



COMPARISON OF BUPIVACAINE HCL AND BUPIVACAINE HCL PLUS DEXMEDETOMIDINE HCL IN WOUND INFILTRATION FOR POST OPERATIVE ANALGESIA IN PATIENT UNDERGOING GYNAECOLOGICAL SURGERY.

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ABSTRACT

Background: Abdominal Laparotomy is a common procedure done for gynaecological malignancy. This study is aimed to determine efficacy of Bupivacaine HCL as analgesic in wound infiltration and effect of Dexmedetomidine as an adjuvant in prolongation of duration of analgesia with Bupivacaine HCL.

Method: In this prospective randomized double-blind study, patients undergoing abdominal laparotomy were randomly allocated into 2 groups.: Group B received 75 mg of Bupivacaine HCl (15 ml) and Group D received 75 mg of Bupivacaine HCl (15 ml) and 1mcg/kg of Dexmedetomidine made up to 30 ml solution with normal saline (NS), 15 ml given on each side of wound. Postoperative haemodynamic changes, visual analogue scale (VAS) pain scores at 0min,30min,1, 2, 4, 6, 8, 12 and 24 hours; rescue analgesia, total amount of analgesia consumed and side effects were recorded.

Result: Time to first analgesic consumption was significantly longer in group D(1067±460.56min) compared to group B (221±174.32min) (P<0.0001). The consumption of diclofenac rescue analgesia was significantly lower in group D than group B without significant side effects

Conclusion: We conclude that adding Dexmedetomidine as an adjuvant to bupivacaine prolongs the analgesic efficacy, decreases postoperative analgesic consumption.

KEYWORDS : Wound Infiltration, Bupivacaine HCL; Dexmedetomidine; Lower Abdominal Laparotomy, VAS SCORE.

INTRODUCTION

Abdominal Laparotomy is a common procedure done for gynaecology carcinomas. Patients suffer from severe postoperative pain which is usually intense during first 24hrs after surgery⁽¹⁾. Poorly controlled acute postoperative pain is associated with increased morbidity, functional and quality of life impairment, delayed recovery time, prolonged duration of opioid use, and prolonged hospital stay. Acute pain if not treated properly leads to the development of chronic pain⁽²⁾. Planning for proper postoperative pain management is an essential component of good anaesthetic practice since the consequences of untreated pain can be devastating. Wound site infiltration is an efficient method in acute post-operative pain management, but has a potential theoretical risk of wound site infection⁽³⁾. With local infiltration or infiltration in the pain sensitive planes, afferent impulses from the site of incision are reduced, and reduces the sensitization and consequent hyperalgesia⁽⁴⁾. It reduces the release of inflammatory mediators from neutrophils, reduce neutrophil adhesion, reduce free oxygen radical formation, and decrease oedema formation. Several clinical studies have reported wound infiltration with local anaesthetic drugs (lignocaine, bupivacaine, levobupivacaine, liposomal bupivacaine and ropivacaine) as safe and effective method for postoperative analgesia with minimal systemic side effects in various surgeries like abdominal, obstetrical and gynaecological, orthopaedic procedures and laparoscopic surgery. Single dose infiltration of a long-term local anaesthetic around the wound can provide effective analgesia^(5,6,7,8). The agent most widely used for this purpose is bupivacaine because it is long acting, effective local anaesthetic⁽⁷⁾. This is limited by the fact that duration of analgesia is provided only till the effects of local anaesthetics action lasts. The addition of various adjuvants such as clonidine⁽¹⁰⁾, opioids⁽¹¹⁾, ketorolac⁽¹²⁾ and dexmedetomidine⁽¹³⁻²³⁾ to local anaesthetics for wound infiltration has increased its duration of action. Various number of studies suggested addition of dexmedetomidine by various route peri- and postoperatively results in effective postoperative pain control. DEX is a strong and highly selective α_2 -adrenoceptor agonist. It could enhance the analgesic efficacy of local anaesthetics when added as an adjuvant for peripheral regional blocks^(24,25,26). The current study was designed to test the hypothesis that dexmedetomidine when added as an adjuvant to local anaesthetic for post-operative wound infiltration after abdominal laparotomy effectively reduces post operative analgesic consumption in first 24 hours of post operative period.

