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"A Comparative Study between Effects of Bupivacaine and Bupivacaine with Dexmedetomidine In Case Of Thoracic Epidural Anaesthesia for Elective Open Cholecystectomy"

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Abstract:
Introduction : *Surgical pain is a universal phenomenon affecting all patients in the peri-operative and post-operative period. So it is the moral to provide adequate peri-operative & postoperative analgesia not only to suppress the adverse physiological responses of pain, but also to improve the quality of patient comfort following surgery.*
Aims and Objectives*: The aim of this study was to compare of thoracic epidural block with Bupivacaine 0.5% and Bupivacaine 0.5% with Dexmedetomididne combination in terms of haemodynamic stability,proper peroperative anaesthesia and postoperative pain relief in adult patients undergoing open cholecystectomy*
Methodology*: This is a A prospective randomized double blind controlled clinical trial carried out on 80 patients at the Department of Anaesthesiology & Surgery, Bankura Sammilani Medical College & Hospital from June 2015- june 2016. 80 patients of ASAPS I and II, aged 25-55 years of either sex undergoing elective open cholecystectomy were included in the study. Haemodynamic status,onset of analgesia,duration of sensory block,duration of analgesia,onset &duration of motor block ,height of block & postoperative analgesia,side effects were analysed*
Results: *The present study showed that thoracic epidural dexmedetomidine 0.5 µg/kg added to 12.0 ml of plain bupivacaine (0.5%) provided prolonged sensory block and longer duration of analgesia compared to 12.0 ml of plain bupivacaine (0.5%) in patients of elective open cholecystectomy. All patients were hemodynamically stable in both groups. Among the side effects, only increase level of sedation was observed in bupivacaine (0.5%) plus dexmedetomidine group than plain bupivacaine group*
Conclusion: *dexmedetomidine 0.5 µg/kg seems to be an effective alternative adjuvant to thoracic epidural bupivacaine in supra-umbilical surgeries like open cholecystectomy with an additional sedative effect and excellent quality of analgesia*

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I. Introduction

The American Pain Society now recommends pain as the "5th vital sign" that is to be monitored regularly along with pulse and blood pressure[1].The International Association for the study of Pain (IASP) defines Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage[2].Surgical pain is a universal phenomenon affecting all patients in the peri-operative and post-operative period. Apart from the agonizing sensory experiences associated with it, acute pain has several deleterious effects on the physique and the psychae[3] .

A system of relieving pain not only must prove its positive influence on the process of recovery but should also measurable both in terms of patient satisfaction, and scientifically, in terms of improved function and progressive effect on healing. Pain management must be prophylactic, integral to surgery and proactive rather than retroactiveCrile et al (1914)[6] first suggested that control of post-operative pain would favourably influence the result of surgery while Weissman C. (1990), described the metabolic effects effects of acute post-operative pain as an effects of the rise of stress hormones such as catecholamines, angiotensin II, cortisol, growth hormone, glucagon, ACTH, and ADH. Pain also reduces insulin and testosterone levels. The increase in stress mediators in the peri-operative period may lead to hyperglycaemia, protein catabolism, a negative nitrogen balance and lipolysis. The excessive levels of aldosterone, cortisol and ADH lead to sodium and water retention and hypokalemia resulting in increased intracellular and extracellular fluid in the periphery and lung parenchyma causing pulmonary edema. Local release of inflammatory factors such as cytokines, interleukin-2, interleukin-6 and TNF may also contribute to abnormal physiological responses[7].The cardiovascular effects of

pain are modulated by catecholamines, aldosterone, ADH and activation of RAS. Angiotensin II causes generalized vasoconstriction while catecholamines increase heart rate and systemic vascular resistance, ultimately leading to hypertension, tachycardia and dyspnea causing significant myocardial ischaemia in patients with coronary artery disease. Circulating catecholamines lead to a hypercoagulable state leading to thromboembolic episodes in the post-operative period. Excessive salt and water retention may precipitate congestive heart failure. Pain increases skeletal muscle tension leading to decreased thoracic compliance, splinting and hypoventilation particularly in patients undergoing abdominal and thoracic surgery causing atelectasis, pulmonary consolidation and pneumonitis in the post-operative period.The increase in sympathetic activity and reflex inhibition of visceral smooth muscles lead to post-operative ileus and urinary retention. There also occurs suppression of immune function resulting in lymphopenia and depression of the RAS resulting in peri-operative infections.Open cholecystectomy is a good modern example of a procedure to which these principal apply[8].so perioperative & postoperative pain control is very much important.There are various method of perioperative & postoperative analgesia.

