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A Prospective, Randomized, Double-Blinded, Comparative Evaluation Of Ropivacaine, And Ropivacaine With Dexamethasone In USG-Guided Transverse Abdominis Plane Block For Laparoscopic Cholecystectomy.

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ABSTRACT

Delayed post-operative mobilization and risk of thromboembolism due to pain remains a concern after laparoscopic cholecystectomy for which transverse abdominis plane (TAP) block is increasingly used. We did this study to evaluate the efficacy of adding 8 mg dexamethasone as an adjuvant to 0.25% ropivacaine in USG-guided TAP block. One hundred patients aged 18 to 60 years, weighing 40 to 80 kg, of either sex, ASA grade 1 and 2, posted for elective laparoscopic cholecystectomy were divided into two equal groups. Group R received 20ml 0.25% ropivacaine plus 2ml NS and RD received 20ml 0.25% ropivacaine with 2ml (8 mg) dexamethasone. Pain was measured by VAS at rest after shifting to PACU at 0, 1, 2, 4, 6, 8, 12, 16 and 24 hours. Whenever VAS >4, paracetamol 1g was administered intravenously (IV) as rescue analgesic and if no reduction in VAS to less than 4, tramadol 1mg/kg IV was given as additional analgesic. No significant difference was seen in VAS at 1 hour. In group R, VAS at 2, 6, 8, and 12 hours was higher (p value <0.05) but was lower at 16 hours and 24 hours than in RD because of rescue analgesia given at 12 hours. No patient was given rescue analgesia at 1, 2 and 4 hours, and requirement at 6 hours was comparable between both groups (p value=0.056). Proportion of patients given PCM as rescue analgesia at 8 and 12 hours was significantly higher in group R (p value <0.0001 respectively). Proportion of patients given rescue analgesia at 16 hours was significantly lower in group R (p value <0.0001). At 24 hours, proportion of patients to whom rescue was not given and tramadol was given, was significantly higher in group R (p value <0.0001). Distribution of total rescue dose was comparable between group R and RD (only PCM given: 92% vs 100% respectively, both PCM and tramadol given: 8% vs 0% respectively) (p value=0.117). Dexamethasone and ropivacaine in TAP block result in early and prolonged analgesia with decreased consumption of opioids after laparoscopic cholecystectomy.

Keywords: Ropivacaine, dexamethasone, transverse abdominis plane block, laparoscopic cholecystectomy

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INTRODUCTION

Cholecystectomy is the second most common surgery performed [1], while laparoscopic cholecystectomy has proven to be a revolutionary method for treating gall stone disease [2]. Laparoscopic cholecystectomy results in a smaller incision, reduced blood loss, reduced postoperative stay and pain, decreased risk of surgery and anaesthesia-related complications, which is reflected in patients' earlier return to routine life and work [3, 4]. This procedure has become new "gold standard" for management of cholelithiasis [5]. One of the major factors that determine the speed of recovery from anaesthesia is the choice of anaesthetic technique [6]. Despite the use of multimodal analgesia, pain remains a major concern after these surgeries [7]. Post-operative pain is a reason for delayed mobilisation of patient. This can increase the risk of venous thromboembolism [8]. Ultrasonography (USG)-guided transversus abdominis plane (TAP) block is a regional block technique used for abdominal surgeries. Ultrasound has improved the safety and success of the block [9]. In this block, plane between internal oblique and transversus abdominis muscle is located with USG and local anaesthetic drug is injected in it which blocks thoracolumbar nerves originating from T7 to L1 spinal roots. Since the pain from anterolateral abdominal wall is carried by fibres arising from the anterior primary rami of spinal nerves from T7 to L1, pain produced by most of the lower abdominal surgeries involves these dermatomes [9, 10].

Many techniques and adjuncts were utilized to prolong duration of analgesia produced by TAP block. These included placement of perineural catheters for continuous block and use of adjuncts such as clonidine, tramadol, epinephrine, and corticosteroids [11-13].

Combinations of dexamethasone and local anaesthetics have been studied in TAP block. Peripheral nerve blocks require a minimum concentration of local anaesthetics [14]. Due to enhanced sensory blockade and less toxic profile of ropivacaine compared to bupivacaine, 0.25% ropivacaine was chosen for this study. Pain scores with doses of local anaesthetics and dexamethasone used in previous studies have been quite varied [15-19]. Whether the difference in results was due to varying local anaesthetic concentration or use of dexamethasone was not evident. Hence, we decreased the local anaesthetic concentration and used 8 mg dexamethasone to assess the quality of TAP block and evaluated efficacy of 8 mg dexamethasone added to 0.25% ropivacaine as an adjuvant to TAP block in patients undergoing laparoscopic cholecystectomy.

