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Original Research Article

Impact of post-operative analgesia with intraperitoneal irrigation of high volume low concentration bupivacaine plus hydrocortisone vs. bupivacaine alone in patients undergoing elective laparoscopic cholecystectomy

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Abstract

Background: Post-operative pain is a common complaint after laparoscopic cholecystectomy. The use of intraperitoneal local anaesthetic agents during laparoscopic cholecystestectomy have known to significantly alleviate this pain and reduce time to recovery. We aim to compare the use of Bupivacaine in combination with Hydrocortisone when administered in high volume low concentration solution, intraoperatively as intraperitoneal irrigation vs Bupivacaine alone, in patients undergoing elective laparoscopic cholecystectomy.
Methods: This is a prospective, double-blinded, randomised comparative study in which 80 patients were randomly allocated into two groups-Group A in whom 20 ml of 0.5% Bupivacaine in 480 ml of normal saline was used vs Group B in whom 20 ml of 0.5% Bupivacaine plus 200 mg of Hydrocortisone in 480 ml of normal saline were instilled intraperitoneally during laparoscopic cholecystectomy and their parameters such as VAS score, shoulder pain, occurrence of post-operative vomiting, time to first rescue analgesic, total rescue analgesic requirement in 24hrs, and time to ambulation were compared.
Results: The two groups were comparable in VAS score, time to first rescue analgesic, total rescue analgesic requirement in 24hrs, and time to ambulation. The side effect profile of the two groups were also comparable with no significant difference between the groups.
Conclusions: Addition of Hydrocortisone to Bupivacaine for intraperitoneal instillation during laparoscopic cholecystectomy does not add any additional benefit in terms of duration of analgesia or time to ambulation, neither does it alter the incidence of adverse effects like vomiting or shoulder tip pain.

Keywords: Intraperitoneal bupivacaine, intraperitoneal hydrocortisone, post-operative analgesia, rescue analgesia, laparoscopic cholecystectomy

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Introduction

Laparoscopic cholecystectomy is the gold standard for the treatment of symptomatic cholelithiasis and chronic cholecystitis. Post-operative pain is a frequent complaint following the procedure. Along with other modalities, intraperitoneal instillation of local anaesthetic have been observed to be effective in providing post-operative analgesia. Intraperitoneal irrigation of Bupivacaine has been known to produce reliable post-operative analgesic effect. Hydrocortisone is also known to have similar effect [1].

Laparoscopic cholecystectomy has become a preferred modality of treatment in gallbladder surgeries. It is the gold standard for the treatment of symptomatic cholelithiasis and chronic cholecystitis [2]. Pain is a frequent complaint following laparoscopic cholecystectomy (LC). Pain in LC can be divided into different components such as parietal, visceral and shoulder pain. Visceral pain accounts for most of the discomfort experienced in the early postoperative period. Intensity quickly decreases after the first 24hrs post operatively. Shoulder tip pain predominates as visceral pain decreases during the later stage [1, 3]. The surgical stress and intraperitoneal CO_2 insufflation of abdomen during laparoscopy leading to rapid distension of the peritoneum, may result in tearing of blood vessels, traumatic traction of the nerves and release of inflammatory mediators causing pain [4]. Pneumoperitoneum with CO_2 is responsible for irritation of the phrenic nerve causing referred shoulder tip pain [3]. Numerous drugs and methods have been studied to effectively counter these adverse effects. Local anaesthetics have been successfully used to treat the postoperative pain in patients undergoing laparoscopic cholecystectomy [5]. Few studies have observed that intraperitoneal Bupivacaine does not reduce pain after laparoscopic cholecystectomy, but these studies used high-concentration low volume bupivacaine intraperitoneally [6, 7]. It has been seen that intraperitoneal irrigation of Bupivacaine in a low concentration and high volume intraoperatively is effective in prolonging the duration of analgesia and reduces postoperative rescue analgesic requirement in the initial 24hrs without significant postoperative adverse effects [8].