The epidural route has been used much more extensively for perioperative pain control, reasons include choice to leave an epidural catheter in place for extended period to maintain analgesia, familiarity with using epidural local anaesthetics and freedom from the risk of post dural puncture headache. The rationale for combination of epidural adjuncts like Alpha 2 Agonist, Dexmedetomidine with local anaesthetic is additive effects. These two types of drugs eliminate pain by acting at two distinct sites. Local anaesthetic at the nerve axon and the Dexmedetomidine acts on pre and post synaptic sympathetic nervous system.The local anaesthetic blocks transmission of impulses at the level of the nerve axon membrane. Those two distinctive actions may contribute to the analgesic effects of surgery[10-11].The unique feature of addition of alpha 2 agonist given neuraxialy for analgesia is lack of sympathetic or motor block which allows patients to ambulate without the risk of orthostatic hypotension or motor in-coordination. These advantages are beneficial for high risk patients undergoing major operation i.e. patients with compromised pulmonary or cardiovascular function, grossly obese patients and elderly patients[12].

So an endeavour was made to compare the efficacy of thoracic epidural block with Bupivacaine 0.5% and Bupivacaine 0.5% with Dexmedetomididne combination in terms of haemodynamic stability and postoperative pain relief in adult patients undergoing open cholecystectomy.

II. Material And Methods

A prospective randomized double blind controlled clinical trial was conducted at surgery & anaesthesiology dept of Bankura Sammilani Medical College. The trial was approved by the Ethical Committee of Bankura Sammilani Medical College, Bankura. 80 adult patients of either sex, ASA physical status I or II, aged 25-55years, body weight 40-70 kg, scheduled for elective open cholecystectomy to be carried out under thoracic epidural anaesthesia were selected. All patients are to be explained regarding the type of anaesthesia and the procedure and informed consent was taken from each patient.

***INCLUSION CRITERIA:**

1. ASA physical status I and II patients undergoing elective surgeries.
2. Age 25-55 years.
3. Sex of both male and female.
4. Scheduled for elective open cholecystectomy.

***EXCLUSION CRITERIA:**

1. Age less than 25 years and more than 55 years.
2. Unwilling patients not giving consent for operation.
3. Emergency cases.
4. ASA physical status class III or more.
5. Patients having known hypersensitivity to amide local anaesthetics and Dexmedetomidine.
6. Patients displaying sign and symptoms of systemic infection.
7. Patients having local infection in thoracic spinal region.
8. Patients with pre-existing Diabetes Mellitus, Hypertension, Ischaemic Heart Disease, COPD or any other major systemic illness.
9. Pre-existing CNS disorder-Epilepsy and raised intracranial tension.
10. Pre-existing respiratory disorder-COPD, Asthma, Chronic Bronchitis.
11. Severe renal, hepatic, cardiological, haematological, metabolic disorder.
12. Cardiovascular malformation.
13. Bleeding diathesis or coagulopathy.
14. Spinal deformity.

15. Haemodynamically unstable patient.
16. Patients on anticoagulant or antiplatelet therapy.

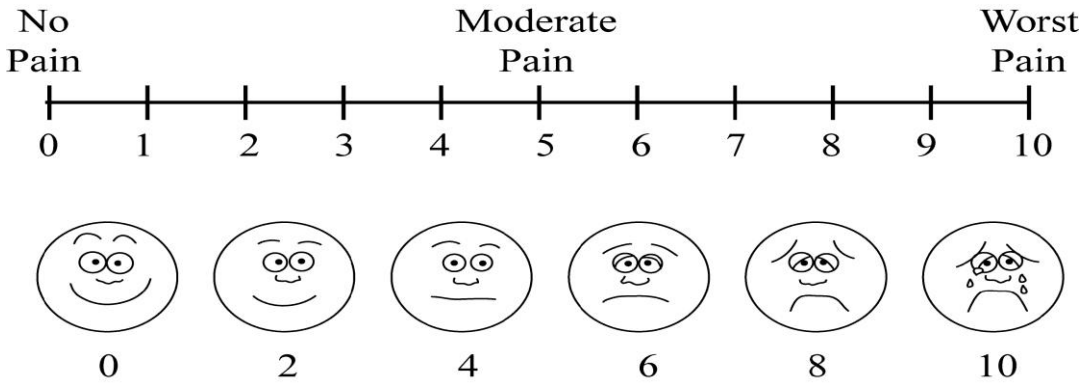
***STUDY TECHNIQUE:**
patients (n=80) will be randomized by simple sealed envelope method into 2 groups(n=40):
Group 1: received :12.0 ml 0.5% Bupivacaine.
Group 2: received :12.0 ml 0.5% Bupivacaine +
0.5 mcg/kg Dexmedetomidine