Aims and objectives

Aim

To compare the efficacy of dexamethasone as an adjuvant to ropivacaine, with plain ropivacaine in USG-guided transversus abdominis plane (TAP) block for laparoscopic cholecystectomy.

Objectives

- To compare the duration of analgesia produced by TAP block with plain ropivacaine, and ropivacaine with dexamethasone.
- To compare the pain scores following (TAP) block with ropivacaine and ropivacaine with dexamethasone.
- To compare the time of first post-procedure rescue analgesic required with ropivacaine and ropivacaine with dexamethasone.
- To estimate and compare the total rescue analgesic dose required following transversus abdominis plane (TAP) block with ropivacaine and ropivacaine with dexamethasone.

MATERIALS AND METHODS

After approval from Institutional Ethics Committee, we conducted this prospective, randomized study in one hundred patients of ASA grades I & II, aged between 18 and 60 years, and weighing from 40 to 80 kg, undergoing elective laparoscopic cholecystectomy.

Patients were informed about the study, and their consent obtained. Using computerized randomization, all patients were allocated to either of two groups of 50 each – group R, that was to receive only ropivacaine and group RD, that was to receive ropivacaine with dexamethasone.

Detailed history of each patient was obtained and systemic examination done. As per institutional protocol, investigations done prior to laparoscopic cholecystectomy include the following: haemogram, coagulation profile, ECG, 2D ECHO, X- ray chest and USG abdomen.

Patients were kept fasting for a duration of 8 hours before the surgery.

On the day of surgery, NBM status, consent and investigations were rechecked.

On arrival in operation theatre, Ringer's lactate was infused at the rate of 4ml/kg/hour intravenously, with continuous monitoring of ECG, SPO2, PR, NIBP, and oxygen was administered by Hudson face mask at rate of 4 L/min. Paracetamol (15–20 mg/kg), followed by glycopyrrolate 0.004 mg/kg, midazolam 0.03 mg/kg, and fentanyl 2 mcg/kg were administered intravenously followed by 2.0 mg/kg of propofol, slowly over 10 minutes and injection vecuronium 0.08 mg/kg. Trachea was intubated and ventilator setting was done according to the body weight of the patient to maintain $EtCO_2$ between 33 and 38 mmHg.

After induction, USG-guided transversus abdominis plane block was performed under all aseptic precautions under ultrasound guidance using a linear array transducer of 6-14 MHz frequency by the in-plane technique. Drug was prepared by another anaesthesiologist who was blinded to the patient group. In supine position, the anterolateral abdominal wall on both sides was prepared with antiseptic solution and draped. The sterilized scanning probe was placed transversely over the lateral abdominal wall between the iliac crest and the costal margin over the midaxillary line to identify the structures from superficial to deep as skin, subcutaneous tissue, fat, external oblique, internal oblique and transverse abdominis muscles, peritoneal cavity, and bowel loops.

A 23G Quincke spinal needle was advanced using an in-plane approach, into the plane between the internal oblique and transverse abdominis muscle, and 2 mL of saline injected to 'open' the fascial plane.

Then 20 ml of 0.25% ropivacaine plus 8 mg in 2 ml of dexamethasone was given to Group RD patients (n = 50) each side, and 20 ml of 0.25% ropivacaine plus 2 ml normal saline was given to Group R patients (n = 50) on each side.

The block was performed by seniormost anaesthesiologist in the operation theatre, and the drug was injected by a post graduate trainee assisting the former.

After surgery, all patients were reversed with neostigmine-glycopyrrolate, and extubated and observed in operation theatre for 10 minutes and then transferred to Post-anaesthesia Care Unit (PACU).

In the PACU, the observations were recorded by another Anaesthesiology trainee, who was blinded to drugs used for the block.

Pain at rest in PACU was measured by VAS (0 = No pain, 10 = intolerable pain) just after shifting to PACU (0 hours) and at interval of 1, 2, 4, 6, 8, 12, 16 and 24 postoperative hours. Whenever VAS >4 on rest, paracetamol 1g IV was given as rescue analgesic and if there was no reduction in VAS to less than 4, tramadol 1mg/kg IV was given as additional analgesic. Ondansetron 4 mg intramuscularly was administered in case of nausea or vomiting. Any other side effects were also noted.