METHODS

After obtaining institutional ethical committee approval REG NO (IRC/2022/P-20) and having all patient's written informed valid consent for use of their anaesthesia related data for research purpose

this prospective, randomized, double blind study was conducted on ASA I---II patients, aged 18---65 years were included in the study and scheduled for gynaecological surgery in Gujarat Cancer and Research Institute from January 2021- September 2021. Patients were excluded if they had a history of allergy to bupivacaine and dexmedetomidine, were pregnant, had coagulation disease, Refusal by the patient, Renaud's disease, Psychiatric illness, Regular narcotic use, Serious cardiac or Pulmonary disease, unable to understand the scoring system for VAS. Prior to the procedure pre-anaesthetic evaluation was done and detailed history of cardiovascular system, respiratory system, central nervous system, drug therapy and drug allergy were taken. A thorough clinical examination of the patient was performed including general physical examination and systemic examination. Airway assessment was done by Mallam Patti grading to anticipate the possibility of difficult airway. Routine investigations like complete blood count, serum electrolytes, X-ray chest, renal and liver function test, 12 lead ECG, FBS, PPBS, PT, APTT, INR, serology, urine-routine and micro were done. To assess pain, visual analogue scale (VAS) (0-10 cm) was utilized and instructions were given for all patients in the context of pain assessment from 0 to 10, with 0 indicating no pain and 10 indicating the worst pain imaginable during pre-anaesthetic visit in the evening prior to surgery. Patients were kept NBM 6 hrs before the surgery and given Tab Lorazepam 1 mg (> 50 kg) or 0.5 mg (< 50 kg) at night prior to surgery. 60 Patients were randomized into two groups via computer generated method, Group B (n=30) and Group D (n=30). After the patient entering into the operation room and just before the induction of anaesthesia, the numbered envelope was opened and the card inside determined into which group the patient would be placed. All the people involved including the patient, the surgeon, the anaesthesiologist, were unaware of the study drugs or the patient group assignment.

- **GROUP B: [Bupivacaine group]- 30 ml 0.25% Of Bupivacaine HCL**
- **GROUP D: [Dexmedetomidine group]- 30 ml 0.25% Of Bupivacaine HCL + 1 µg/kg of Dexmedetomidine.**

Dose of dexmedetomidine was based on the previous ref study done by SINGH⁽²⁰⁾. Upon arrival in the operating room, standard ASA monitors like non-invasive blood pressure (NIBP), heart rate, electrocardiogram, (lead 2, lead 4) SpO2 monitoring and EtCO2 were attached and baseline vitals were recorded. Intravenous cannula 18 G was inserted in a peripheral vein and a Ringer lactate solution was started. All patients were premedicated with Inj. Fentanyl citrate (2mcg/kg) and midazolam (0.25 mg.kg-1). After 3mins of preoxygenation with 100% oxygen, anaesthesia was induced with Inj.

