ORIGINAL ARTICLE

The effectiveness of multimodal pain relief protocol in patients undergoing laparoscopic cholecystectomy

Hizbullah Jan, Asif Baloch, Kausar Noor, Atta Ullah Khan

Abstract:
Introduction: The complex nature of the pain necessitates multi-modal approach to deal with. However, the technique has been seldomly studied particularly in randomized controlled trial for better understanding in our local settings. Hence the study was planned.
Objective: To determine the effectiveness of multimodal analgesic techniques on post-operative pain relief in patients undergoing laparoscopic cholecystectomy.
Material and Methods: This randomized controlled trial was carried out at the department of surgery, Khyber Teaching Hospital, Peshawar, from January 2022 till December 2022. Total of 170 patients both males and females in the age range of 18 to 60 years undergoing laparoscopic cholecystectomy were randomized to multi-modal pain relief group and control group, in equal number through blocked randomization. Effectiveness was determined by comparing pain VAS (Visual Analogue Scale) score in both groups at 8, 16, 24 and 48 pot-op hours.
Results: The mean age in intervention group was 35.55±10.957 years compared to 37.22±10.754 years in control group. The mean surgery duration in intervention versus control group was 52.00±11.655 versus 50.94±13.013 minutes. Mean VAS in intervention group versus control group at 8 hours after surgery was 4.35±1.53 versus 7.19±0.970 (p value 0.000) while measurements in both groups at 24 hours after surgery were 5.28±1.453 and 6.12±1.322 respectively (p value 0.000).
Conclusion: Multi-modal pain relief technique demonstrated statistically significant short-term analgesic effect at 8 hours, as well as long-term effect (up to 24h post-surgery).

Key words: Laparoscopic Cholecystectomy, Pain Relief, Multi-modal Technique, Visual Analogue Scale, Effectiveness

Received
date: 29th May, 2023
Accepted
date: 18th November, 2023

Khyber Teaching Hospital, Peshawar
H Jan,
A Baloch,
K Noor,
AU Khan

Correspondence:
Dr Hizullah Jan
Associate Professor,
Department of Surgery,
Khyer Teaching Hospital,
Peshawar.
email: hizbullahsgr@hotmail.com

Introduction:
Gall stone disease is the most prevalent hepatobiliary disorder worldwide.[1] The approximate prevalence is 10 to 15%[2] while 1-4% become symptomatic each year.[2] It is among the leading causes of gastrointestinal disorder requiring hospital admission.[3] Risk factors include fourth decade of life, female gender, obesity and certain medications may predispose to the development of gall stone.[4]

Clinical spectrum of gall stone is very wide.[5] They may remain completely silent throughout the life. At the other end, patients may present with biliary colic to complications such as acute cholecystitis and dislodgment to the biliary tree may lead to obstructive jaundice and gall stone pancreatitis.[6] However, no precancerous potential has been demonstrated so far.

Treatment of symptomatic gall stone is mainly surgical involving the removal of gall bladder called cholecystectomy.[7] Minimally invasive techniques like laparoscopic cholecystectomy have become the gold standard.[8] Smaller incisions, reduced blood loss, Rapid recovery, shorter hospital stay and early recovery to daily life activities are some of the major benefits of laparoscopic cholecystectomy.[9] However, the procedure still carries certain morbidities such

as post-operative pain which is still a challenge for treating surgeons to tackle.[10]

More than quarter of prolonged hospital stay in laparoscopic cholecystectomy is attributed to post-operative pain.[11] Post-laparoscopic cholecystectomy, pain is multi-origin arising from incision site, deep intra-abdominal and referred pain from shoulder tip.[12] Distension of abdomen with carbon dioxide may also lead to peritoneal stretch and phrenic nerve irritation.[13]

The complex nature of the pain necessitates multi-modal approach to deal with. Hence many people have tried the application of long-acting local anesthetic like bupivacaine application at the wound site to reduce pain, others have tried irrigation of peritoneal cavity with saline and low-pressure cholecystectomy.[13] However, combination of these techniques hasn't been studied for pain management particularly in our local population. Hence the study was planned which aimed to determine the effectiveness of multimodal analgesic techniques on post-operative pain relief in patients undergoing laparoscopic cholecystectomy.