Glucocorticoids are known to have an anti-inflammatory action and play a role in providing postoperative analgesia [9, 10]. They reduce inflammation by inhibition of prostaglandin synthesis and are released endogenously during surgical stress [9]. Hydrocortisone is the main glucocorticoid secreted in humans whose levels can increase up to ten folds during severe stress. The intraperitoneal administration of Hydrocortisone has been observed to reduce pain and analgesic requirement after laparoscopic cholecystectomy [11]. The post-operative analgesia seen with the intraperitoneal use of Hydrocortisone is similar to that provided with intraperitoneal bupivacaine [12]. In our study, we have compared the efficacy of Bupivacaine in combination with Hydrocortisone when administered in high volume low concentration solution, intraoperatively as intraperitoneal irrigation vs Bupivacaine alone, in providing postoperative analgesia in patients undergoing elective laparoscopic cholecystectomy.

Objectives

To study the efficacy of hydrocortisone in providing post-operative analgesia as an adjuvant to bupivacaine when given as intraperitoneal irrigation during laparoscopic cholecystectomy and to compare:

1. Efficacy of Hydrocortisone as adjuvant to bupivacaine vs bupivacaine alone on duration of postoperative analgesia (DOA) with in patients undergoing elective laparoscopic cholecystectomy.
2. Total rescue analgesic requirement in 24 hrs post operatively.
3. Incidence of postoperative shoulder pain.
4. Time to ambulation.
5. Occurrence of vomiting postoperatively.

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Methodology

This study was conducted on patients undergoing elective laparoscopic cholecystectomy in our hospital. This is a prospective, double-blinded, randomised comparative study done in the months of August and September 2022. The Inclusion and exclusion criteria for patient allocation are given in Table 1.

Table 1: Inclusion and Exclusion criteria

Inclusion Criteria	Exclusion Criteria
Patients willing to give written informed consent	Patients refusing to participate in the study
Patients with ASA grade I and II	Patients with allergy to local anaesthetics
Patients aged 20-60 years of either sex	Patients with Acute pancreatitis, Chronic pain, Choledocholithiasis
Patients scheduled for elective laparoscopic cholecystectomy	Patients with Chronic opioid use, NSAIDS
	Inability to comprehend VAS
	Patients requiring conversion of laparoscopic cholecystectomy to open cholecystectomy

After obtaining clearance and approval from Institutional Ethical Committee, patients fulfilling inclusion criteria and those who were willing to give written informed consent were included. After routine pre-anaesthetic evaluation, and familiarizing them with VAS, patients were administered oral medications-Tab Alprazolam 0.5mg and Tab Ranitidine150mg the night before surgery and were kept fasting for 8 hours before surgery. Hemodynamic and respiratory parameters (blood pressures, blood oxygen saturation, Heart rate, pulse rate, ECG, respiratory rate were measured. The patients were given uniform premedication with Midazolam at 0.025mg/kg intravenously (i.v.), Fentanyl at 2 microgram/kg i.v. and Ondansetron at 0.1mg/kg i.v. and preoxygenation was done with 100% O2 for 3min. General anaesthesia was induced with intravenous injection of Propofol at 2mg/kg, muscle relaxation was provided with intermittent intravenous injection of Vecuronium bromide at 0.1mg/kg and tracheal intubation was done with appropriate sized cuffed endotracheal tube. Anaesthesia was maintained with 0.2-1% Isoflurane in a mixture of 50 % oxygen and 50% nitrous oxide. Muscle relaxation was maintained with intermittent intravenous injection of Vecuronium bromide at 0.02mg/kg. Ventilation flow and pressure parameters were monitored continuously throughout with goal of keeping Et CO_2 between 35-40. Intrabdominal pressures following CO_2 insufflation were restricted to $\leq$12cm H_2O. All the patients received intravenous injection of Diclofenac sodium at 1.5mg/kg for analgesia during surgery.

Patients were randomly allocated into one of the two groups using numbers generated from www.random.org. 80 patients of either sex were randomly allocated into two different groups of 40 each as described below:

- **Group A (n=40):**20 ml of 0.5% Bupivacaine in 480 ml of Normal saline.
- **Group B (n=40):** 20 ml of 0.5% Bupivacaine plus 200 mg of Hydrocortisone in 480 ml of Normal saline.

