VOLUME - 10, ISSUE - 09, SEPTEMBER - 2021 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Anaesthesiology

ANALGESIC EFFICACY AND HAEMODYNAMIC PROFILE OF DEXMEDETOMIDINE VERSUS FENTANYL AS EPIDURAL ADJUVANTS – A PROSPECTIVE STUDY

Dr. Santhi K S — Professor (cap) Dept Of Anaesthesiology Government Medical College, Kottayam.

Dr. Elizabeth Joseph* — Associate Professor (cap) Dept. Of Anaesthesiology Government Medical College, Kottayam. *Corresponding Author

Dr. Rachana C Nair — Junior Resident Dept. Of Anaesthesiology Government Medical College, Kottayam.

ABSTRACT

BACKGROUND: Combined spinal epidural anaesthesia is the most popular anaesthetic technique for major gynaecological surgeries. Epidural adjuvants enhance the quality and duration of surgical anaesthesia. Adjuvants like opioids or alpha 2 agonists provide a dose sparing effects on local anaesthetics and accelerate the onset of sensory blockade of epidural anaesthesia. Our study was aimed to compare the hemodynamic, sedative and analgesia potentiating effects of Dexmedetomidine and Fentanyl when added to epidural Bupivacaine for gynaecological surgeries.

METHODOLOGY: Patients of ASA Grade I and II, aged between 30 and 65 years who were scheduled for major gynaecological surgeries were included in the study. Patients were randomly divided into two groups, Group D (N = 51) and Group F (N = 51). Group D received epidural injection of 0.5 mcg/kg of Dexmedetomidine diluted to 5ml with Normal Saline (NS) and Group F received 0.5mcg/ kg of Fentanyl diluted to 5 ml with NS, in addition to a spinal dose of 3ml of 0.5 % Bupivacaine. When two segment regression of sensory level was noted, epidural block was supplemented with 0.5 mcg /kg of the study drug in combination with 1.5 ml/segment of 0.5% Bupivacaine. Duration of sensory block, motor block, and incidence of bradycardia, hypotension, nausea and pruritus were assessed.

RESULTS: The duration of analgesia and motor block were significantly longer in the Dexmedetomidine group. The incidence of bradycardia was more in the Dexmedetomidine group, but the incidence of hypotension was nearly the same.

CONCLUSION: Dexmedetomidine seems to be a better alternative to Fentanyl as an epidural adjuvant due to early onset of sensory anaesthesia and prolonged postoperative analgesia.

KEYWORDS : Epidural analgesia; Bupivacaine; Dexmedetomidine; Fentanyl.

BACKGROUND

Pain is an unpleasant sensory and emotional experience perceived only by the sufferer. Major gynaecological surgeries are intensely painful. Stress hormone release, pro inflammatory state induced by surgery and the delayed ambulation resulting from poor pain relief may lead to major systemic complications. Most of the time, these surgeries are done under central neuraxial blockade using local anaesthetic agents. Combined spinal epidural block has been extensively used in gynaecological surgeries as it combines the benefits of both spinal and epidural anaesthesia. It is more versatile in comparison to spinal anaesthesia alone, as it provides post operative pain relief also, by the indwelling epidural catheter. Bupivacaine is the most commonly used drug in central neuraxial blockade. It belongs to amide group of local anaesthetics. Combining adjuvant drugs with Bupivacaine is expected to prolong the duration of block and improve the quality of analgesia. They also help to reduce the dose of local anaesthetic drugs, which in turn reduce the incidence of hypotension and bradycardia. Commonly used adjuvant drugs are opioids like Morphine, Fentanyl and Tramadol, alpha 2 agonists like Clonidine, Dexmedetomidine and other drugs like Magnesium and Diltiazem. Opioids like Fentanyl is associated with side effects such as sedation, pruritus, nausea, vomiting, respiratory depression and decreased GI motility. Epidural Dexmedetomidine has been shown to reduce intraoperative anaesthetic requirements, improve postoperative analgesia and prolong both sensory and motor blockade without the side effects of opioid adjuvants. The aim of our study was to compare the analgesic efficacy and hemodynamic profile of the two drugs, Fentanyl and Dexmedetomidine as epidural adjuvants with the local anaesthetic agent 0.5 % Bupivacaine, in patients undergoing major gynaecological surgeries and to compare the hemodynamic effects observed with them.