Thiopentone sodium (5mg/kg) i.v and Inj. Atracurium (0.5mg/kg) i.v to facilitate endotracheal intubation with cuffed endotracheal tube. After checking bilateral equal air entry, tube was fixed. Nasogastric tube of appropriate size was inserted. Intraoperative anaesthesia was maintained with 50% N₂O:50% O₂ plus Sevoflurane and intermittent Inj. Atracurium 0.1mg/kg. Volume-controlled positive pressure ventilation was adjusted at a tidal volume of 6 ml/kg and respiratory rate to keep ET_{CO}2 at 35-45 mmHg with continuous monitoring which include non-invasive blood pressure at 5-minute interval, spo₂, heart rate. Patients were monitored using Drager infinity vista XL Model. Heart rate (HR) and mean arterial pressure (MAP) was maintained within 20% of the pre-operative value. Hypotension (MAP <20% of the baseline or <60 mmHg) was treated with infusion of normal saline and if required injection mephentermine 3-6 mg boluses IV. Bradycardia (HR <40 beats/min) was treated with IV atropine 40 µg/kg bolus. Intraoperative injection Paracetamol was given I.V. according to dosage 15 mg/kg in every patient in both groups. At the end of surgical procedure and after haemostasis was achieved, local infiltration with the study drug was given into the MUSCULO FASCIAL +SUBDERMAL planes, 15 ml of group drug either side by the operating surgeon. Study drugs were prepared by an anaesthesiologist not involved in the study. Anaesthesiologist who observed the patient and surgeon were unaware of the study group until the end of the study. The wound was closed in layers and the dressing were applied and neuromuscular blockade was reversed with Inj. Neostigmine sulphate (0.05mg/kg) and Inj. Glycopyrrolate (0.01mg/kg). Patients were extubated when standard criteria for extubation achieved. After the operation, patients were transferred to postoperative care unit and given supplemental oxygen for 2hrs at 2 L/min. Postoperative pain was assessed by anaesthetist who is not aware of patients group. Assessment done first at 0 hr, i.e., after extubation, when the patient was able to follow commands and then at 30min, 1, 2, 4, 6, 8, 12 and 24hrs. The duration of analgesia was considered from the time the study drugs were infiltrated to the first demand for analgesia or VAS score was ≥4. Rescue analgesia was carried out with Inj. Diclofenac 75mg I.M. repeat dose of rescue analgesia given as needed. Our primary objectives are to look for VAS score, total rescue analgesia requirement and Ramsay sedation score in 24 hrs.

Secondary objectives are to look for HR, SBP, and SpO₂, respiratory rate, Side effects such as nausea, vomiting, hypotension. Nausea or vomiting treated with inj. ondansetron 0.15 mg /kg.

The sedation score on a 6-point Ramsey sedation scale was used.

- 1 Patient awake, anxious, agitated or restless
- 2 Patient awake, cooperative, oriented and tranquil
- 3 Patient Drowsy, with response to commands
- 4 Patient asleep, brisk response to glabella tap or loud auditory stimulus
- 5 Patient asleep, sluggish response to stimulus
- 6 Patient has no response to firm nail-bed pressure or other noxious stimuli.

When the patient had a sedation score of 4 and above, supplement oxygen 6 L/min was administered and alert was given to the anaesthesiologist.

STATISTICAL ANALYSIS:

Before the study, the number of patients required in each group was determined via previous study⁽²⁰⁾. The calculation of sample size revealed that at least 27 patients in each group would be required for appropriate study with level of significance - 0.05 and a power of 0.8. So, 60 patients were taken in case of any exclusion. Data are presented as mean with standard deviation or median IQR with range or 95% confidence interval (CI) as appropriate. Statistical significance for analgesic requirement was determined by one-way analysis of variance (ANOVA). P <0.05 was considered statistically significant. The time to first dose of rescue analgesic, i.e., the duration of analgesia, was analysed using the Mann-Whitney U test. Statistical analysis done by Statistical Package for Social Sciences Version 15.0 software (Chicago, USA). Data in the text and table are statistically described in terms of mean± standard deviation, or frequencies (number of cases) and percentages when appropriate. Un-paired t-test was used to compare two population means. Microsoft word Excel has been used to generate graphs and tables.

