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International Journal of Current Research
Vol. 7, Issue, 07, pp.18629-18632, July, 2015

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

EVALUATION OF INTRAPERITONEAL INSTALLATION OF BUPIVACAINE FOR POST OPERATIVE ANALGESIA IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY: A RANDOMIZED CONTROL TRIAL

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ARTICLE INFO

Article History:
Received 23rd April, 2015
Received in revised form
27th May, 2015
Accepted 10th June, 2015
Published online 31st July, 2015

Key words:

Intraperitoneal Installation of Bupivacaine,
Laparoscopic Cholecystectomy,
Postoperative analgesia.

ABSTRACT

Background: Laparoscopic Cholecystectomy being promoted as a Day care surgery now a day, therefore, adequate pain relief in post operative period is a must for patient's compliance. Incorporation of intraperitoneal installation of Bupivacaine as a part of multimodal analgesic regime provides significant post operative analgesia. This study evaluates the role of intraperitoneal spraying of bupivacine in patients undergoing laparoscopic cholecystectomy for adequate post operative analgesia.

Methods and Materials: Sixty ASA I, II patients with uncomplicated cholelithiasis, undergoing laparoscopic cholecystectomy were randomly divided in two groups. Group 1 was the study group where 20 ml of 0.5% bupivacaine was instilled and group 2 was the control group where 20 ml of normal saline was instilled into the gall bladder fossa and sub-diaphragmatic space at the end of the surgery. The VAS, total requirement of rescue analgesia and time to the first dose of rescue analgesia was noted at regular intervals over the 24 hour postoperative period.

Results: In the study group, 50% (i.e. 15 out of 30) of the patients required only a single dose of rescue analgesia over the 24 hour observation period. Another 40% (i.e. 12 out of30) required two doses and the remaining 10% (i.e. 3 out of 30) required three doses of rescue analgesia. In the control group 56.7 % (i.e. 17 out of 30) of the patients required three doses of rescue analgesia, another 30% (i.e. 9 out of 30) required two doses while the remaining 13.3% (i.e. 4 out of 30) patients required four doses of rescue analgesia over the period of observation. These results are highly significant.

Conclusion: Intraperitoneal instillation of bupivacaine in the gall bladder fossa and sub diaphragmatic surface is safe and has an effect in alleviating postoperative pain thereby minimizing the requirements of analgesics and it can be incorporated as a routine practice and as a part of multimodal analgesic regime.

Citation: Dr. Kapil Panchbhai, Dr. Divish Saxena, Dr. Prabhat Nichkaode and Dr. Abhay Chowdhary, 2015. "Evaluation of Intraperitoneal installation of Bupivacaine for post operative analgesia in patients undergoing laparoscopic Cholecystectomy: A randomized control trial", *International Journal of Current Research*, 7, (7), 18629-18632.

INTRODUCTION

Laparoscopic cholecystectomy has become gold standard operation for the diseases of gall bladder. It results in less postoperative pain and reduced analgesic requirement as compared to open cholecystectomy. Small incision, rapid recovery and shorter hospital stay have made laparoscopic surgery very popular amongst the surgeons and the patient population. Hence there is a need for adequate post operative pain relief in such cases. The highest incidence of pain is in the upper abdomen (Dobbs *et al*., 1987).

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Shoulder pain may occur in as many as 63% or as few as 35% of the patients (Dobbs *et al*., 1987; Riedel *et al*., 1980). With increasing trend of laparoscopic cholecystectomies as day care surgeries, the use of spinal or epidural analgesia is not a practical technique for pain management. Therefore, anaesthesiologists are turning to multimodal or "balanced" analgesic techniques involving the use of smaller doses of opioids in combination with non-opioid analgesic drugs, such as local anaesthetics, ketamine, acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) for adequate pain relief. Intracavitary instillation of local anaesthetics is said to be a simple and effective technique for providing pain relief during the early postoperative period after laparoscopic procedure. Bupivacaine, an amide type local anaesthetic is sprayed over the gall bladder bed and the diaphragmatic

surface of the liver. The rationale for this route of administration is that the peritoneum is exposed to a local anaesthetic block of visceral nociceptive conduction, thereby providing an additional mechanism of analgesia. In this present study we are assessing the effectiveness of intraperitoneal instillation of bupivacaine for providing effective post operative analgesia following laparoscopic cholecystectomies.