METHODS

The present study was a prospective observational study conducted in the Department of Anaesthesia. A total of 102 female patients scheduled for elective gynaecological surgeries like total abdominal hysterectomy, cytoreduction, and staging laparotomy were selected. ASA Grade 1 and 2 patients aged between 30 and 65 years were included in the study. Patients who refused regional anaesthesia, patients with spine deformity, coagulation disorders, allergy to local anaesthetics, and local infection at the site of epidural injection were excluded from the study. After obtaining written informed consent from the patients and after approval from the institutional review board, patients were randomized using sealed envelope technique into two groups (group D and group F) of 51 each. Preanaesthetic evaluation was done on the previous day of surgery. Those scheduled for surgery received Tab Alprazolam 0.25 mg, Tab Ranitidine 150 mg and Tab Metoclopramide 10mg as premedication. Preoperative fasting of 8 hours was ensured. On the day of surgery, patient was shifted to operating room. Arrangements for epidural and sub arachnoid block, general anaesthesia and resuscitation were kept ready. All patients were secured 18-guage IV cannula and started on IV fluid. Monitors such as non-invasive blood pressure, ECG, pulsoximeter were attached. Basal parameters like blood pressure, pulse rate, respiratory rate, spo2 and ECG were recorded. Under aseptic precautions, spinal-epidural anaesthesia was performed using Combined Spinal Epidural (CSE) set at L3-L4 interspace. All patients received 3 ml of hyperbaric Bupivacaine intra thecally. Epidural puncture was done at L2-L3 space and epidural catheter was inserted and fixed, such that 5 cm remained inside the epidural space. At the start of the surgery, group F received bolus of Fentanyl 0.5mcg/kg diluted to 5ml with Normal Saline (NS) and group D received bolus of Dexmedetomidine 0.5mcg/kg diluted to 5 ml with NS, epidurally. The onset of sensory block was assessed by pin prick method. Motor block was assessed by Bromage 3-point score for lower extremity.

The following block characteristics were observed and recorded.

1. Duration of analgesia: Duration of analgesia was taken from the time of epidural drug administration to the time of first supplementation with rescue analgesic.
2. Duration of motor block: Duration of motor block was recorded from the time of onset of motor block to the time when the patient was able to lift the extended leg.
3. Grading of sedation: Sedation was graded using Ramsay sedation scale
4. Incidence of pruritus
5. Incidence of vomiting

Intraoperatively, supplemental oxygen was given. Hemodynamic parameters were monitored from pre-operative period up to 24 hours post surgery. Episodes of bradycardia and hypotension were also documented. Pulse rate <60 /min and mean blood pressure < 20% of basal value were treated with Inj Atropine, IV fluids and vasopressors.

Intraoperatively, sensory level was assessed every 5 minutes for the first 15 minutes and every 30 minutes after that. When two segment regression of the sensory level was noted, epidural top up was done with 0.5 % Bupivacaine 1.5 ml / segment and 0.5 mcg/kg Fentanyl in Group F and 0.5 mcg/kg Dexmedetomidine in Group D.

Postoperative pain was recorded using Visual Analog Scale (VAS) ranging from 0 – 10.

Modified Bromage Scale

0 - No motor blockade
1 – Inability to raise extended leg
2 – Inability to flex the knee
3 – Inability to flex the ankle joint
4 – No movement possible in legs

Visual Analog Scale

0: Absolutely no pain
1–3: Mild pain
4-6: Moderate pain
7-9: Severe pain
10: Worst imaginable pain

Ramsay Sedation Scale

1 - Anxious and agitated or restless
2 - Co-operative, oriented and tranquil
3 - Awake on verbal command only
4 - Brisk response to gentle tactile stimulation
5 – Sluggish response to gentle tactile stimulation
6 – Unarousable

STATISTICAL ANALYSIS

Data were analysed using IBM SPSS version 20. Association between various factors were assessed using Chi Square test for qualitative variables and t test for quantitative variables. The level of statistical significance was taken as 'p' value less than 0.05.

RESULTS

A total of 102 patients were included in the study. 51 were allocated to Group D and 51 were allocated to Group F. Both groups were comparable with regard to their age, sex and body weight.