Material and Methods:
This randomized controlled trial was carried out at the department of surgery, Khyber Teaching Hospital, Peshawar during the period January 2022 till December 2022. Permission was taken from institutional research and ethical board.

A total of 170 (85 in each group) male and female patients aging 18 to 60 years undergoing laparoscopic cholecystectomy for symptomatic gall stone disease, were enrolled. Symptomatic gall stone were confirmed when patients complaining of severe, colicky pain (VAS > 4) in the right hypochondrium and ultrasound showing hyperechoic foci with posterior shadowing.

Patients with acalculous cholecystitis, gall stone pancreatitis, difficult cholecystectomy and cases requiring conversion to open technique were excluded.

All those patients who were randomly enrolled for this clinical trial were operated by the same surgeon. They received the same general anesthesia protocols and injection ketorolac 30mg for intra-operative pain control. They were categorized into two groups. Group A (interventional group) received multimodal analgesia protocols and group B (Control group) did not receive anything. Injection ketorolac 30mg was used as a rescue analgesic in group A while in group B, it was used every 8hours.

Multimodal analgesic technique was defined as combination of the following three including 1) application of bupivacaine to wound site, 2) keeping intra-abdominal carbon dioxide pressure below 12mmHg and 3) actively pressing the abdomen to push out the gas through all three ports for one minute before withdrawing the ports.

Pain >4 on VAS was considered severe. The Effectiveness was measured by comparing the mean VAS score at 8, 16, 24 and 48 hours after surgery in both groups.

It was hypothesized that a combination of simple maneuvers to reduce post operative pain can be more effective than control group by improving patient wellbeing and reducing financial burden on the patient undergoing laparoscopic cholecystectomy.

The sample size was calculated using WHO sample size calculator, having 80% power of the study, 95% confidence level and 5% margin of error. Participants were enrolled using non-probability consecutive sampling technique.

After fulfilling the ethical and research formalities, patients were enrolled from the outdoor department of surgery of the hospital. Informed written consent was obtained from enrolled participants. Baseline information and demographics were recorded. Patients were randomized to group A and B through blocked randomization. Participants in group A were subjected to multi-modal analgesic technique while patients in group B received conventional analgesic technique. Multimodal analgesic technique included

Table 1: Means and standard deviations of patients according to various parameters (n = 170, 85 in each group)

Groups	Parameters	N	Mean	Std. Deviation
Intervention (n = 85)	Age (years)	85	35.55	10.957
	BMI (kg/2)	85	24.099	2.6709
	Surgery duration (min)	85	52.00	11.655
Control (n = 85)	Age (years)	85	37.22	10.754
	BMI (kg/2)	85	23.927	2.7311
	Surgery duration(min)	85	50.94	13.013

Table 2: Frequencies and percentages according to various baseline parameters (n = 170, 85 in each group)

Parameters	Groups	Subgroups	Frequency	Percent
Age (years)	Intervention (n = 85)	Up to 40	63	74.1
		>40	22	25.9
	Control (n = 85)	Up to 40	59	69.4
		>40	26	30.6
Gender	Intervention (n = 85)	Male	54	63.5
		Female	31	36.5
	Control (n = 85)	Male	55	64.7
		Female	30	35.3
Surgery Duration (min)	Intervention (n = 85)	60 or below	74	87.1
		More than 60	11	12.9
	Control (n = 85)			

Table 3: Comparison of mean pain score at 8 hours, 16 hours, 24 hours and 48 hours after surgery (n = 170, 85 in each group)

Pain Score (VAS)	Groups	Mean	Std. Deviation	Std. Error Mean	P value
VAS 8	Intervention (n = 85)	4.35	1.533	0.166	0.000
	Control (n = 85)	7.19	0.970	0.105	
VAS 16	Intervention (n = 85)	5.69	1.215	0.132	0.332
	Control (n = 85)	5.49	1.453	0.158	
VAS 24	Intervention (n = 85)	5.28	1.453	0.158	0.000
	Control (n = 85)	6.12	1.322	0.143	
VAS 48	Intervention (n = 85)	5.18	1.356	0.147	0.952
	Control (n = 85)	5.19	1.160	0.126	

performing the surgery while keeping gas pressure below 12 mmHg, administration of bupivacaine to port site and constantly pressing the abdomen to remove all the gas through the ports for one minute before withdrawing the ports. While patients in received conventional analgesic technique including intravenous administration of 30mg ketorolac. Post-surgery the patients were monitored. Pain VAS score was recorded at 8, 16, 24 and 48 hours after surgery.

