural anesthesia and analgesia on perioperative outcome: A randomized, controlled Veterans Affairs cooperative study. Ann Surg 2001;234:560-9.
3. Holte K, Kehlet H. Epidural anesthesia and analgesia — Effects on surgical stress responses and implications for postoperative nutrition. ClinNutr 2002;21:199-206.
4. Rigg JR, Jamrozik K, Myles PS, Silbert BS, Peyton PJ, Parsons RW, et al. Epidural anesthesia and analgesia and outcome of major surgery: A randomised trial. Lancet 2002;359:1276-82.
5. Moraca RJ, Sheldon DG, Thirlby RC. The role of epidural anesthesia and analgesia in surgical practice. Ann Surg 2003;238:663-73.
6. Mauro VA, Brandão ST. Clonidine and dexmedetomidine through epidural route for post-operative analgesia and sedation in a cholecystectomy. Rev Bras Anestesiol 2004;4:1-10.
7. Förster JG, Rosenberg PH. Clinically useful adjuvants in regional anesthesia. CurrOpinAnaesthesiol 2003;16:477-86.
8. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, et al. Dexmedetomidine and clonidine in epidural anesthesia: A comparative evaluation. Indian J Anaesth 2011;55:116-21.
9. Swami SS, Keniya VM, Ladi SD, Rao R. Comparison of dexmedetomidine and clonidine (a2 agonist drugs) as an adjuvant to local anesthesia in supraclavicular brachial plexus block: A randomised double-blind prospective study. Indian J Anaesth 2012;56:243-9.
10. Eisenach J, Detweiler D, Hood D. Hemodynamic and analgesic actions of epidurally administered clonidine. Anesthesiology 1993;78:277-87.
11. Klimscha W, Chiari A, Krafft P, Plattner O, Taslimi R, Mayer N, et al. Hemodynamic and analgesic effects of clonidine added repetitively to continuous epidural and spinal blocks. AnesthAnalg 1995;80:322-7.
12. Castro MI, Eisenach JC. Pharmacokinetics and dynamics of intravenous, intrathecal, and epidural clonidine in sheep. Anesthesiology 1989;71:418-25.
13. 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
14. Grewal A. Dexmedetomidine: New avenues. J AnaesthesiolClinPharmacol 2011;27:297-302.
15. Eisenach JC, Shafer SL, Bucklin BA, Jackson C, Kallio A. Pharmacokinetics and pharmacodynamics of intraspinaldexmedetomidine in sheep. Anesthesiology 1994; 80:1349-59.
16. Sudheesh K, Harsoor S. Dexmedetomidine in anesthesia practice: A wonder drug? Indian J Anaesth 2011;55:323-4
17. Burlacu CL, Buggy DJ. Update on local anesthetics: focus on levobupivacaine. Therapeutics and clinical risk management 2008; 4(2): 381-392.
18. Groban L. Central nervous system and cardiac effects from long acting amide local anesthetic toxicity in the intact animal model. RegAnesth PainMed2003;28(1):3-11.

ISSN:0975-3583,0976-2833 VOL14,ISSUE05,2023

19. Avila Hernandez AN, Singh P. Epidural Anesthesia. 2022 Mar 9. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
20. Nawani DP, Agrawal S, Asthana V. Single shot epidural injection for cervical and lumbosaccral radiculopathies: a preliminary study. Korean J Pain. 2010 Dec;23(4):254-7.
21. Mann C, Pouzeratte Y, Boccara G, Peccoux C, Vergne C, Brunat G, Domergue J, Millat B, Colson P. Comparison of intravenous or epidural patient-controlled analgesia in the elderly after major abdominal surgery. Anesthesiology. 2000 Feb;92(2):433-41.
22. Pascoe PJ. Advantages and guidelines for using epidural drugs for analgesia. Vet Clin North Am Small Anim Pract. 1992 Mar;22(2):421-3.
23. Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. Drugs. 2000 Mar;59(3):551-79.
