Original Research Article

Intraperitoneal nebulization of ropivacaine 0.75% vs intraperitoneal nebulization of bupivacaine 0.5% for post-operative analgesia in laparoscopic surgeries: Prospective double blinded randomised controlled trial

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Abstract

Background: Laparoscopic surgeries being minimally invasive surgeries are associated with a relatively minor surgical trauma. Excessive pain, nausea and vomiting and fatigue will delay the discharge. Bupivacaine and Ropivacaine, the long acting Local Anaesthetics when given intraperitoneally provide effective pain relief when the pain peaks within 4-6 hours of surgery.
Aim: To compare the efficacy of intraperitoneally nebulised Ropivacaine 0.75% and Bupivacaine 0.5% for postoperative analgesia in Laparoscopic surgeries.
Materials and methods: This study was a double blinded randomised controlled trial in ASA grade I and II patients" was conducted in 60 patients of both sexes, of age group 20-45 years. They were randomly divided into two groups of 30 patients each: Group R (Ropivacaine) – received intra-peritoneal nebulization of Ropivacaine 0.75% 4 ml (30 mg) after the placement of umbilical port and

Group B (Bupivacaine) – received intra peritoneal nebulization of Bupivacaine 0.5% 4 ml (20 mg) after the placement of umbilical port.

Results: There was no significant difference in age and weight between the two groups. Intra-operatively statistically significant differences were observed SBP - At 15 and 30 min post nebulization and at extubation. No significant differences were observed with respect to DBP and HR. Postoperatively DBP and HR differences were found to be statistically significant at 4th post-operative hour. There were no statistically significant differences in SBP and MAP between both the groups. Dynamic VAS scores were statistically significant at extubation and in first 6 hours and not significant at 24 hours between both the groups. Static VAS scores were not statistically significant at all times compared between both the groups. Mean Time for first rescue analgesic requirement was 8.23$\pm$0.511 hours in group R vs.7.59$\pm$0.52 in group B and was statistically significant (p=0.0001). Mean total rescue analgesic required was 95$\pm$33.3 mg Diclofenac in group R vs. 112.6$\pm$38.4 in group B with 26% of group R requiring 2nd dose of rescue analgesic and 50% of patients in group B required 2nd dose and was not statistically significant. Mean time for unassisted ambulation was 12.8$\pm$0.61 hours in group R vs.13.16$\pm$0.6 hours in group B which was not statistically significant (p=0.52).

Conclusion: From the present study, it is concluded that both Bupivacaine and Ropivacaine are safe and similarly efficacious in reducing postoperative pain following intra-peritoneal nebulization in laparoscopic surgeries.

Key words

Ropivacaine, Bupivacaine, Intraperitoneal, Nebulization, Laparoscopic surgery, Analgesia.

Introduction

Minimally Invasive Surgery is one of the rapidly expanding fields of surgery. The reason behind the increasing number of Laparoscopic Surgeries are improved postoperative pain and improved healing time as compared to open surgeries resulting in earlier recovery and discharge from the hospitals. Post-operative complications though lesser as compared to open procedure but have been found to be significant enough to affect the recovery process and delay the discharge from Post Anesthesia Care Units [1].

Pain after Laparoscopic Surgeries has been associated with: the surgical manipulations - the incision sites, the pneumo-peritoneum - causing peritoneal and diaphragmatic stretching resulting in visceral and shoulder tip pain, ischemia and acidosis locally and the hypercarbia: causing systemic sympathetic stimulation thus amplifying local tissue inflammatory response and Post-Cholecystectomy wound in the liver in case of Laparoscopic Cholecystectomy [1]. Several modalities have been employed for achieving the safe and effective analgesia as pain is the dominating complaint and also it has been hypothesized that intense acute pain after Laparoscopic Surgeries may predict the development of chronic pain [2].