The intraperitoneal irrigation was given during dissection of gall bladder and aspirated after gallbladder dissection was complete. After gallbladder extraction, irrigation of the surgical bed and the peritoneal cavity with the remaining irrigating fluid was done. Patient was placed in Trendelenburg position with right lateral tilt to facilitate dispersion of irrigating solution in the subhepatic region for 5min. Irrigating fluid was then aspirated, drain placed and surgical ports were closed. Isoflurane and nitrous oxide were stopped. Extubation was done after reversal of the neuromuscular blockade with a mixture of Neostigmine (0.05mg/kg) and Glycopyrrolate (0.01mg/kg). Once cardiopulmonary stability was ensured, patients were shifted to the recovery room. Post operatively the patients were given intravenous injection of

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Paracetamol 20mg/kg at 8 and 16hrs. A proforma was used to collect the data which includes patient's particulars; indication, date and time of surgery, time of intubation, time of extubation; VAS score, presence of shoulder pain, occurrence of vomiting (episodes) at extubation, at 30mins, 1hr, 2hrs, 4hrs, 6hrs, 8hrs, 12hrs and 24hrs postoperatively; time to first rescue analgesic, total rescue analgesic requirement in 24hrs; and time to ambulation.
Rescue analgesic-Intravenous injection of Tramadol at 2mg/kg whenever VAS score equals or exceeds 4. The time interval between extubation and request for first rescue analgesic was taken as the duration of analgesia (DOA). These efficacy parameters which were to be compared in both the groups are listed in Table 2.

Table 2: Efficacy parameters

Efficacy parameters to be compared in Group A and B
Time to first rescue analgesic
Total rescue analgesic requirement in first 24 hours
Time to ambulation
Total episodes of vomiting in first 24 hours
Incidence of shoulder pain

Statistical analysis

Results obtained were analysed by descriptive statistics. Chi-Square study, Fisher exact test, student-T test and other appropriate statistical methods were adopted at the time of data analysis. SPSS version 21.0 was used for calculation. $p<0.05$ was considered statistically significant.

Results

The patients were randomly allocated into 2 groups-Group A(n=40): who received 20 ml of 0.5% Bupivacaine in 480 ml of Normal saline and Group B (n=40): who received 20 ml of 0.5% Bupivacaine plus 200 mg of Hydrocortisone in 480 ml of Normal saline. Both groups were female predominant due to the disease etiology but were matched for gender (Table 3 and 4). The two groups were also matched for Age as shown in Table 5.
The duration of analgesia and total rescue analgesic requirement in 24 hours post operatively were comparable between the two groups and statistically insignificant. ($p>0.05$). There was no significant difference between the time to ambulation between the 2 groups (Table 6 & 7). Incidence of vomiting and shoulder pain was also statistically insignificant between the two groups ($p>0.05$) (Table 8 & Table 9). Incidence of shoulder tip pain due to diaphragmatic irritation at the end of 24 hours was low were also comparable between the two groups (Table 10 & 11).

Tables

Table 3: Gender distribution in Group A

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Female	35	87.8	87.8	87.8
Male	5	12.2	12.2	100.0
Total	40	100.0	100.0	

Table 4: Gender distribution in Group B

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Female	26	68.4	68.4	68.4
Male	12	31.6	31.6	100.0

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Total	38	100.0	100.0	

Table 5: Age Distribution of Group A and B

	Number	Mean (in yrs)	Standard deviation (in yrs)
Group A (bupivacaine Alone)	40	43.32	13.62
Group B (Bupivacaine With Hydrocortisone)	40	39.92	11.22

Table 6: Duration of Analgesia and requirement of analgesics in Group A

	Age	Duration of Analgesia (In HRS)	Time to First Rescue Analgesia	Total Rescue Analgesic Requirement in 24 Hours (In MG)	Time to Ambulation (In HRS)
Mean	39.93	11.451	11.451	112.20	4.24
Std. Deviation	11.226	8.6587	8.6587	92.723	.538
Range	37	24.0	24.0	300	2
Minimum	23	.0	.0	0	4
Maximum	60	24.0	24.0	300	6