Proper history taken & physical examination done. & kept npm for 6 hrs The night before surgery tab Diazepum 10 mg orally, inj. Metochlopramide 10 mg and inj. Ranitidine 50 mg i.m. or i.v. have to be given 1-2 hours before operation.Patient under the study were explained about the epidural technique. They were also informed that in case of failure of technique, general anaesthesia would be administered. Visual analogue pain scale was shown to all patients in the preoperative. On the scale at the extreme left end of a line, (10 cm long) represented no pain and the other end represented no pain. The patients had to place a mark on this scale corresponding to the degree of pain experienced, during and after operation.Patient's compliance was taken similarly on a 10 point scale (0-10).Surgeons were told to mark their satisfaction on a 4 point scale regarding muscle relaxation, analgesia, ease of operation, any difficulty during procedure. They were assured that GA would be given if they face any problem during operation under Epidural anaesthesia.
#Anaesthetic Procedure: After proper identification of patients and checking of machine, breathing circuits and monitors are to be carried out beforehand and the full range of drugs and equipments including appropriate size laryngoscopy blades, airways and ET tubes are to be kept in hand. After arrival of patient in the operation theatre a baseline, pulse rate, BP, ECG, respiratory rate, SpO_2 are to be noted. Each patient is to be given 10-20 ml/kg Ringer's solution at body temperature as fluid preload over approximately 15 minutes before epidural anesthesia and infusion continued thereafter.

The patients are to be kept in sitting position. Proper cleaning of the back with betadine lotion and identification of space, 3 ml Bupivacaine 0.5% is to be used to infiltrate the skin and subcutaneous tissue at T_{8-9} or T_{9-10} interspace. For epidural anaesthesia, an 18 G Tuohy needle is introduced through the same lace till the resistance of ligamentum flavum was met. The stylet is withdrawn and 5 ml glass syringe with a smoothly moving piston containing 3 cc. saline tightly attached to the needle hub. The needle is gradually introduced with constant pressure on the piston and the epidural space is identified by loss of resistance and smooth injection of air. Epidural catheter insertion done and the needle is withdrawn. After negative aspiration, 0.5% Bupivacaine is administered and signs and symptoms of intravascular injection if any is noted. If no sign of intravascular injection of drugs are noted then 0.5% Bupivacaine 1.5 ml/of desired block along with 0.5 mcg/kg of Dexmedetomidine are to be administered. After injection of the drug, the epidural catheter is secured in place with adhesive tapes and sterile gauge, then bacterial filter are added and patient is placed ready to undergo operation.

***PARAMETERS ASSESSED:**
1. Haemodynamic status:
Continuous ECG, HR, BP(MAP), pulse, SpO_2.
2. Onset of analgesia(sensory block):
to be assessed by pin prick method. Time duration(minute)-from injection of local anaesthetics solution epidurally to the start of loss of pain sensation to pin prick.
3. Duration of sensory block:
Time duration(minute)-from onset of sensory block to regression of dermatome of two segments.
4. Duration of analgesia: assessed by 4 point verbal rating scale to record the observer's assessment of pain. The scores are-
I. Comfortable(no pain)
II. Mild pain(only elicited by questioning)
III. Moderate pain(bothering the pains, but often controlled by lying still, analgesic accepted gladly)
IV. Severe pain(dominating the consciousness and calling out for urgent relief)
Time duration(minute)-from the onset to the first request for systemic analgesia.
5. Onset of motor block: By modified Bromage scale as follows:
0- No paralysis
1- Inability to raise extended leg
2- Inability to flex knee

3- Inability to flex ankle and fast toe
Time duration(minute)-from injection of local anaesthetics solution to achieve motor block scale two or more.
6. Duration of motor block: By modified Bromage scale.
Time duration(minute)-from onset of motor block to regaining of full motor power and joint movements.
7. Height of block: By pin prick method over dermatomal segments.
8. Postoperative analgesia assessed VAS (Visual Analouge Scale-numeric pain scale 0-10. (0= no pain, 10= worst possible pain



9. Ramsay Sedation score:
1. Drowsy
2. Drowsy but arousal to touch/call
3. Drowsy but arousal on deep stimulation

10. Side effects: nausea, vomiting, headache, pruritus, respiratory depression, hypotension, shivering, urinary retention, drowsiness etc. also noted.
The surgery is allowed to start when the condition of the patient is stable.
The intra-operative monitoring of pulse, MAP, SpO_2, ECG are noted. When the patients complain of pain 2-4 ml of 0.5% Bupivacaine bolus dose are given by epidural catheter and rescue analgesic(inj. Diclofenac i.m.) is given and during post operative period 0.125% Bupivacaie are given at a rate of 8 ml/every 12 hrs.The HR, MAP are recorded before the start of procedure and then 5 minute interval up to 30 minute, then 10 minute interval up to 1 hour and finally 15 minute interval up to 90 minute or till the operation. Then every 1 hour interval up to 6 hour post operative period. SBP<70 mm Hg is promptly managed with I.V. fluid and vassopressor (Phenylephrine).SpO_2 and respiratory rate also recorded as above said interval.