Statistical analysis

The presentation of categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as mean ± SD and as median with 25th and 75th percentiles (interquartile range). The data normality was checked by using Kolmogorov-Smirnov test. The cases in which data was not normal, we used non-parametric tests. The following statistical tests were applied for results:

- The comparison of variables which were quantitative and not normally distributed in nature were analysed using Mann-Whitney Test (for two groups) and independent t-test was used for comparison of normally distributed data between two groups.

- The comparison of variables which were qualitative in nature was done with using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

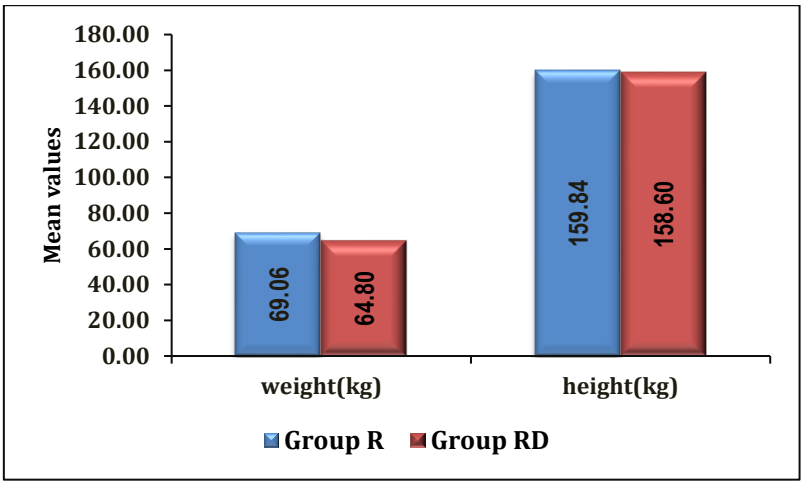
Data entry was done in Microsoft Excel and final analysis was done with use of Statistical Package for Social Sciences (SPSS) software (IBM, Chicago, USA, ver 21.0).

A *p* value of less than 0.05 was considered statistically significant.

RESULTS

Distribution of age, gender and ASA grade was comparable between group R and RD. Significant difference was seen in weight between group R and RD (*p* value <.05) Mean ± SD of weight (kg) in group R was 69.06 ± 9.24 which was significantly higher as compared to group RD 64.8 ± 10.42(*p* value=0.033). No significant difference was seen in height between group R and RD.

Figure 1: Comparison of anthropometric parameters between group R and RD.



No significant difference was seen in VAS score at 1 hour (*p* value=1), at 4 hours (*p* value=0.157) between group R and RD. Median (25th-75th percentile) of VAS score at 1 hour, at 4 hours in group R was 0(0-0), 1(1-1) respectively and in group RD was 0(0-0), 1(1-1) respectively with no significant difference between them.

Significant difference was seen in VAS score at 2 hours, at 6 hours, at 8 hours, at 12 hours, at 16 hours, at 24 hours between group R and RD (*p* value <0.05). Median (25th-75th percentile) of VAS score at 2 hours, at 6 hours, at 8 hours, at 12 hours in group R was 0(0-1), 2(1-3), 3(2-4.75), 3(2-5) respectively which was significantly higher as compared to group RD (0(0-0) (*p* value=0.014), 1(1-2) (*p* value<.0001), 2(2-2) (*p* value<.0001), 3(2-3)) (*p* value=0.002)) respectively.

VAS score at 16 hours, at 24 hours in group RD was significantly higher as compared to group R (*p* value=0.003, *p* value<.0001) respectively because till 12 hours rescue analgesia was not given to patients in group RD and on the contrary, majority of patients in group R were given rescue analgesia up to 12 hours due to high VAS score so the score decreased at 16 and 24 hours in group R as compared to group RD.

Table 1: Comparison of VAS score between group R and RD.