Studies indicate that Bupivacaine and Ropivacaine, the long acting Local Anesthetics when given intraperitoneally provide effective pain relief when the pain peaks within 4-6 hours of surgery. Further Ropivacaine with its local vasoconstrictor property, high sensorimotor differential blocking property may lead to differences in duration of pain relief or total analgesic requirements [3].

Intraperitoneal Local Anaesthetics as a method of reducing post-operative pain were first evaluated in patients undergoing Gynaecological Laparoscopic surgery. Intraperitoneal Instillation of Local Anaesthetics can provide pain relief after a Laparoscopic Surgery, but Local Anaesthetic distribution may not always be uniform throughout the peritoneal surface. Intraperitoneal Nebulization of Local

Anaesthetics is a relatively novel method for pain control as this approach should provide uniform dispersion of Local Anaesthetics throughout the peritoneal cavity. This study was done to compare the efficacy of intraperitoneally nebulised Ropivacaine 0.75% and Bupivacaine 0.5% for post-operative analgesia in Laparoscopic surgeries.

Materials and methods

Sixty patients of American Society of Anaesthesiologists grades I and II scheduled for elective laparoscopic surgeries were randomly assigned to two groups: Group R and Group B of 30 patients each. The study protocol was approved by the Institutional Ethics Committee of Patients coming to the hospital scheduled for elective Laparoscopic Cholecystectomy and Laparoscopic Appendicectomy. A written informed consent was taken from all the patients.

Inclusion criteria: Females and males: 20 - 45 years, ASA grades: I and II, Scheduled for Laparoscopic Cholecystectomy and Laparoscopic Appendicectomy surgeries.

Exclusion criteria: Emergency/ Urgency surgery, Requirement for prolonged post-operative admission into ICU, Cognitive impairment or mental retardation progressive degenerative disorders of CNS, Seizures or chronic therapy with Anti-epileptics, Severe Hepatic or Renal impairment, Pregnancy or Lactation, Allergy to one of the drugs under study, Acute infections or chronic inflammatory disease, Laparoscopic surgery converted to open technique.

Patients were divided 30 each in a group as

Group R: Patients of this group received intra-peritoneal nebulization of Ropivacaine 0.75% (4 ml) (30 mg) after the placement of umbilical port.

Group B: Patients of this group received intra-peritoneal nebulization of Bupivacaine 0.5% (4 ml) (20 mg) after the placement of umbilical port.

Patients enrolled for the study had a comparable demographic profile. All the patients underwent thorough pre-anaesthetic evaluation one day prior to surgery. Clinical assessment with detailed history was taken. All systems were examined including the airway. The procedure to be carried out was explained and the patients were made familiar with Visual Analog Scale (0-100 mm; 0-no pain and 100-the worst possible pain) and its employment in pain assessment. All the patients were kept nil per oral as per the fasting guidelines. All of them received Tab. Diazepam 10 mg and Tab. Ranitidine 150 mg night before the surgery.

The all basic investigations were performed preoperatively as required. 20% Intra-lipid and emergency cart was kept ready to combat Local Anaesthetic Systemic Toxicity.

Significant VAS score: A scale more than 30 on visual analog scale requiring additional analgesic to reduce pain.

Rescue analgesia: The analgesic given to control acute episodes of pain (VAS score >30) in a patient on pain management regimen according to the protocols.

Static VAS Score: Pain score recorded when the patient is quietly breathing.

Dynamic VAS score: Pain scores recorded when the patient is deeply breathing or coughing.

Laparoscopic surgery was performed according to standard Anaesthesia and surgical protocols. Preoperative blood pressure and heart rate were recorded; intravenous access with an 18 guage cannula into a peripheral vein was established. Patients were pre-medicated with inj. Midazolam 2 mcg /kg, inj. Glycopyrrolate 4 mcg /kg, inj. Ondansetron 80 mcg /kg and inj. Fentanyl 2 mcg/kg body weight intravenously. General Anesthesia was administered using inj. Thiopentone Sodium 5 mg/kg or inj. Propofol 2 mg/kg as inducing agents and inj. Vecuronium 80 mcg/kg facilitated tracheal intubation and muscle relaxation intravenously. After confirming the intra-peritoneal location of the umbilical port (10 mm) carbon dioxide

insufflation was followed by intra-peritoneal nebulization of the study drugs using nebulizer. Intra-operative hemodynamics was monitored.