III. Statistical Analysis

All raw data were entered into a predesigned excel spreadsheet and analysed using standard statistical software SPSS. Numerical data was expressed as means, medians and standard deviation of mean. Categorical data was expressed as percentages. Numerical data between two groups which was normally distributed was analysed using student's t-test and Mann Whitney U test as appropriate. All tests were two tailed. A P value of less than 0.05 was considered statistically significant.

IV. Result

All the 80 patients who enrolled themselves in this double blinded randomized comparative study , completed the study. There was no drop out and the study results are shown below**.**

GROUP	MINIMUM WEIGHT(kg)	MAXIMUM WEIGHT(kg)	MEAN	MEDIAN	STD. DEV	P-VALUE
B	44	60	50.30	50	4.304	0.820
D	42	60	50.48	50	4.403	

DISTRIBUTION OF BODY WEIGHT OF PATIENTS IN TWO GROUPS

Table 1 shows distribution of body weight in two study groups. There was no statistically significant difference in body weight distribution among the study groups as 'p' value >0.05 and hence the groups were comparable to each other in terms of body weight

TABLE – 2DISTRIBUTION OF HEIGHT OF PATIENTS IN TWO GROUPS

GROUP	MINIMUM HEIGHT(cm)	MAXIMUM HEIGHT(cm)	MEAN	MEDIAN	STD. DEV	P-VALUE
B	140	166	153.33	154	6.137	0.667
D	146	164	153.88	152	5.209	

Table 2 shows distribution of height in two study groups. There was no statistically significant difference in height distribution among the study groups as 'p' value >0.05 and hence the groups were comparable to each other in terms of height.

TABLE – 3 DISTRIBUTION OF DURATION OF SURGERY IN TWO GROUPS

GROUP	MINIMUM TIME(min)	MAXIMUM TIME(min)	MEAN	MEDIAN	STD. DEV	P-VALUE
B	70	110	87.73	88	8.578	0.368
D	65	102	85.98	87	8.699	

Table 3 shows distribution of duration of surgery in two study groups. There was no statistically significant difference in duration of surgery as 'p' value >0.05 and hence the groups were comparable to each other.

TABLE – 4 DISTRIBUTION OF ONSET OF SENSORY BLOCK IN TWO GROUPS

GROUP	MINIMUM TIME(min)	MAXIMUM TIME(min)	MEAN	MEDIAN	STD. DEV	P-VALUE
B	15	19	17.03	17	0.974	<0.001
D	10	14	12.18	12	1.059	

Table 4 shows distribution of onset of sensory block in two study groups. There was statistically significant difference in onset of sensory block among the study groups as 'p' value <0.05.Patients in Group- B had significantly early onset of sensory block than Group- D.

TABLE – 5 DISTRIBUTION OF TIME OF ONSET TO MAXIMUM SENSORY BLOCK LEVELS IN TWO GROUPS

GROUP	MINIMUM TIME(min)	MAXIMUM TIME(min)	MEAN	MEDIAN	STD. DEV	P-VALUE
B	20	25	22.65	23	1.075	<0.001
D	15	18	16.78	17	0.832	

Table 5 shows distribution of time to maximum sensory block levels in two study groups. There was statistically significant difference in time to reach maximum of sensory block levels among the two study groups as 'p' value <0.05.Group-B clearly shows delay of time to reach maximum block level than Group-D.

TABLE – 6 DISTRIBUTION OF TIME OF ONSET FOR COMPLETE MOTOR BLOCK IN TWO GROUPS

GROUP	MINIMUM TIME(min)	MAXIMUM TIME(min)	MEAN	MEDIAN	STD. DEV	P-VALUE
B	26	31	29.05	29	1.131	<0.001
D	21	25	22.93	23	0.917	

Table 5 shows distribution of onset of time for complete motor block in two study groups. There was statistically significant difference in duration of sensory block among the study groups as 'p' value <0.05.Patients in Group- D had significantly early onset of time for complete motor block than Group- B.