24. Weerink MAS, Struys MMRF, Hannivoort LN, Barends CRM, Absalom AR, Colin P. Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine. Clin Pharmacokinet. 2017 Aug;56(8):893-913.
25. Yasaei R, Saadabadi A. Clonidine. 2022 Jul 19. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
26. Acharya, Dr. (2017). A Study of Clonidine and Dexmedetomidine as Adjuvant to Epidural Levobupivacaine for Post Operative Analgesia in Infraumbilical Surgeries. Journal of Medical Science And clinical Research. 05. 17292-17298. 10.18535/jmscr/v5i2.10.
27. Arunkumar S, Hemanth Kumar VR, Krishnaveni N, Ravishankar M, Jaya V, Aruloli M. Comparison of dexmedetomidine and clonidine as an adjuvant to ropivacaine for epidural anesthesia in lower abdominal and lower limb surgeries. Saudi J Anaesth. 2015 Oct-Dec;9(4):404-8.
28. Gullapalli hanumantharao et al., Dexmedetomidine and Clonidine as an Adjuvant to Ropivacaine for Epidural Anaesthesia. JMSCR Volume 06 Issue 10 October 2018.
29. Arumugam et al. Sri Lankan Journal of Anaesthesiology: 24(2):70- 75(2016)
30. Dr. Amutha Rani et al., “A Comparative Study to Evaluate the Post Operative Analgesia Comparing Dexmedetomidine and Clonidine with Epidural Levobupivacaine for Pelvis and Lower Limb Orthopaedic Surgeries”. JMSCR Volume 10 Issue 02 February 2022.
31. Karthik, G.S., et al. "A comparative evaluation of dexmedetomidine and clonidine as adjuvants to levobupivacaine in epidural anaesthesia for lower limb orthopaedic surgeries." Journal of Evolution of Medical and Dental Sciences, vol. 4, no. 12, 9 Feb. 2015
32. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, Kulshrestha A, Singh A, Parmar S, Singh A, Goraya S. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. Indian J Anaesth. 2011 Mar;55(2):116-21.
33. Sarvesh B, Shivaramu BT. Epidural 0.125% levobupivacaine with dexmedetomidine Versus Clonidine for Total Abdominal Hysterectomies: A Prospective Double Blind Randomized Trial. Indian J Anesth Analg. 2019;6(3):1012-17.
34. Kejriwal AK, Singh R, Agrawal M, et al. A comparative study of levobupivacaine with clonidine and levobupivacaine with dexmedetomidine in thoracic epidural block for laparoscopic cholecystectomy. J. Evolution Med. Dent. Sci. 2016;5(14):615-619.
35. Dr. Plabon Hazarika, Dr. Prabir Pranjal Das. The efficacy and safety of epidural dexmedetomidine and clonidine with 0.5% levobupivacaine in patients undergoing elective lower abdominal gynaecological procedure. International Journal of Medical and Health Research, Volume 5, Issue 6, 2019, Pages 29-33
36. Kabi S, Verma R, Singh D, Singh P, Agarwal J, Kushwaha BB, Chaudhary AK, Singh N. A Comparison Between Dexmedetomidine and Clonidine as Adjuvants to Levobupivacaine in Labour Analgesia. Cureus. 2021 Dec 7;13(12):e20237.
37. Anjana Hazarika, Yuwaraj Majumdar. Comparative analysis of the efficacy of epidural dexmedetomidine and clonidine with bupivacaine in patients undergoing infraumbilical surgeries. International Journal of Contemporary Medical Research 2020;7(6):F3-F7.
38. Agarwal S et al. Int J Res Med Sci. 2015 Nov;3(11):3254-3261
39. Vibhor Rai, Sweety Malik. (2016). Epidural Dexmedetomidine and Clonidine as a adjunct with Bupivacaine in patients undergoing lower limb orthopedic Surgeries. A Clinical Study. Int. J. Adv. Res. Biol. Sci. 3(11): 1-8.