The following parameters were recorded intra-operatively:
Pulse oximetry, Non-invasive blood pressure, electrocardiography and end-tidal carbon dioxide. The end-tidal carbon dioxide was maintained between 30-35 mm Hg intra-operatively by adjusting minute ventilation appropriately. SpO2 was maintained between 97 -100 % intra-operatively.

Subsequent analgesia and depths of anaesthesia were maintained with Inj. Fentanyl supplemented as half the loading dose (1 mcg/kg) every 40 min.

Signs of Local anaesthetic toxicity such as, brady-arrhythmias, hypotension and signs of allergy such as, rashes, hypotension etc. were keenly observed throughout the procedure. Duration of surgeries was around 70-100 min in all the cases.

Port-site local infiltration was given with Lignocaine 1% 10 ml at the end of surgery in both the groups.

Patients were extubated after complete recovery smoothly without producing much extubation response. Hemodynamics and immediate post extubation VAS scores and incidence of shoulder tip pain were noted. Patients were then shifted to postoperative care unit where further parameter monitoring was done.

Post-operative course
Postoperatively the patients were given oxygen support with Hudson's mask 6L/min for 2 hours. They were given inj. Tramadol 50 mg IV thrice daily for 48 hours.

Static and dynamic VAS scores, shoulder tip pain, SBP, DBP, MAP, HR and complications – PONV, were recorded at 0min, 30 min, 1 hour, 2 hour, 3 hour, 4 hour, 5 hour, 6 hour and 24 hours. VAS scores more than 30 mm were considered to be significant and any additional requirements of rescue analgesia were met by inj. Diclofenac 75 mg intramuscular. Time for requirement of first Rescue Analgesic dose and total doses of further analgesic required were noted. Time for first unassisted ambulation was noted. Occurrence of any adverse events was recorded.

Inj. Ondansetron was administered on complaining nausea and vomiting. Saturations recorded were within 95-100% in first 24 hours in both the groups of patients

Results were statistically analyzed using Un-paired t test and Fisher exact test and Chi-square test. A 'p' value of <0.05 was considered as significant and calculated by Graphpad software. All the values are mentioned as Mean +/- standard deviation.

Results

There were no clinical or statistically significant differences in the demographic and hemodynamic profile of patients and the two groups were comparable.

There was no statistically significant difference in age and weight between the two groups. Both groups had male population in greater proportions, accounting for 60% or more of the total study population in each group. Both the groups were comparable in terms of ASA status of either ASA I or II with 60- 70% of the sample falling within ASA I group (**Table – 1**).

Sample population in both the study groups were comparable with respect to SBP, DBP, MAP, and HR with p value >0.05 (**Table – 2**).

Intra-operatively the differences in systolic blood pressure were statistically significant at 15 and 30 min post nebulization and at extubation. There were no significant differences in diastolic blood pressures in both the groups throughout the intraoperative period. There were no significant

differences in heart rate in both the groups during intraoperative period (**Table – 3**). No significant differences were noted in SBP trends postoperatively between both the groups (**Figure – 1**).

Significant differences in DBP were observed at 4 hours post-operatively (**Figure – 2**).

Post-operatively heart rate differences were significant only at 4th hour (**Figure – 3**).