TABLE-7 DISTRIBUTION OF THE TIME TO TWO SEGMENTAL REGRESSION

GROUP	MINIMUM TIME(min)	MAXIMUM TIME(min)	MEAN	MEDIAN	STD. DEV	P-VALUE
B	110	116	113.15	113	1.210	<0.002
D	237	250	242.95	243	2.581	

Table-7shows distribution of duration to two segmental regression. It clearly shows for Group-D it is significantly more delayed than Group-B as p-value <0.05

TABLE-8 DISTRIBUTION OF TIME DURATION FOR REGRESSION TO BROMAGE 1

GROUP	MINIMUM TIME(min)	MAXIMUM TIME(min)	MEAN	MEDIAN	STD. DEV	P-VALUE
B	148	155	152.23	152	1.210	<0.001
D	237	250	242.95	243	2.581	

Table-8shows distribution of time duration for regression to Bromage 1. It shows that Group-D has significantly more duration of time for regression to bromage-1 than Group-B as p-value <0.05

TABLE9 DISTRIBUTION OF TIME TO SENSORY REGRESSION AT S1

GROUP	MINIMUM TIME(min)	MAXIMUM TIME(min)	MEAN	MEDIAN	STD. DEV	P-VALUE
B	177	185	181.70	182	1.757	<0.001
D	326	338	330.15	330	2.392	

Table-9 shows the distribution of time to sensory regression at S1 between two groups. It shows that Group-D needs significantly more time to sensory regression at S1 than Group-B as p-value <0.001

TABLE – 10 DISTRIBUTION OF THE TIME POINT AT WHICH RESCUE ANALGESIC (VAS ≥4) REQUIRED IN TWO GROUPS

GROUP	MINIMUM TIME(min)	MAXIMUM TIME(min)	MEAN	MEDIAN	STD. DEV
B	200	230	215.15	215	6.274
D	240	272	259.65	261	8.223

Table10 shows distribution of duration of analgesia before rescue analgesic is given. The time to first request of rescue analgesic (min) was significantly earlier in B group than in D group, as 'p' value <0.05

TABLE – 11 COMPARISON OF SEDATION SCORE BETWEEN TWO GROUPS:

TIME	GROUP B (MEAN±SD)	GROUP D (MEAN±SD)	SIGNIFICANCE (p VALUE)
5 Min	2.35 ± 0.58	2.15 ± 0.54	0.101
10 Min	2.70 ± 0.46	3.40 ± 0.55	**0.001**
15 Min	2.40 ± 0.50	3.78 ± 0.73	**0.001**
20 Min	2.38 ± 0.50	4.30 ± 0.72	**0.001**
25 Min	2.58 ± 0.50	3.78 ± 0.80	**0.001**
30 Min	2.75 ± 0.49	3.98 ± 0.86	**0.001**
45 Min	2.60 ± 0.49	3.98 ± 0.83	**0.001**
60 Min	2.70 ± 0.46	3.63 ± 0.77	**0.001**
90 Min	2.35 ± 0.62	2.88 ± 0.33	**0.001**

Table 12 COMPARISON OF SpO_2 (OXYGEN SATURATION) BETWEEN TWO GROUPS:

TIME	GROUP B (MEAN)	GROUP D (MEAN)
0 Min	99.00	100.00
5 Min	99.50	99.50
10 Min	100.00	100.00
15 Min	100.00	100.00
20 Min	100.00	100.00
25 Min	100.00	100.00
30 Min	100.00	100.00
45 Min	100.0	100.00
60 Min	99.50	100.00
90 Min	100.00	100.00

There was no statistically significant difference between the patients of Group B and Group D as p value > 0.05 (student's independent t-test) found in SpO_2 in every time of measurement.

TABLE – 13 COMPARISON OF HEART RATE (HR) BETWEEN TWO GROUPS:

TIME	GROUP B (MEAN±SD)	GROUP D (MEAN±SD)	SIGNIFICANCE (p VALUE)
0 Min	97.58 ± 17.35	97.88 ± 13.92	0.932
5 Min	94.63 ± 18.31	95.23 ± 14.82	0.872
10 Min	88.60 ± 15.68	89.73 ± 13.04	0.728
15 Min	83.55 ± 16.36	85.85 ± 12.27	0.479
20 Min	82.75 ± 16.18	84.25 ± 13.02	0.649
25 Min	80.78 ± 16.11	80.35 ± 12.12	0.894
30 Min	79.25 ± 15.42	78.00 ± 10.07	0.669
45 Min	78.43 ± 14.57	78.58 ± 8.78	0.956
60 Min	79.48 ± 14.14	79.13 ± 8.96	0.895
90 Min	80.00 ± 13.13	80.25 ± 7.72	0.918
120 Min	80.13 ± 11.28	79.30 ± 6.76	0.693
180 Min	81.48 ± 8.91	82.00 ± 7.66	0.778
240 Min	81.40 ± 10.79	83.85 ± 9.38	0.282
300 Min	82.43 ± 11.20	84.15 ± 9.34	0.457
360 Min	81.03 ± 8.63	83.85 ± 8.16	0.137

There was no statistically significant difference between the patients of Group – B and Group – D as p value > 0.05 (student's independent t-test) found in heart rates in any time of measurement.