Duration of motor block

Table 1

	Group	N	Mean	Std. Deviation	t	P value
Duration of motor block(hrs)	F	51	2.6137	.50893	6.6	.000
	D	51	3.3490	.60212		
Duration of sensory block (hrs)	F	51	4.967	1.3328	14.3	.000
	D	51	9.422	1.7646		

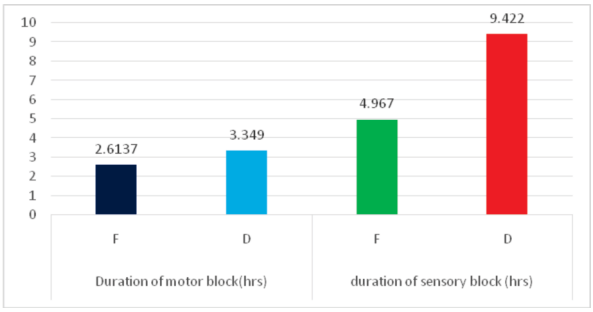


Figure 1

Mean duration of motor blockade in group F patients were 2.6137 hours with a standard deviation of 0. 50893. Mean duration of motor blockade in group D was 3.349 hours with a standard deviation of 0.60212. The p value is 0.000 which is significant (student t test). (Table1, figure 1)

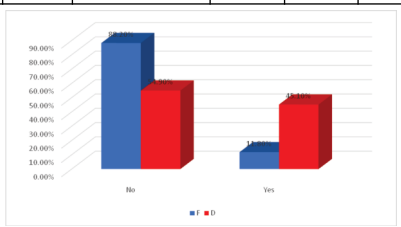
Duration of sensory block

In the group F, mean duration of sensory block is 4. 967 hours with a standard deviation of 1.3328. Mean duration of sensory block in group D is 9.422 hours with a standard deviation of 1.768. The p value 0.000 (student t test) is significant. (Table1, figure 1)

Episodes of bradycardia and hypotension

The incidence of bradycardia in group D was significantly more than that of group F, although there was no statistically significant difference in the incidence of hypotension. (Table2 , Figure 2)

			Episodes of bradycardia	Total			
			No	Yes		X^2	P value
Group	F	Count	45	6	51	13.92	.000
		%	88.2%	11.8%	100.0%		
	D	Count	28	23	51		
		%	54.9%	45.1%	100.0%		
Total		Count	73	29	102		
		%	71.6%	28.4%	100.0%		



Episodes of hypotension Table 3

			Episodes of hypotension		Total		
			No	Yes		X^2	P value
Group	F	Count	42	9	51	.703	.402
		%	82.4%	17.6%	100.0%		
	D	Count	45	6	51		
		%	88.2%	11.8%	100.0%		
Total		Count	87	15	102		
		%	85.3%	14.7%	100.0%		

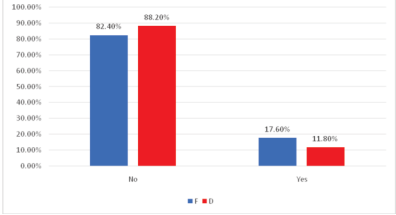


Figure 3

The sedation scores were higher in Group D, while the incidence of pruritus, nausea and vomiting were higher in group F.

DISCUSSION

Pain relief in the perioperative period is an essential requirement of anaesthesia. For gynaecological surgeries, general anaesthesia is less preferred to regional anaesthesia, considering the poly pharmacy involved, inadequate post operative analgesia, post operative problems like delayed ambulation, and cardiovascular and respiratory complications. Even though spinal anaesthesia is easy to perform and has rapid onset of action with less side effects, the duration of action is limited. Hence, we selected CSEB technique for our study, so as to combine the favourable aspects of spinal and epidural anaesthesia. Bupivacaine, an amide local anaesthetic agent, is the most commonly used drug for regional anaesthesia. Several studies have suggested that addition of adjuvants to local anaesthetics significantly prolong analgesia and reduce consumption in perioperative period. The synergism between epidural local anaesthetics and opioids is well established, but evidence regarding the combination of LA with Dexmedetomidine through epidural route is scarce in literature. Alpha -2 adrenoceptor agonists are the focus of interest due to their sedative, analgesic anxio lytic and sympatholytic properties. Dexmedetomidine is a highly selective alpha receptor agonist with a high ratio of alpha 2 / alpha 1 activity. Earlier onset of sensory and motor block, lesser time for complete sensory and motor block, prolonged analgesia and motor block can be explained by the fact that epidural Dexmedetomidine has greater selectivity for -2 receptors with greater lipid solubility. Hence, it easily penetrates the meninges. They also cause augmentation of local anaesthetic effects as they cause hyperpolarization of nerve tissues by altering transmembrane potential and ion conductance at locus coeruleus in the brainstem. The increase in analgesic action of local anaesthetics by the use of -2 agonists in the epidural space may be related to the reduction of the systemic absorption of the local anaesthetics, caused by local vasoconstrictor subtypes mediated by the C2 in smooth muscle and venous epidural plexus.