VAS score	Group R(n=50)	Group RD(n=50)	Total	*p* value
At 1 hour				
Mean ± SD	0 ± 0	0 ± 0	0 ± 0	1†
Median (25th-75th percentile)	0(0-0)	0(0-0)	0(0-0)	
Range	0-0	0-0	0-0	

At 2 hours				
Mean ± SD	0.42 ± 0.54	0.18 ± 0.39	0.3 ± 0.48	0.014†
Median (25th-75th percentile)	0(0-1)	0(0-0)	0(0-1)	
Range	0-2	0-1	0-2	
At 4 hours				
Mean ± SD	1.14 ± 0.57	1.02 ± 0.14	1.08 ± 0.42	0.157†
Median (25th-75th percentile)	1(1-1)	1(1-1)	1(1-1)	
Range	0-3	1-2	0-3	
At 6 hours				
Mean ± SD	2.22 ± 1.25	1.34 ± 0.48	1.78 ± 1.04	<.0001†
Median (25th-75th percentile)	2(1-3)	1(1-2)	2(1-2)	
Range	1-6	1-2	1-6	
At 8 hours				
Mean ± SD	3.64 ± 1.52	2.1 ± 0.36	2.87 ± 1.35	<.0001†
Median (25th-75th percentile)	3(2-4.75)	2(2-2)	2(2-3)	
Range	2-7	1-3	1-7	
At 12 hours				
Mean ± SD	3.6 ± 1.63	2.58 ± 0.61	3.09 ± 1.33	0.002†
Median (25th-75th percentile)	3(2-5)	3(2-3)	3(2-3)	
Range	2-7	2-4	2-7	
At 16 hours				
Mean ± SD	2.72 ± 0.83	3.36 ± 1.06	3.04 ± 1	0.003†
Median (25th-75th percentile)	3(2-3)	3(2-4)	3(2-4)	
Range	1-5	2-5	1-5	
At 24 hours				
Mean ± SD	2.12 ± 0.8	3.4 ± 1.03	2.76 ± 1.12	<.0001†
Median (25th-75th percentile)	2(2-2.75)	3(3-4)	3(2-3.25)	
Range	1-4	2-5	1-5	

† Mann Whitney test
Mean ± SD of duration of analgesia (in hours) in group RD was significantly higher as compared to group R (*p* value <.0001)

Table 2: Comparison of duration of analgesia (in hours) between group R and RD.

Duration of Analgesia (in hours)	Group R(n=50)	Group RD(n=50)	Total	*p* value
Mean ± SD	9.8 ± 2.69	19.3 ± 3.54	14.55 ± 5.71	<.0001*
Median (25th-75th percentile)	8(8-12)	18(16-24)	16(8-18)	
Range	6-16	16-24	6-24	

* Independent t test

None of the patients had to be given rescue analgesia at 1, 2 hours and 4 hours. Distribution of rescue analgesia at 6 hours was comparable between group R and RD (*p* value=0.056). Proportion of patients given PCM as rescue analgesia at 8 hours was significantly higher in group R as compared to group RD (*p* value <0.0001). Proportion of patients given rescue analgesia at 12 hours was significantly higher in group R as compared to group (*p* value <0.0001).

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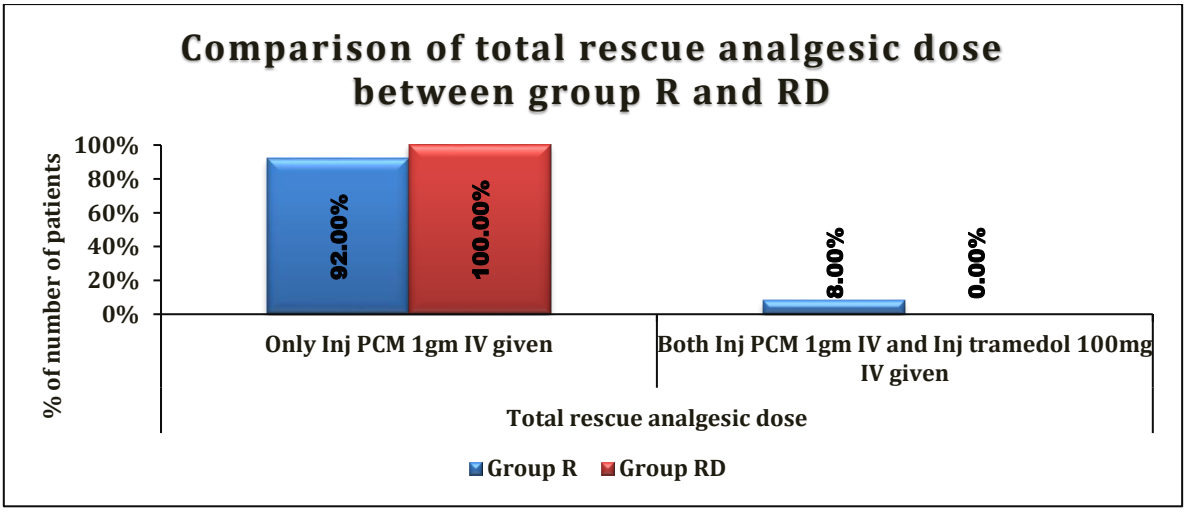
Proportion of patients with rescue analgesia at 16 hours was significantly lower in group R as compared to group RD (*p* value <0.0001). At 24 hours, proportion of patients to whom rescue analgesia was not given and to whom tramadol was given, was significantly higher in group R as compared to group RD. (*p* value <0.0001). At 24 hours, proportion of patients to whom rescue analgesia with PCM was given, was significantly lower in group R as compared to group RD (*p* value <0.0001).