TABLE – 14 COMPARISON OF MEAN ARTERIAL PRESSURE (MAP) BETWEEN TWO GROUPS:

TIME	GROUP B (MEAN±SD)	GROUP D (MEAN±SD)	SIGNIFICANCE (p VALUE)
0 Min	96.00 ± 13.38	97.60 ± 11.17	0.563
5 Min	86.23 ± 11.82	89.35 ± 13.83	0.281
10 Min	78.88 ± 12.24	80.63 ± 13.59	0.547
15 Min	74.65 ± 10.07	77.78 ± 13.09	0.235
20 Min	70.85 ± 8.91	76.10 ± 11.16	**0.023**
25 Min	70.30 ± 9.35	73.53 ± 11.08	0.164
30 Min	70.75 ± 7.47	74.28 ± 8.89	**0.059**
45 Min	70.80 ± 7.40	74.73 ± 8.73	**0.033**
60 Min	73.88 ± 8.12	75.55 ± 7.48	0.340
90 Min	77.73 ± 7.99	77.63 ± 7.99	0.956
120 Min	80.48 ± 7.71	79.18 ± 9.40	0.501
180 Min	92.63 ± 8.31	83.28 ± 8.20	**0.001**
240 Min	88.18 ± 8.75	94.18 ± 6.40	**0.001**
300 Min	86.38 ± 9.65	87.43 ± 9.62	0.627
360 Min	86.25 ± 6.29	89.40 ± 8.87	0.071

The statistically significant difference in p value (p value < 0.05) by student's independent t-test and Mann-Whitney test was found in mean arterial pressure at 20 min, 30 min, 45 min, 180 min and 240 between two groups.

TABLE- 15 INCIDENCE OF SIDE-EFFECTS IN GROUP-B AND GROUP- D

SIDE EFFECTS	GROUP- B	GROUP- D	TOTAL
NAUSEA & VOMITING	2(5%)	5(12.5%)	7(8.75%)
PRURITUS	4(10%)	0	4(5%)
RESPIRATORY DEPRESSION	0	0	0
SHIVERING	4(10%)	6(15%)	10(12.5%)
HEADACHE	0	0	0
URINARY RETENSION	1(2.5%)	0	1(1.25%)

HYPOTENSION	9(22.5%)	9(22.5%)	18(22.5%)
BRADYCARDIA	7(17.5%)	4(10%)	11(13.75%)

V. Discussion

Open cholecystectomy still remains a more frequently performed procedure in the developing countries, mostly in far flung areas due to non-availability of the laparoscopic equipment as well as the lack of trained hands. One of the major side effects of open cholecystectomy is substantial impairment of pulmonary function after a large sub-costal upper abdominal incision. Marked diaphragmatic dysfunction occurs postoperatively, caused by both reflex diaphragmatic changes and incisional pain. Vital capacity and functional residual capacity (FRC) may be reduced by 20-40% of pre-operative values, and they may not return to normal until 2-3 days after surgery.[13] though GA is commonly administered still it has own pulmonary complication & incidence of postoperative nausea & vomiting & also there is no scope for using postoperative analgesia.so we concentrated over epidural anaesthesia. Local anesthetics and adjuvants co- administered epidurally improves the quality of intraoperative and postoperative analgesia, allowing a reduction in the dose of both the classes of drugs.

The present study was undertaken to compare the onset and duration of effective anesthesia by time interval between the onsets of block to time for request for first rescue analgesic assessed by Visual Analogue Scale (VAS)[14]. Perioperative hemodynamic changes and any obvious side effects like shivering and nausea-vomiting were also taken into consideration. This comparative, randomized, double blinded, parallel group clinical trial was conducted between March 2015 to August 2016 at Bankura Sammilani Medical College & Hospital, Bankura, in General Surgery operation theatre, involving 80 patients of ASA physical status I and II who received either thoracic epidural 0.5% bupivacaine 12 ml (group-B) or 0.5% bupivacaine 12 ml and dexmedetomidine 0.5mcg/kg (group-D). The comparison of clinical efficacy of group-B and group-D, in terms of onset and duration of anesthesia and analgesia, was assessed along with heart rate, blood pressure (SBP, DBP, MAP) at regular intervals throughout the perioperative period in elective open cholecystectomy. This method also well matches with the study of Seema Shreepad Karhade and co-workers [15] who studied 60 patients of ASA grade I & II undergoing vaginal hysterectomy under epidural anaesthesia, recruited and randomized into 2 groups to receive 15 ml of bupivacaine (0.5%) for group I and 15 ml of bupivacaine (0.5%) with 0.5 μg/kg of dexmedetomidine for group II.