The analgesic effect of Dexmedetomidine is possibly produced by the stimulation of spinal cord at the dorsal root neuron level, where -2 agonists inhibit the release of substance P in the nociceptive pathway and also inhibit the release of norepinephrine, at the nerve endings. The spinal mechanism is considered to be mainly responsible for the analgesic effects though there is some evidence of both the supraspinal and peripheral sites of action of Dexmedetomidine.

Epidural Dexmedetomidine causes prolonged post operative analgesia, and lower consumption of local anaesthetic agents ([1,2,3]). Dexmedetomidine is found to be a better epidural adjuvant compared to Clonidine [(6)] . Dexmedetomidine was found to be providing early onset of analgesia, adequate sedation and prolonged post-operative analgesia [(7,8)]. Fentanyl is 800 times more lipid soluble than morphine and rapidly absorbed from epidural space [(9)]. Fentanyl acts primarily as an agonist at -opioid receptors to enhance the analgesia. The dorsal roots (primary afferent tissues) contain opioid-binding sites and Fentanyl either acts directly on the spinal nerve or by penetrating the duramater to act at the spinal roots. The spread through CSF is limited and segmental level of analgesia is achieved with precise location of epidural catheter.

In the present study, Dexmedetomidine group showed an earlier onset of sensory blockade and lesser time to achieve maximum sensory level as compared to Fentanyl group. Time for two-segment regression, the duration of analgesia, and motor blockade were significantly prolonged in patients in whom Dexmedetomidine was used as an adjuvant with Bupivacaine. Our data support previous studies that used Dexmedetomidine and Fentanyl as additives to epidural anaesthesia.

In our study, group D patients had a significantly higher duration of analgesia with a mean of 9.422 hours compared to group F with a mean duration of 4.22 hours. S. Kiran et al [1] demonstrated that 10 microgram Dexmedetomidine as adjuvant to 0.5% Ropivacaine was more effective with respect to duration and intensity of analgesia compared to 0.5% Ropivacaine alone or 0.5% Ropivacaine with 20 micrograms of Fentanyl in patients undergoing infraumbilical surgeries.
The duration of motor block in group F was 2.611 hours and among group D was 3.349 hour. In a study by Nilesh Banu Sona Ware, J. Balavenkatt Subramaniam et al[2], the receding time for motor block and sensory block was higher in patients who received Dexmedetomidine as epidural infusion compared to patients who received Ketamine as epidural infusion for hip surgeries under CSE. Our study results are matching with this. The initial epidural bolus of the adjuvant drug given after the fixation of the spinal drug, helps to build up the CSF level and the supplement doses given later maintains it. Saadawy et al [3] studied the effects of Dexmedetomidine on the characteristics of Bupivacaine in caudal anaesthesia in children. Their findings also are similar, with epidural Dexmedetomidine prolonging post operative analgesia and lowering consumption of local anaesthetics. Sarkar A et al ([4]) also had similar findings with the conclusion that Dexmedetomidine is a better alternative to Fentanyl as epidural adjuvant.

Bradycardia was noted among 6 patients of group F and 23 patients of group D. One patient in the Dexmedetomidine group was treated with inj. Atropine 0. 6 mg. Severe or resistant bradycardia was not seen in any of the patient. Dexmedetomidine causes bradycardia by its central action of reducing the sympathetic flow and inhibition of norepinephrine release. Among the 102 patients studied, 85.3% had no hypotension. In both groups, hypotension was not severe and responded to Inj. Mephenteramine. Among group F, 9 patients had hypotension and among group D, 6 patients had hypotension. Synthetic opiate drug Fentanyl can induce centrally mediated bradycardia and hypotension. Dexmedetomidine causes hypotension by stimulating the pre synaptic alpha 2 receptors decreasing the norepinephrine release.

"Throughout the procedure all the patients were calm in both groups. Among the group F patients, 58.8% had no sedation. 41.2% of group F had a sedation score of 1. Among group D, 55% had a sedation score of 1 and 41.2% had a sedation score of 2. Severe unarousable level of sedation was not observed in any of the patients. Respiratory depression also was not observed in the intra operative or post-operative period. These results tally with the findings of Kumkum Gupta et al [(5)] and Bajwa et al [(9)].

Pruritus was complained by 4 patients of group F (7.8%), and responded to treatment with single dose of antihistamine Inj. Pheniramine maleate. No patients in the Dexmedetomidine group had pruritus. This was statistically significant with p value of 0.041.