RESULT

The present study includes 60 {Table-1} adult patients aged 18-65 years belonging to ASA grade I and II undergoing gynaecological surgery. both the groups were comparable with respect to age, weight and mean duration of surgery with no statistical difference between them (p.>.0.05). There is no significant changes in heart rate in both the groups during 30 min, 2 hr, 4hrs, 6hrs and 24hrs. But at 1sthr (P=0.0003) , 8thhr (P=0.0060) and 12 hrs (P=0.0149) significant increase in heart rate were observed in group B compared to group D. There is no significant changes in SBP in both the group upto 30 minutes. But at 30th min (P=0.0463) significant increase in SBP in group B compared to group D. At 1st, 4th and 12thhr SBP was raised in group D compared to group B with nonsignificant P value. There is no significant change in spo₂ in both group at any period of time. {Graph - 1} There is no significant changes in Respiratory Rate in both the group (P value >0.3). There is no significant changes in spo₂ in both the group. During 0min and 30min there was nonsignificant difference in VAS score. VAS was higher at 1st and 2nd hour in group B which is statistically significant (P<0.05) than group D, because of onset of pain. Group D patients had later onset of pain at 4th and 6th hour with statistically non-significant VAS score difference, and again became statistically significant at 8th,12th and 24th hours. (p<0.05){Table - 2,Graph-2} .RSS was higher at 2nd hour in group D which is statistically significant (P<0.05) than group B. In group B at 6th hr RSS score was high compared to group D. which is statistically significant (P<0.05).{Graph-3} .Total Diclofenac consumption in the group D was found to be significantly lower than the group B (P <0.05). All patients in Group B (100%) required rescue analgesia, while only 13 patients in Group D(43.3%) required it and it was statistically significant (P <0.002).{Table-4,Graph-5s} incidence of side effects like nausea and vomiting was 13.3% (4 pts) in group D and 20%(6 pts) in group B. There was no report of other adverse effects like bradycardia, hypotension, pruritis and respiratory depression. Nausea and vomiting treated with Inj. Ondansetron 4mg iv.

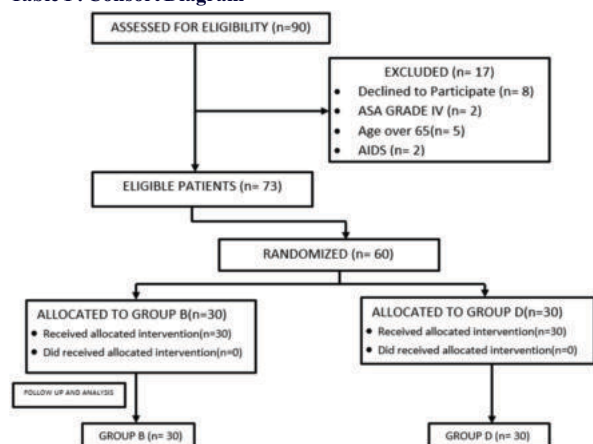
DISCUSSION

Pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage". Pain after surgery is inevitable and the treatment of pain is central to the case of postoperative patients⁽²⁷⁾. The concept of an acute pain service (APS) as an anaesthesiology-based postoperative pain management service was introduced by Ready and colleagues in 1988⁽²⁸⁾. Abdominal Laparotomy is a surgical procedure is associated with significant acute severe postoperative pain which is mediated by nociceptors and mechanoreceptors activation in the peritoneum, nerve endings, muscles and fascial sheaths. Innervation is by the posterior rami of the spinal nerve roots, which are linked to the autonomic nervous system. Inflammation of these structures or mechanical compression of the nerves in this area results in pain^(29,30). There are numerous clinical studies have confirmed wound infiltration is effective and safest technique for postoperative analgesia after surgical procedures performed under general or regional anaesthesia. In the less extensive surgical procedures like open inguinal hernia repair⁽³¹⁾ or breast cancer operations, it reduces consumption of opioid⁽³²⁾ and is sufficient as single effective method of postoperative analgesia. It is also used as effective method in the moderate invasive general surgery, gynaecological surgery, urologic surgery, caesarean section, orthopaedic procedures, lumbar spine surgery, after hip and knee replacement, shoulder surgery and in cardiothoracic surgical procedures. Wound infiltration with local anaesthetics with or without adjuvant drugs has been studied to produce significant postoperative analgesia. **S Singh et al**⁽²⁰⁾ in their study found that local wound infiltration with bupivacaine and Dexmedetomidine had significant analgesia compared to Bupivacaine alone group. In their study post operative rescue analgesia requirement was significantly less in dexmedetomidine group compared to bupivacaine alone group with p value < 0.003, statistically significant. The concentration 0.25% was chosen because it has been found to be effective in blocking sensory nerves when used for postoperative analgesia. This has been proven by various studies indicating that 0.25% have more sensory blockade than motor blockade^(9,10). And another important consideration is the volume and concentration of local anaesthetic delivered to the surgical site, so we infiltrated the surgical wound with 30ml of study drug, 15 ml on each side. The analgesic effects and uses of dexmedetomidine in regional anaesthesia was studied by **Neerja Bharti et al**⁽²⁴⁾ they found that the duration of sensory, as well as motor, block was significantly prolonged in the dexmedetomidine group, compared with local anaesthetic agent alone (P < 0.0001). and **Abdulla FW et al**⁽²⁵⁾ concluded that the addition of