Table 4, show the time for onset of sensory block in the two groups. The mean onset time of sensory block to reach T_6 in Group B were 17.03±0.974 minutes and in Group D were 12.18±1.059 minutes. It shows that in Group D receiving 0.5% bupivacaine 12ml and 0.5 mcg/kg of dexmedetomidine, had early onset of sensory block than in patients in Group B receiving 12ml 0.5% bupivacaine alone. Appropriate statistical test shows, significant difference ($p<0.001$) in the onset of sensory block between the two groups. This observation is close to the result of Seema Shreepad Karhade et al. [15] who examined the onset times of sensory and motor block during the study for efficacy and quality of epidural dexmedetomidine in combination with bupivacaine for vaginal hysterectomy.

In table-5 It was observed that the onset of sensory block to the maximal level for the plain bupivacaine group(B) was 22.65 ±1.075 min and for the dexmedetomidine(D) group was 16.78 ± 0.832 min as there was significant difference in the mean onset of sensory block with appropriate test p-value became <0.001 which corroborate with the result of observation done by Seema Shreepad Karhade et al.

Table 6, show the time for onset of complete motor block in the two groups. The mean onset time of motor block to maximum level in Group B were 29.05±1.131 minutes and in Group D were 22.93±0.917 minutes. With appropriate statistical test, p value became <0.001. Hence it shows that there was significant difference as $p<0.05$ in the time of onset of motor block between the patients in Group D and Group B. All the findings are corroborative with the study of Seema Shreepad Karhade et al[15]. regarding the onset of motor block to the maximal level with epidural anaesthesia in vaginal hysterectomy where in plain bupivacaine group was 27.16±4.2 min and in dexmedetomidine group was 22.98±4.78 min, with a $p<0.001$, denoting that there was significant difference in the time to complete motor blockade in both groups.

Table 8, show the duration of sensory block in the two groups. This duration was calculated by counting time to regression of sensory block to 2 segment dermatome. Statistically there was significant difference in duration of sensory block distribution among the study groups as 'p' value is <0.002.The mean duration of sensory block in Group B were 113.12±1.210 minutes and in Group D were 242.95±2.581 minutes. It shows that in Group D had longer duration of sensory block than in patients in Group B. The data corroborates with the value of study of Seema Shreepad Karhade et al [15]. In their study they found that duration of sensory block was shorter in the plain bupivacaine(0.5%) group than in the dexmedetomidine with bupivacaine(0.5%) group ($P < 0.001$). Time to 2 segment regression was 110.32±10.21 minutes in plain bupivacaine group, whereas in dexmedetomidine group it was 240.84±9.48 minutes. Table 9, figure 9 show distribution of mean duration for regression to Bromage 1. In this study the value for Group B was 152.23±1.210 whereas in Group D, it was 242.95±2.581. This shows there was significant difference in the

duration of sensory regression to Bromage 1 for both group as p-value was <0.001. This value corroborates with the study of Seema Shreepad Karhade et al[15] where they found the value for plain bupivacaine group was 150.52±21.38 and in case of dexmedetomidine group it was 320.62± 23.86 with p-value <0.001.

Table 10, show distribution of mean duration to sensory regression at S1. In this study the value for Group B was 181.70±1.757 whereas in case of Group D, it was 330.15±23.92 with the p-value <0.001. This shows there was significant difference in mean duration for sensory regression at S1 for both the groups. This data corroborates with the study of Seema Shreepad Karhade et al[15] where they found the value for plain bupivacaine group was 179.68±26.34 and in case of dexmedetomidine group it was 328.28±28.14 with a p-value <0.001.

Table 10, show distribution of duration before rescue analgesia was given in two study groups. Duration of analgesia was assessed every 30 minutes postoperatively by a 10 cm Visual Analogue Scale (VAS). Duration of analgesia in minute was assessed from onset of sensory block to first request for rescue analgesic when VAS≥4. There was statistically significant difference in duration of analgesia when rescue analgesic was given, among the study groups as 'p' value is <0.05. Patients in Group- D had significantly long duration before rescue analgesia was given than Group- B. The mean time duration before rescue analgesic is given was 215.15±6.274 minutes in bupivacaine group and 259.65 ± 8.223minutes in dexmedetomidine group, p value =0.001. Our findings were well supported by the study of Seema Shreepad Karhade et al [15] , in which the patients in the bupivacaine(0.5%) group requested rescue analgesia earlier than patients in the dexmedetomidine group as the average times to first request for rescue analgesia were 150.24 ± 24.42 and 320.62 ± 23.86 respectively.