MATERIALS AND METHODS

60 patients of Class I and Class II risk as per American Society of Anaesthesiology (ASA) of either sex were posted for elective laparoscopic cholecystectomy. These patients participated in prospective open randomized study for post operative pain relief after laparoscopic cholecystectomy. After the informed and written consent was obtained, these patients were randomly allocated to one of the two groups:

Group 1- Study Group (20cc 0.5%Bupivacaine) –30 patients
Group 2- Control Group (20cc Normal Saline) –30 patients

Patients who were sensitive to Bupivacaine, those having acute cholecystitis on admission and those belonging to ASA group III or IV were excluded from the study. A preoperative assessment in the form of detailed history, general and systemic examination and investigations like complete blood count, liver function tests, and kidney function tests, blood sugar levels, ECG and ultrasound of abdomen were performed.

Methodology

All the patients were operated in general anaesthesia with four port {umbilical as camera port(10 mm), right mid axillary line port for gall bladder retraction (5 mm), epigastric port (10 mm) and right midclavicular port (5 mm) as working ports} laparoscopic cholecystectomy. Intra abdominal pressure was maintained between 10 – 12 mm of Hg. After the gall bladder was extracted, 15^{o} of head low and right tilt position was given. A pre aspirated syringes of 20 cc 0.5% mg. Bupivacaine or Placebo (20cc Normal saline) was sprayed in the same position over the gall bladder fossa and right sub diaphragmatic space under direct vision by the operating surgeon. After the drug was sprayed the head low and right till position was maintained for the next 10 minutes. Pneumoperitoneum was completely evacuated by the surgeon before closing port sites by manual compression of the abdomen. The total duration of surgery was recorded for all the patients. In the post operative period following points were assessed in all the patients:

1. **VAS Assessment:** The patients were asked to indicate their pain scores on a 10 cm visual analogue pain scale where 'O' indicated no pain and '10' indicated worst possible pain. The VAS was recorded at 0, 2, 4, 8, 12, 18 and 24 hrs after surgery.
2. **Rescue analgesia:** Rescue analgesic (Inj. Diclofenac Sodium I.M) was administered when the VAS was ≥ 5 or when the patient demanded an Analgesic. The time taken to the first dose of rescue analgesia and the total dose of rescue analgesics received by each patient were recorded.
3. **Site of Pain:** The site of pain was determined by asking the patient to indicate the site of discomfort. Also the patient was asked whether he was experiencing shoulder tip pain.
4. **Topic effects of bupivacaine:** Patients were monitored postoperatively for any toxic side effects of bupivacaine such as respiratory depression, restlessness, tremors, convulsions and arrhythmias.

The results were subjected to statistical analysis. Statistical analysis was done by the independent't' test and chi-square test. P value < 0.05 was considered statistically significant.

RESULTS

Being a Randomised Control Trial (RCT), the two groups were comparable with regard to their age, sex, Body Mass Index and patients belonging to ASA Class I and II. The duration of surgery was also comparable in both the groups (Table 1)

Table 1. Comparison of two groups with respect to age, sex, BMI, ASA and operating time

	Study group (bupivacaine) n=30 Mean±S.D.	Control group (saline) n=30 Mean±S.D.	'p' Value
Age (yrs)	41.97±17.045	38.90±12.246	0.427*
Sex(M/F)	7/23	10/20	0.390#
BMI(kg/m^2)	26.53±3.550	26.07±3.503	0.61*
ASA Class(I/II)	26/4	26/4	1.000#
Duration of surgery (min.)	86.67±20.441	83.83±15.849	0.551*

** p > 0.05- Not significant, By Independent 't' test , # p > 0.05- Not significant, By Pearson Chi-Square test*

The VAS was measured at rest, at regular intervals over a period of 24 hours. VAS was found to be significantly reduced in the study group as compared to the control group at the end of the 2nd, 4th and 24th hour after surgery (Table 2).