Table 7: Duration of Analgesia and requirement of analgesics in Group B

	Age	Duration of Analgesia (In HRS)	Time to First Rescue Analgesia	Total Rescue Analgesic Requirement in 24 Hours (In MG)	Time to Ambulation (In HRS)
Mean	43.32	**11.803**	12.329	**89.47**	4.37
Std. Deviation	13.646	8.6004	8.7211	76.369	.675
Range	45	24.0	24.0	300	3
Minimum	20	.0	.0	0	3
Maximum	60	24.0	24.0	300	6

Table 8: Frequency of Vomiting in Group A

Vomiting Episodes	Frequency	Percent	Valid Percent	Cumulative Percent
0	32	80.5	80.5	80.5
1	7	17.1	17.1	97.6
2	1	2.4	2.4	100.0
Total	40	100.0	100.0	

Table 9: Frequency of Vomiting in Group B

Vomiting Episodes	Frequency	Percent	Valid Percent	Cumulative Percent
0	29	71.1	71.1	71.1
1	11	28.9	28.9	100.0
Total	40	100.0	100.0	

Table 10: Incidence of Shoulder tip pain in Group A

Any complaint of Frequency shoulder pain in 24 hours?		Percent	Valid Percent	Cumulative Percent
No	38	92.7	92.7	92.7
Yes	2	7.3	7.3	100.0
Total	40	100.0	100.0	

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Table 11: Incidence of Shoulder tip pain in Group B

Any complaint of Frequency shoulder pain in 24 hours?		Percent	Valid Percent	Cumulative Percent
No	31	81.6	81.6	81.6
Yes	9	18.4	18.4	100.0
Total	40	100.0	100.0	

Discussion

Laparoscopic Cholecystectomy is said to result in less post-operative pain and generally requires less post-operative analgesia as compared to open cholecystectomy. Nevertheless, patients of LC experience considerable discomfort during first 24 post-operative hours and a fraction of them develop shoulder tip pain due to the irritation of phrenic nerve. There are numerous methods of analgesia with varying rates of success to treat this postoperative pain following laparoscopic Cholecystectomy. The commonly used modalities include-local anaesthetic infiltration at trocar site, sub-diaphragmatic instillation of a local anaesthetic, low-pressure pneumoperitoneum, use of conventional opioids and non-opioids analgesics in the postoperative period.

We used Bupivacaine in our study for intraperitoneal instillation during laparoscopic cholecystectomy for post-operative pain relief because it is used in most studies existing in literature for pre-emptive analgesia. Hydrocortisone was added as an adjunct to bupivacaine in this study to one of the groups to compare the efficacy of the combination over only bupivacaine. It has been previously shown that glucocorticoids can play a crucial role in the regulation of inflammatory response through both genomic and nongenomic mechanisms and therefore may reduce pain. However, in our study we have found no additional benefit in terms of pain relief or decrease in side effects as compared to administration of Bupivacaine alone.

A similar study was done by Sarvestani *et al*. in 2014 which used higher concentration of Bupivacaine (100mg of Bupivacaine in 250mg of normal saline) with and without hydrocortisone which showed similar results as our study [12]. In our study, the same effect was observed with a low concentration and high volume of Bupivacaine. By using a low concentration solution of Bupivacaine, we can further reduce local side effects of intraperitoneal instillation of Bupivacaine. The efficacy of producing an adequate analgesic effect using high volume and low concentration of Bupivacaine has been established by previous studies [8, 13, 14].

Limitations

In our study, the surgeries were performed by 5 different surgeons which could be a limitation. We did not include a placebo group with only intraperitoneal saline irrigation in our study as we had enough evidence provided by previous studies and systematic reviews over the efficacy of Intraperitoneal Bupivacaine over only saline instillation [5, 15, 16]. Most of our comparative parameters-VAS score, time to ambulation etc. were subjective and patient dependant factors.

Conclusion

The addition of Hydrocortisone to Bupivacaine for intraperitoneal instillation during laparoscopic cholecystectomy does not add any additional benefit in terms of duration of analgesia or time to ambulation. It does not alter the incidence of adverse effects like vomiting and shoulder tip pain.

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