Table – 11, show the comparison of sedation score between two groups which was assessed by Ramsay Sedation Score and it was measured at 5, 10, 15, 20, 25, 30, 45, 60 and 90 min from the administration of study drug. There was statistically significant difference in sedation score among the study groups as 'p' value is <0.05. This study corroborates with the study of Sukhminder Jit Singh Bajwa, Vikramjit Arora, Jasbir Kaur, Amarjit Singh, S. S. Parmar et al.[16] where they selected 50 patients of ASA grade I & II undergoing lower limb orthopaedic surgery who were randomized into two category-one group received 15 ml 0.75% Ropivacaine with Fentanyl and another group received 15 ml 0.75% Ropivacaine with 1 µg/kg Dexmedetomidine. They observed in their study as 38% and 42% of patients exhibited grade II and grade III sedation as compared to 16% and 2% of patients in the RF group, respectively. These sedation scores were highly significant on statistical comparison (P<0.001). Only 12% of the patients in the RD group had sedation scores of 1 as compared to 82% wide and awake patients in RF group which was a highly significant statistical entity (P<0.001).

Table–13, figure 13 shows comparison of SpO_2 between two groups with pulse oximeter. There was no statistically significant difference in mean SpO_2 among the study groups as 'p' value is >0.05 at every time of measurement. This study aso corroborates with the study of Sukhminder Jit Singh Bajwa, Vikramjit Arora, Jasbir Kaur, Amarjit Singh, S. S. Parmar et al.[16] where they found avoidance of respiratory depression in the patients who were administered dexmedetomidine was one of the most remarkable observations and the evidence is similar to the earlier studies where researchers have found complete absence of clinically detectable respiratory depression in the previous multiple human studies.[17,18,19]

Intraoperative and postoperative HR and MAP were monitored to evaluate hemodynamic stability. Table 14-15 and figure 14-15 show distribution of intraoperative and postoperative HR and MAP and their comparison between two study groups at various time points.

From Table 13 it was observed regarding the heart rates that there was no statistically significant difference between the patients of Group - B and Group – D as p>0.05. Bradycardia was treated with IV atropine 0.3-0.6 mg. Our finding also corroborates with the study of Sukhminder Jit Singh Bajwa, Vikramjit Arora, Jasbir Kaur, Amarjit Singh, S. S. Parmar et al.[16] where they also found there was no significant changes in heart rate in both groups.

But from Table 14, it was observed there was statistically significant difference in mean arterial pressure in 20 min, 30 min, 45 min, 180 min and 240 min (p value < 0.05) between the patients of Group B and Group D. Hypotension was treated with IV mephentermine 3-6 mg or phenylephrine 100µg and additional lactated Ringer's solution. MAP was slightly more in patients receiving dexmedetomidine than in the plain bupivacaine group. Though it had been postulated by Sukhminder Jit Singh Bajwa, Vikramjit Arora, Jasbir Kaur, Amarjit Singh, S. S. Parmar et al.[16] that increased incidence of hypotension following co-administration of dexmedetomidine and bupivacaine could be due to higher sensory level achieved. But as p-value was >0.05, so this is insignificant i.e, in both group MAP wasn't changed by a significant way. Our findings are also consistent with the author's finding as we did not encounter a significant increased incidence of hypotension in both of our groups though there were hypotension in each group patients. But the value wasn't significant.

Table 15 show the comparison of side effects between the study groups. Two patients in Group B and five patients in Group D had incidence of nausea and vomiting. Four patients in Group B complained of

pruritus, whereas, no patients in Group D complained of pruritus. Shivering was observed in four patients of Group B and six patients in group D. Only one patient of Group B presented with urinary retention where as no one in group D had urinary retention.

Hence, it was observed that 0.5 mcg/kg dexmedetomidine with 12 ml bupivacaine provided effective epidural anaesthesia than with same amount of bupivacaine only in terms of longer duration of sensory block and superior analgesia in elective open cholecystectomy. Patients receiving bupivacaine plus dexmedetomidine are more somnolent than the patient receiving bupivacaine alone without any episodes of respiratory depression throughout the surgery.

VI. Conclusion

The present study showed that thoracic epidural dexmedetomidine 0.5 µg/kg added to 12.0 ml of plain bupivacaine (0.5%) provided prolonged sensory block and longer duration of analgesia compared to 12.0 ml of plain bupivacaine (0.5%) in patients of elective open cholecystectomy. All patients were hemodynamically stable in both groups. Among the side effects, only increase level of sedation was observed in bupivacaine (0.5%) plus dexmedetomidine group than plain bupivacaine group. dexmedetomidine 0.5 µg/kg seems to be an effective alternative adjuvant to thoracic epidural bupivacaine in supra-umbilical surgeries like open cholecystectomy with an additional sedative effect and excellent quality of analgesia

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