Table 2. Comparison of VAS in both groups

VAS	Study group (bupivacaine) N=30	Control group (saline) N=30	'p' Value
0 hrs	0.43±1.194	1.20±1.901	0.066
2 hrs	1.90±1.826	4.43±1.591	0.000*
4 hrs	2.60±1.653	3.80±2.156	0.019*
8 hrs	3.37±1.810	3.67±1.807	0.523
12 hrs	4.03±2.189	4.27±1.893	0.66
24 hrs	2.67±1.241	3.60±1.754	0.021*

** p < 0.05- Significant, By Independent't' test*

The most common site of pain recorded was in the right hypochondrium. No significant difference as to the location of pain was observed between the groups (Table 3).

Table 3. Table showing the site of pain in both groups

Site of pain	Study group (bupivacaine) N=30	Control group (saline) N=30	Total (60)
	No. of patients (%)	No. of patients (%)	
Right hypochondrium	25 (83.3%)	21 (70%)	46 (76.7%)
Generalized Abdomen	5 (16.7%)	5 (16.7%)	10 (16.7%)
Upper Abdomen	0	4 (13.3%)	4 (6.7%)

p= 0.114(Not significant), By Pearson Chi-Square test

In the study group, 50% (i.e. 15 out of 30) of the patients required only a single dose of rescue analgesia over the 24 hour observation period. Another 40% (i.e. 12 out of 30) required two doses and the remaining 10% (i.e. 3 out of 30) required three doses of rescue analgesia. In the control group 56.7% (i.e. 17 out of 30) of the patients required three doses of rescue analgesia, another 30%(i.e. 9 out of 30) required two doses while the remaining 13.3%(i.e. 4 out of 30) patients required four doses of rescue analgesia over the period of observation. It states that requirement of rescue analgesics was significantly higher in the control group (Table 4).

Table 4. Table showing number of rescue analgesic doses required in both groups

Total dose	Study group (bupivacaine) N=30 No. of patients (%)	Control group (saline) N=30 No. of patients (%)	Total (60)
1	15 (50%)	0	15 (25%)
2	12 (40%)	9 (30%)	21 (35%)
3	3 (10%)	17(56.7%)	20 (33.3%)
4	0	4 (13.3%)	4 (6.7%)
Total doses (Mean +/- S.D.	1.60±0.675	2.83±0.648	p value 0.000*

**p=0.000- Significant, By Pearson Chi-Square test*

DISCUSSION

The advent of laparoscopic cholecystectomy was the catalyst that aroused the interest of general surgeons worldwide in laparoscopy and closed abdominal surgery. The technique was first described by Phillipe Mouret in 1988 and it was refined and popularized in the United States by Reddick and Olsen (1983). In 17-41% of the patients, pain is the dominating complaint and the primary reason for prolonged convalescence after laparoscopic cholecystectomy (Bisgaard *et al*., 2001). Interestingly, the type of pain after laparoscopy differs considerably from that seen after laparotomy. Whereas laparotomy results mainly in parietal pain (located in the abdominal wall), patients complain more of visceral pain (deep, dull, difficult to localize, inside the abdomen, resembling biliary colic) after operative laparoscopy. Shoulder pain secondary to diaphragmatic irritation as a result of CO_2 pneumo-peritoneum is a frequent postoperative observation after laparoscopy. Mechanism of pain after laparoscopy has been reviewed by Schoeffler, Diemunsch, and Fourgeaud (Bisgaard, 2001). Rapid distension of the peritoneum may be associated with tearing of blood vessels, traumatic traction of the nerves and release of inflammatory mediators. Comyn (Narch *et al*., 1991) reported that peritoneal biopsy performed 2-3 days after laparoscopy showed peritoneal inflammation and neuronal rupture, and there was a linear inverse relationship between abdominal compliance at the time of laparoscopy and severity of postoperative pain. Pain is most intense on the day of surgery and subsequently declines to low levels within 3-4 days (Bisgaard *et al*., 2001). Although NSAIDs appear to be highly efficacious for managing post laparoscopic cholecystectomy pain, they have the disadvantage that they may cause gastric irritation in addition to impairing platelet and renal function.