Table 3: Comparison of rescue analgesia between group R and RD.

Rescue analgesia	Group R(n=50)	Group RD(n=50)	Total	*p* value
At 1 hour				
Not given	50 (100%)	50 (100%)	100 (100%)	-
At 2 hours				
Not given	50 (100%)	50 (100%)	100 (100%)	-
At 4 hours				
Not given	50 (100%)	50 (100%)	100 (100%)	-
At 6 hours				
Not given	45 (90%)	50 (100%)	95 (95%)	0.056‡
IV PCM 1g given	5 (10%)	0 (0%)	5 (5%)	
At 8 hours				
Not given	27 (54%)	50 (100%)	77 (77%)	<.0001‡
IV PCM 1g given	23 (46%)	0 (0%)	23 (23%)	
At 12 hours				
Not given	31 (62%)	50 (100%)	81 (81%)	<.0001‡
IV PCM 1g given	19 (38%)	0 (0%)	19 (19%)	
At 16 hours				
Not given	47 (94%)	22 (44%)	69 (69%)	<.0001‡
IV PCM 1g given	3 (6%)	28 (56%)	31 (31%)	
At 24 hours				
Not given	46 (92%)	28 (56%)	74 (74%)	<.0001‡
IV PCM 1g given	0 (0%)	22 (44%)	22 (22%)	
Inj tramadol 100mg IV given	4 (8%)	0 (0%)	4 (4%)	

‡ Fisher's exact test

Distribution of total rescue analgesic dose was comparable between group R and RD. (Only PCM given: 92% vs 100% respectively, both PCM and tramadol given: 8% vs 0% respectively) (*p* value=0.117).
Figure 2: Comparison of total rescue analgesic dose between group R and RD.



DISCUSSION

In our study, significant difference was seen in weight between group R and RD. Mean ± SD of weight (kg) in group R was 69.06 ± 9.24 which was significantly higher as compared to group RD. In study by Deshpande et al [15], mean weight(kg) in R group was 63.8 ± 10.1 and in RD group it was 66.5 ± 12.1. This value is similar to outcome in our study.

No significant difference was seen in VAS score at 1 hour and 4 hours between group R and RD. Significant difference was seen in VAS score at 2 hours, 6 hours, 8 hours, 12 hours, 16 hours, 24 hours between group R and RD. VAS score at 16 and 24 hours in group RD was significantly higher as compared to group R respectively because till 12 hours rescue analgesia was not given to patients in group RD and on the contrary, majority of patients in group R were given rescue analgesia by 12 hours due to high VAS score, so VAS decreased at 16 and 24 hours in group R.

Study done by Gnanasekar et al [20], shows similar results with time to first analgesic consumption and total morphine consumption, whereas pain scores were significantly lower in Group A, only till the 8th postoperative hour probably because of surgeries involving multiple specialties, leading to differences in visceral pain perception. They found a significant decrease in pain scores in saline group from the 10th to 12th postoperative hours probably due to accumulated morphine consumed, compared to dexamethasone group. The pain scores were comparable between the groups from 16th postoperative hour. Deshpande et al [15] in their randomized double-blinded study have shown that ropivacaine 0.5% with 4 mg dexamethasone in TAP block produced significant reduction in pain scores from 4th to 12th postoperative hours with significant increase in time to first analgesic demand (13.2 ± 7.6 vs. 7.1 ± 4.6 H, $P < 0.001$) in abdominal hysterectomies done under subarachnoid block.