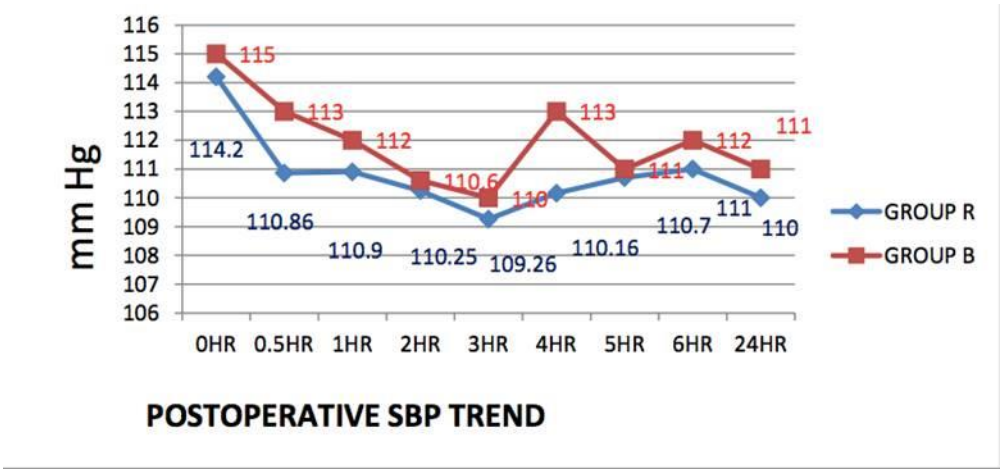
Table - 1: Demographic data in present study.

		Group R	Group B	P Value
Age (in years)	Mean	35.37	33.63	0.3891
	SD	8.528	6.93	
Weight (in kg)	Mean	66.96	65.33	0.258
	SD	6.16	4.81	
Gender	Male N(%)	18(60%)	20(66.6%)	0.688
	Female N(%)	12(40%)	10(33.3%)	
ASA status	ASA I	21(70%)	18(60%)	0.59
	ASA II	9(30%)	12(40%)	

Table - 2: Preoperative hemodynamic data.

	SBP	DBP	MAP	HR
Group B	123±10.5	78.53±7.95	93.5±7.1	92.3±12.94
Group R	120±10.4	77.2±9.99	91.3±8.52	90.7±11.9
p value	0.2708	0.57	0.28	0.62

Figure - 1: Post-operative systolic blood pressure between both the groups.



Mean Static VAS scores were not statistically significant at any of the measured points of time frame.

Mean Dynamic VAS scores were significant in first 6 hours with a p value < 0.05 however individually patients never reached a VAS score beyond 30 within first 6 hours. At 24 hours the scores were not statistically significant. There was a slight increase in vas scores both static and dynamic beyond 3 hours of postoperative period in both the groups probably due to increasing intensity of pain and waning off of the effect of Bupivacaine or Ropivacaine. At 24 hours the scores were reduced indicating reduction in intensity of postoperative pain (**Table – 4**).

Table – 3: Intraoperative hemodynamics in study.

Time	Group R		Group B		P Value
	Mean	SD	Mean	SD	
Systolic blood pressure					
pre –neb	147.7+/-5.58		149+/-8.4		0.48
post-neb					
0 min	145.9+/-7.37		146+/-7.93		0.95
5 min	140+/-6.5		141+/-7.05		0.57
10 min	132.46+/-6.5		135+/-5.97		0.12
15 min	121.6+/-7		129+/-6.27		0.0001
30 min	116.2+/-5.1		122+/-7.53		0.0009
60 min	113.3+/-4.2		115+/-5.11		0.16
end of surgery	113.2+/-4		115+/-6.46		0.12
at extubation	142.6+/-5.2		146+/-5.9		0.02
Diastolic blood pressures					
pre- neb	92.8+/-4.34		93.4+/-3.8		0.57
post-neb					
0 min	88.6+/-4.1		88+/-3.36		0.53
5 min	84.9+/-3.94		85.2+/-4.89		0.79
10 min	81.4+/-5.19		82+/-4.2		0.62
15 min	78.7+/-5.1		80.6+/-4.79		0.14
30 min	77.3+/-4.8		78.8+/-4.06		0.19
60 min	76.16+/-5		76+/-4.71		0.89
end of surgery	75.6+/-6.2		76.4+/-6.74		0.63
at extubation	89.6+/-3.3		91.1+/-2.52		0.052
Heart rate					
pre-neb	103.9+/-9.1		103+/-10.1		0.78
post-neb					
0 min	102.2+/-9		101+/-9.7		0.62
5 min	94.3+/-7.4		93.7+/-8.29		0.76
10 min	88.1+/-5.37		89.3+/-6.93		0.45
15 min	82.7+/-4.1		83.5+/-4.8		0.49
30 min	80.9+/-3.8		80+/-4.6		0.41
60 min	78.9+/-2.8		79+/-4.9		0.92
end of surgery	79.7+/-3.96		78+/-4.5		0.12
at extubation	92.9+/-6		95+/-5.5		0.16