In our study 5 patients of group F (9.8%) and 1 patient of group D (2.1%) had nausea. Vomiting was seen in 3 patients (5.9 %) of group F and 1 patient of group D. But this difference was not statistically significant (p value: 0.308)

In the perioperative period there are many factors contributing

to nausea and vomiting like use of opioids and their dose [10], early ambulation, delayed gastric emptying, female gender, history of motion sickness and vascular headache. Opioids cause direct stimulation of chemoreceptor trigger zone. Along with delayed gastric emptying, dehydration and electrolyte imbalance may also play a role in causing vomiting. "Dexmedetomidine prevent nausea and vomiting in the perioperative period and adding Dexmedetomidine to Morphine have been shown to delay morphine induced vomiting [11,12,13].

All our patients had stable hemodynamic status in the post operative period. The dose requirement of local anaesthetic drug was very low and the doses of adjuvant drugs were suitably selected. The difference in haemodynamic profile between the two groups was not statistically significant.

CONCLUSION

We conclude that Dexmedetomidine as an adjuvant to epidural Bupivacaine is a better alternative to Fentanyl, as it shows faster onset of sensory block, prolonged duration of analgesia, better motor blockade and higher sedative property without any significant respiratory depression

REFERENCES

1. S . Kiran , Kavitha Jinil , Urvashi Tandon , Soumita Kumar. Evaluation of Dexmedetomidine and Fentanyl as additives to Ropivacaine for epidural anaesthesia and analgesia. 2018 Journal of Anesthesiology Clinical Pharmacology 34 : 41 -5
2. Nilesh Balu Sona Ware , J . Balavenkatt Subramaniam , P . Gurumoorthy , Poonam Ashok Jadhav. Quality of post operative analgesia after epidural Dexmedetomidine and Ketamine – A comparative study . IJA vol 60 issue 10 October 2016 .
3. Saadawy I , Broker A , Elashahaway M A , Almazrova A , Melibery S , Abdul Latif AA et al . Effect of Dexmedetomidine in the characteristics of Bupivacaine in caudal blocks in paediatrics . Acta Anesthesiology Scandinavia 2009 : 53 : 251 – 6
4. Sarkar A , Bafila N S , Singh RB , Rasheed MA , Choubey S , Arora V. Anaesthesia Essays Res. 2018 April – June 12 (2) : 572- 580 .
5. Kum Kum Gupta , Bhavana Rasthogi , Prasanth K Gupta , Manish Jain , Saneeta Gupta , Deepthi Mangle. Epidural 0. 5 % Levo Bupivacaine with Dexmedetomidine versus Fentanyl for vaginal hysterectomy – A prospective study . Indian Journal of pain. 2014 29 issue 3 page 149 – 154 .
6. Safiya Sheikh and Sarala B Mahesh . Efficacy and safety of epidural Dexmedetomidine and Clonidine in patients undergoing lower limb orthopaedic surgery. Journal of Anesthesiology Clinical Pharmacology . 2016 April – june : 32 (2) :203 – 209
7. Suni Chiruvilla , Balaji Dhonthu , Dora Babu Salla . Post operative analgesia with epidural Dexmedetomidine compared to Clonidine following total abdominal hysterectomy . A prospective double blind randomized trial. Anaesthesia essays Res . 2018 jan – March 12 (1) : 103 – 108 .
8. Bajwa S K, Bajwa A K , Kaur J sing G , Arora V Gupta S et al . Dexmedetomidine and Clonidine in epidural anaesthesia . A comparative evaluation . IJA 2011 : 55 : 116 – 21
9. Bajwa SJ , Bajwa SK , Kaur J , Siny A , Paramar SS , Comparative evaluation of Dexmedetomidine and Fentanyl foe epidural analgesia in lower limb Orthopaedic surgeries . Saudi Journal of Anaesthesia , 2011 : 365 – 70 .
10. Jayan Kandasamy MBBS , MD , Walderman A , Carlo MD. Assisted ventilation of the neonate, 6 th edition 2017
11. Mitra Jabalameli , Safoura Roulamine and Fatemech Gourtanian. A comparison of the effects of Fentanyl and RemiFentanyl on nausea , vomiting and pain after caesarean section . Iran J Med Sci. 2011 Sep; 36(3): 183–187.
12. Shenbui Jin et al medicine. Dexmedetomidine prevents post operative nausea vomiting in patients during general anaesthesia - A PRISMA complaint meta analysis of randomised controlled trials . Medicine (Baltimore). 2017 Jan; 96(1): e5770. Huai Jin Li , Shah Liu , Yue Yins l. Adding Dexmedetomidine in addition to morphine based analgesia reduces early PONV in patients undergoing laproscopic gynecological surgeries. A randomised controlled trial . BMC Anesthesiology, Volume 20, Article number: 11 (2020)