Sharma et al [16] also found similar results with 8 mg dexamethasone added to 0.5% ropivacaine in TAP block for inguinal hernia surgeries done under spinal anaesthesia. Since the above studies were done under subarachnoid block, early postoperative pain assessment could be misleading.

Comparison of rescue analgesia between group R and RD

No patient had to be given rescue analgesia at 1, 2 and 4 hours. Distribution of rescue analgesia at 6 hours was comparable between group R and RD (not given: 90% vs 100% respectively, PCM given: 10% vs 0% respectively) (p value=0.056). Proportion of patients given PCM as rescue analgesic at 8 hours was significantly higher in group R as compared to group RD (46% vs 0% respectively) (p value <0.0001). Proportion of patients given PCM as rescue analgesic at 12 hours was significantly higher in group R as compared to group RD (38% vs 0% respectively) (p value <0.0001).

Proportion of patients given PCM as rescue analgesic at 16 hours was significantly lower in group R as compared to group RD (6% vs 56% respectively) (p value <0.0001). Proportion of patients given tramadol as rescue analgesia at 24 hours, was significantly higher in group R as compared to group RD (not given: 92% vs 56% respectively, and tramadol given: 8% vs 0% respectively). Proportion of patients given PCM as rescue analgesia at 24 hours was significantly lower in group R as compared to group RD. (PCM given: 0% vs 44% respectively) (p value <0.0001).

Ammar et al[18] demonstrated in their study, that addition of 8 mg dexamethasone as an adjunct to 20 ml 0.25% bupivacaine significantly prolongs the duration of analgesia of TAP block where the time to first request of analgesic was 459.8 ± 75.3 min.

Study done by Gnanasekar et al [20], shows similar results with 8 mg dexamethasone added to 0.25% ropivacaine in terms of pain scores, but the time to the first analgesic request was 525.85 ± 81.3 min which could be explained by the enhanced sensory blockade of ropivacaine.

Abdalla et al [19] and Kartalov et al [13] in their prospective controlled trials have shown significant prolongation of time to first additional analgesic requirement and reduction in total morphine consumption with significant reduction in pain scores till 24 h after radical cystectomies and inguinal hernia surgeries, respectively.

Comparison of duration of Analgesia (in hours) between group R and RD

In our study, mean ± SD of duration of analgesia (in hours) in group RD was 19.3 ± 3.54 which was significantly higher as compared to group R (9.8 ± 2.69) (p value <.0001).

Ropivacaine is a safe amide local anaesthetic when used even at 0.25% in TAP block produced effective analgesia for abdominal surgeries as evidenced by the study conducted by Pai *et al*[14], which showed that ropivacaine 0.2% produces similar analgesia compared to 0.5% in TAP block for caesarean section surgery done under general anaesthesia.

Comparison of total rescue analgesic dose between group R and RD

In our study, distribution of total rescue analgesic dose was comparable between group R and RD. (Only PCM given: 92% vs 100% respectively, Both PCM and tramadol IV given: 8% vs 0% respectively) (p value=0.117).

Deshpande et al [20] in their randomized double-blinded study showed that mean ± SD of total tramadol dose(mg) requirement in first 24 hours was 94.0 ± 35 in R group and in RD group it was 50.2 ± 34.

Various animal models have postulated the mechanism of action of dexamethasone. Barnes et al [21] documented the anti-inflammatory effects of glucocorticoids. Analgesia due to systemic absorption of peripherally-injected dexamethasone-bupivacaine microcapsules in intercostal nerve blocks has also been documented in healthy volunteers.

Devor et al [22] reported the prevention of ectopic neuronal discharge when freshly cut nerve endings were treated with corticosteroids in experimental neuromas.

Study done by Gnanasekar et al [20] evaluated the quality of TAP block with dexamethasone as an adjuvant for surgeries done under general anaesthesia in multiple specialties. They postulated that lower abdominal surgeries in multiple specialties share the same somatic pain perception pathways, and TAP block offers equipotent postoperative analgesia after these surgeries. With the added advantage of dexamethasone, the quality of analgesia proved to be superior with no complications.

CONCLUSION

Addition of dexamethasone to ropivacaine for TAP block results in early, prolonged, and safe analgesia with decreased consumption of opioids and overall patient satisfaction in laparoscopic cholecystectomy. Dexamethasone 8 mg, with 0.25% ropivacaine may be used routinely in TAP block for laparoscopic cholecystectomy surgery for better analgesic efficacy with no complications.

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