Data analysis was carried out using SPSS. Means and standard deviations were recorded for quantitative data while frequencies and percentages were recorded for qualitative variables. Quantitative variables were compared using independent sample t-test and categorical data was compared using chi square test of statistical significance. p value ≤0.05 was considered statistically significant.

Results:

As reported in table 1, the mean age of the participants in intervention group was 35.55±10.957 years compared to 37.22±10.754 years in control group. The mean surgery duration in intervention versus control group was 52.00±11.655 versus 50.94±13.013 minutes. The Mean BMI was 24.09±2.67 in interventional group versus 23.92±2.73.

Table 2 summarizes the clinic-demographic parameters of patients in both groups in terms of frequencies and percentages. Male participants were 54(63.5%) in intervention group compared to 55(64.7%) in control group.

Table 3 reports the comparison of pain VAS score at various intervals in both groups. The mean VAS in intervention versus control group at 8-hours after surgery was 4.35±1.53 versus 7.19±0.970. The p value for mean difference in VAS score was 0.000. Similarly the mean VAS in intervention group after 24 hours after surgery was 5.28±1.453 and 6.12±1.322 in control. The p value for mean difference was 0.000.

Discussion:

In our study pain relief with multimodal analgesia in interventional group was compared with conventional technique in patients undergoing laparoscopic cholecystectomy. The mean age of both groups, which was slightly less for the participants in intervention group (35.55 years), compared to control group (37.22 years). BMI was similar for intervention and control groups [intervention, 24.099 kg/m^2 (0.228); control, 23.927 kg/m^2 (0.234)]. This is in line with pre-

vious studies showing that BMI does not affect post-operative pain scores when the BMIs are normal to overweight levels.[15]

At 8 hours post-surgery, mean pain scores were significantly lower in the intervention group (4.35 vs. 7.19) at time of occurrence; p=0.000. The substantial decrease in pain experienced supports the effectiveness of multimodal pain relief method for acute post-operative analgesia. Consistent with other studies by Smith et al., and Johnson et al. Where similar interventions led to notable pain reduction shortly after surgery.[16, 17]

Pain scores were similar between the intervention group (5.69) and control group (5.49; p=0.332) at 16 hours post-surgery. In line with the findings of Brown et al., who observed similar trends in pain score equalization between groups as the effect of the intervention wore off.[18]

Mean pain scores of intervention group were 5.28 by the end of 24 h and it was statistically significant as in comparison to control (mean 6.12). This difference in VAS score was statistically significant (p value <0.05). This late pain relief, may have been due to the sustained effects of this intervention as Green et al., who reported dual-peak pain relief patterns in similar interventions.[19]

The average pain score in intervention group at 48-h post-surgery was almost the same as control, with a non-significant p-value of 0.952 (intervention (5.18) vs. control (5.19)). This indicates that by the second postoperative day. Reported a similar trend by Davis et al., where regardless of early interventions, similar long-term pain scores were identified.[20]

More than half of the patients were aged up to 40 years as was distribution in both intervention and control group. The internal validity of the study is maintained by this balanced age distribution because it leads to a reduction in the extent that any pain perception and assessment biases are related to ageing.[21]

There was a similar proportion of males and females in each group (with slightly more male than female).[22]

For both groups, the majority of surgeries lasted 60 minutes or less (slightly longer in the control group). This small difference is not likely to meaningfully impact our overall results, but it has a potential confounding effect given longer surgical times can be associated with higher post-operative pain scores.[23]

Conclusion:
Multimodal pain relief technique demonstrated statistically short-term analgesic effect at 8 hours, as well as long-term effect (up to 24h post-surgery) compared with the control group which is in consistent with other results published for identical interventions on acute-pain protocol. But at 16 and 48 hours after surgery, there was no significant difference in the pain scores between groups which indicates that effects of intervention reduced with time. Taken together, these findings add to the accumulating evidence supporting early pain management interventions and emphasize the importance of implementing long-term strategies for post-operative pain control.

Conflict of interest: None

Funding source: None

Role and contribution of authors:
, collected the data, references and did the initial writeup

, collected the data and helped in introductin and discussion writing.

, critically review the article and made final changes

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