Mean Time taken for administration of rescue analgesia was 8.23±0.5 hours in Ropivacaine group and 7.6±0.52 hours in Bupivacaine group which was statistically significant (p=0.0001). Earliest and longest time of administering rescue analgesia in group R was required 7 and 9.1 hours respectively and in group B was 6.6 and 8.5 hours respectively.

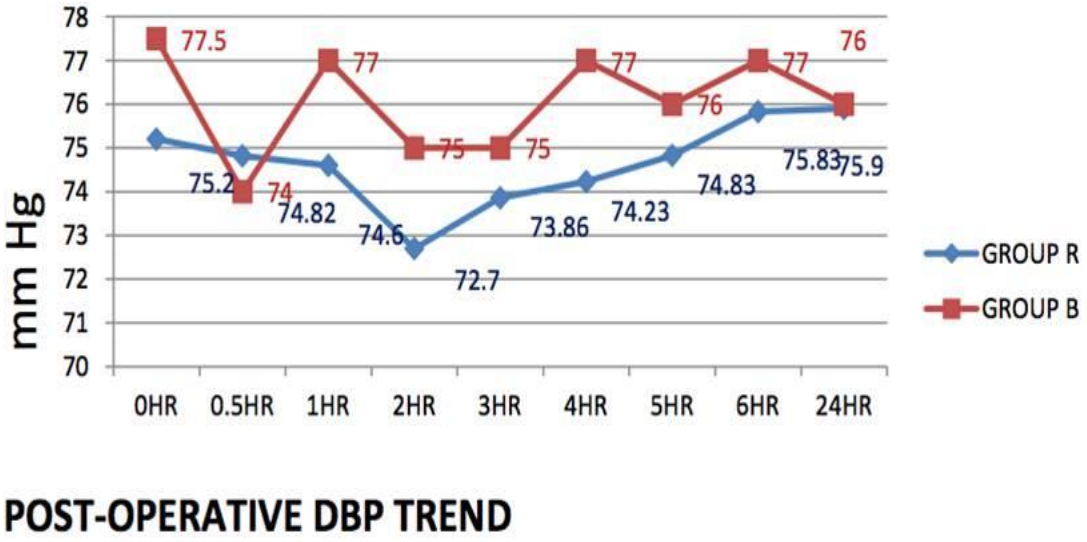
Mean of Total rescue analgesic dose required in group R was 95±33.3 mg vs. 112.5±38.4 mg in group B which was not very statistically significant (p=0.06). However a total of 15 individuals in group B (50% of study group) and 8 individuals in group R (26.6% of study group) required 2nd dose of rescue analgesia in 24 hours. This probably reflects the difference of

efficacy in analgesia provided by Ropivacaine and Bupivacaine (**Table – 5**).

Mean time required for unassisted ambulation was 12.8 +/-0.61 hrs vs.13.16+/- 0.6 hrs in groups R and B respectively and the difference was not statistically very significant (p=0.0519).