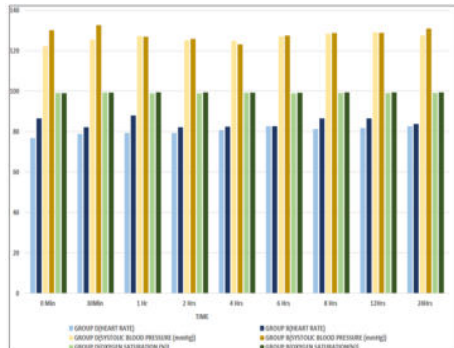
dexmedetomidine to bupivacaine for nerve block prolongs the duration of analgesia and reduces postoperative pain. In their study the duration of analgesia was 10.9 h (10.0 to 11.8 h) and 9.8 h (9.0 to 10.6 h) for the DexP group (dexmedetomidine perineurally) and DexIV group (dexmedetomidine I.V), respectively, compared with 6.7 h (5.6 to 7.8) for the control group (local anaesthesia alone) (P < 0.001). So we added dexmedetomidine 1mcg/kg to study their efficacy and duration of analgesia compared to 0.25% bupivacaine alone. In our study, VAS score was comparable in both groups and No significant difference up to 1st hour, but significant rise in VAS score seen from 1st to 4th hours in Group B compared to Group D. Then it became Nonsignificant due to early rescue analgesia in Group B, and again became significant from 8thhrs up to 24 hr. The time for first rescue analgesia in group D was 1067±460.56mins and group B was 221±174.32 which was statistically significant(p<0.0001). Total amount of rescue analgesia (Inj. Diclofenac) was found to be statistically significantly higher in group B (162.5±44.4 mg) compared to group D (42.5±54.59 mg) (P <0.05). Total Number of Patients required Rescue Analgesia is 13 in group D (43.3%) compared with 30 in Group B (100%) (P<0.002). In our study Ramsey Sedation Score is significantly high in Group D during second Hr maybe due to systemic effect of Dexmedetomidine⁽²⁷⁾. then remains non-significant 24 Hours. Limitations of our study was that we did not measure the data after 24hrs of surgery and we could not observe postoperative wound infection. Only 1 concentration of Dexmedetomidine and Bupivacaine evaluated in our study, additional studies are needed to investigate more concentrations. Plasma concentration Dexmedetomidine was not detected in our study, so more study with plasma concentration needed to confirm either it is systemic effect or not.

GRAPHS AND TABLES

Table 1 : Consort Diagram



GRAPH - 1.