In 1991, it was suggested by Narchi *et al*. (1991), that instillation of local anaesthetic into the abdominal cavity during laparoscopic procedures may reduce the post operative shoulder pain. Subsequent studies with intra peritoneal local anaesthetic have shown mixed results. In 1993, Chundrigar and colleagues (Chundrigar *et al*., 1993) used 20 ml of 0.25% bupivacaine directly onto the gall bladder bed, with significant pain relief following laparoscopic cholecystectomy. The study comprised 60 consecutive patients listed for elective laparoscopic cholecystectomy. Patients were assessed for pain using a visual analogue pain scale at five time intervals after surgery; 1, 2, 4, 8 hrs and at discharge. There was a significant reduction in pain scales at the 1st and 2nd hr time intervals after surgery in the study group. In 1997, Weber *et al*. (1997) sprayed 10 ml of 0.5% bupivacaine postoperatively into the sub-diaphragmatic space in 50 patients. The evaluation of postoperative pain was done according to a numerical verbal scale and the dose of analgesia required. Their results showed significantly reduced pain scores at 2, 6, and 12 hrs. In 2002, a similar study by Bhardwaj *et al*. (2002) found good pain relief with 20 ml of 0.5% of bupivacaine with adrenaline 1:200,000 following laparoscopic cholecystectomy. The Visual Analogue Score was significantly lower in the study group as compared to the control group at the 1st, 4th and 8th postoperative hour. This was also observed in our study where the total number of doses of analgesic was higher in the control group as compared to the study group.

The risk of bupivacaine instillation was studied by Raetzell *et al*. (1995). They concluded that maximum plasma concentrations of bupivacaine after intraperitoneal application of 50 or 100 mg occurred after 5- 30 minutes with a mean of 0.48 and 1.0 mg/L, which resembles other techniques of regional anaesthesia like brachial plexus or epidural blockade. No side effects attributable to the local anaesthetic were noted. Of the 41 RCT's reviewed, 13 trials with 18 treatment arms compared intraperitoneal bupivacaine 50-155 mg (in 17 treatment arms) with saline or no treatment. In all trials the local anaesthetic was administered in the right sub diaphragmatic or gall bladder region in concentrations between 0.1% and 0.5%.Overall 7 of the 13 trials found improved pain relief for at least one of the evaluated pain measures. In 7 trials with 10 treatment arms, overall pain scores and pain scores for abdominal pain and shoulder tip pain were significantly reduced compared with the control patients. In most studies pain scores were reduced only in the early post operative period however in two trials (Pasqualucci *et al*., 1994; Pasqualucci *et al*., 1996), pain reduction lasted up to 24 hrs. In both studies 20cc of 0.5% bupivacaine was used in the study group. In the remaining 6 trials no effect on pain scores and supplement analgesia was observed.

The differences in the between the results of the various RCT's are difficult to explain. The most plausible explanations could be:-

i. Application of insufficient dose of local anaesthetic as has been implied in most of the negative studies (Rademaker *et al*., 1994).
ii. Instillation in supine position preventing the drug from flowing over the celiac plexus and the phrenic nerve (Rademaker *et al*., 1994).
iii. Anatomic flux diverting the drug away from the site of instillation.

iv. Rapid dilution of the drug in the peritoneal cavity.
v. Small sample size in some of these trials (Raetzell *et al*., 1995; Rademaker *et al*., 1994).
vi. The technique as such may not block relevant nociceptive input. It is possible that the cutaneous sensation is unrelieved by the intraperitoneal administration of local anaesthetic.

As suggested in a study by Charvarty *et al*. (2014), bupivacaine, if used in proper concentration and dosages, is a simple technique for providing adequate analgesia in post operative period.

Conclusion

Intraperitoneal instillation of bupivacaine in the gall bladder fossa and sub diaphragmatic surface is safe and has an effect in alleviating postoperative pain thereby minimizing the requirements of analgesics and it can be incorporated as a routine practice and as a part of multimodal analgesic regime. Further trials are needed in laparoscopic cholecystectomy to provide evidence for the optimal multimodal analgesic regimen.

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