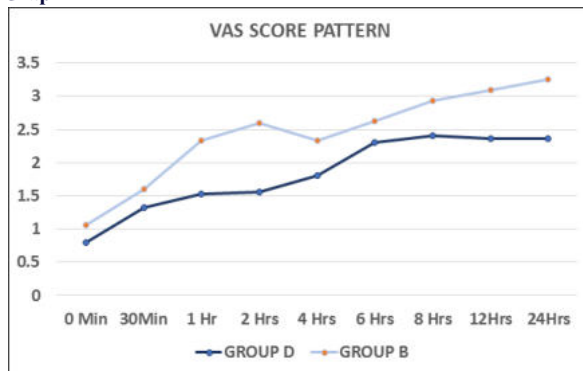
Graph 1 - Comparison Between Group B And Group D For Heart Rate, Systolic Blood Pressure, And Oxygen Saturation At Different Time Interval.

Table 2: Comparison of VAS SCORE At Different Time Intervals:

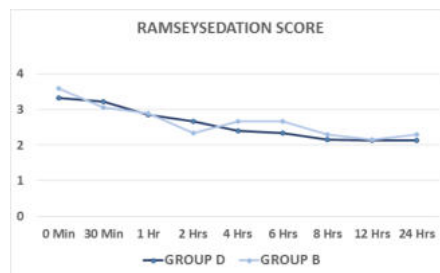
TIME	VAS SCORE		
	GROUP D	GROUP B	P VALUE
0 Min	0.80±0.84	1.06±1.14	0.3188
30Min	1.33±1.00	1.60±1.30	0.3710
1 Hr	1.53±0.97	2.33±1.45	0.0148
2 Hrs	1.56±1.01	2.6±1.22	0.0007

4 Hrs	1.8±0.85	2.33±1.44	0.0879
6 Hrs	2.3±0.92	2.63±1.27	0.2538
8 Hrs	2.40±0.96	2.93±0.90	0.0314
12Hrs	2.36±0.89	3.10±0.88	0.0001
24Hrs	2.36±1.09	3.26±0.98	0.0014

Graph - 2



Graph 2: - VAS SCORE Pattern Comparision Between Group B And Group D.

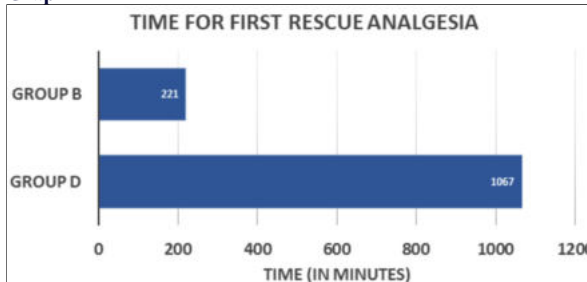


Graph 3: - Ramsey sedation Score

Table 3: Time For First Rescue Analgesia

TIME OF FIRST RESCUE ANALGESIA IN BOTH GROUPS (min)		
GROUP D	GROUP B	P VALUE
1067.00±460.56	221±174.32	0.0001

Graph 4

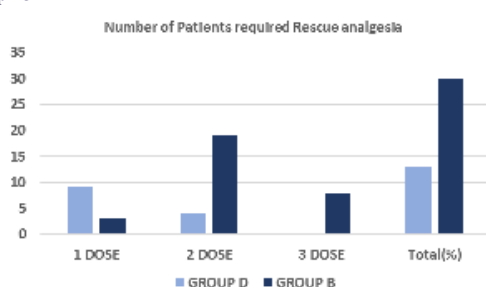


Graph 4: - Comparison of First Rescue Analgesia In Both Groups

Table 4 : Number Of Patients Required Rescue Analgesia

Group	1 dose	2 dose	3 dose	Total(%)	P<0.001
D	9	4	0	13(43.3%)	
B	3	19	8	30(100%)	

Graph 5



CONCLUSION

From this study we concluded that Wound infiltration with long-acting bupivacaine is effective for postoperative pain relief after Abdominal surgery. Adding Dexmedetomidines an adjuvant to bupivacaine prolongs the analgesic efficacy, decreases post operative analgesic consumption and postoperative pain score.

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Nil.

Conflicts of interest:

There are no conflicts of interest.

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