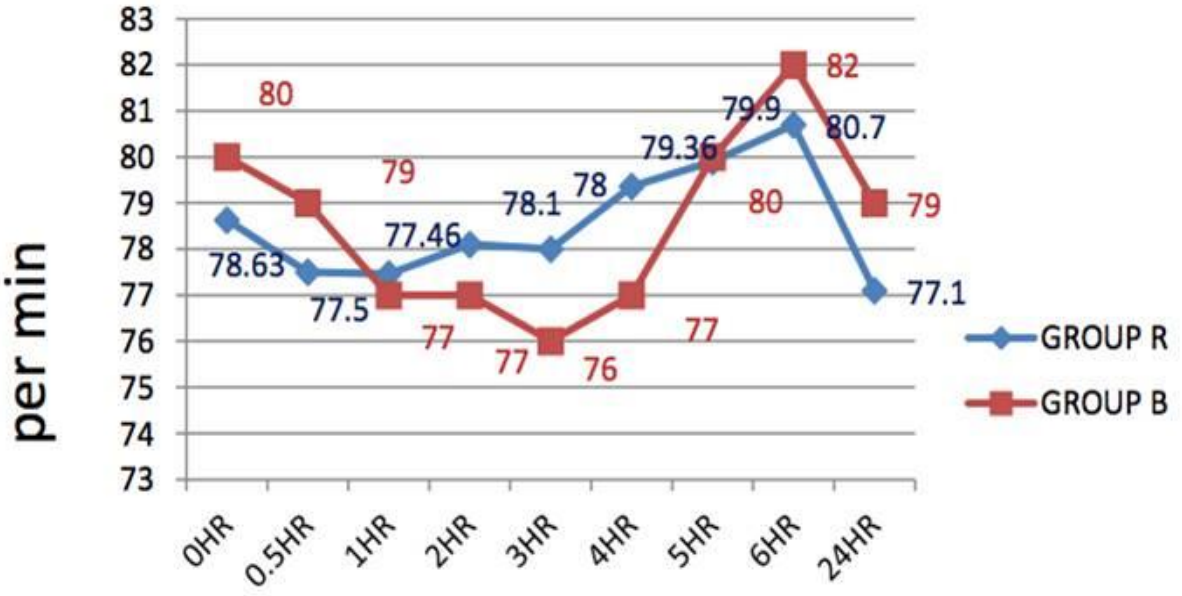
Earliest ambulatory time noted was 12.1 hours in both the groups. The incidence of PONV was 20% vs. 26.6% in groups R and B respectively and was statistically not significant (p value: 0.54) as per **Figure – 4**.

Figure - 2: Post-operative diastolic blood pressure trend.



POST-OPERATIVE DBP TREND

Figure - 3: Post-operative heart rate trend.



POSTOPERATIVE HR TREND

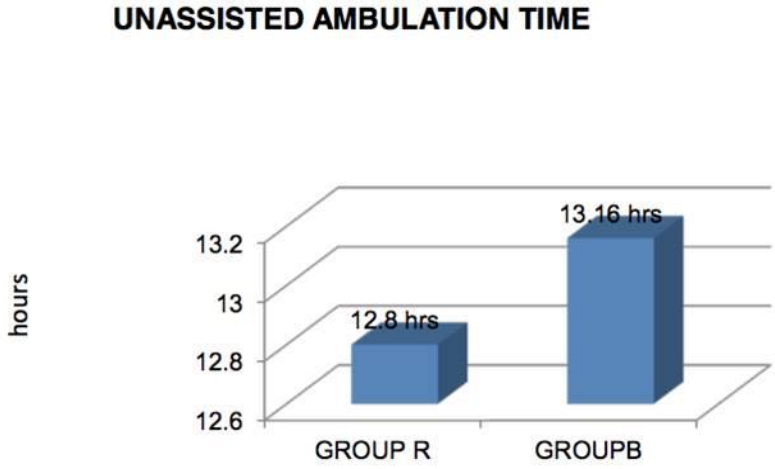
Table - 4: Static and Dynamic VAS scores.

	VAS -Static			VAS Dynamic		
	Group R	**Group B**	**P Value**	**Group R**	**Group B**	**P Value**
At extubation	14.5+/-1.75	14.73+/- 1.4	0.86	23.3+/-1.21	25.3+/-1.8	0.0001
post-op						
0 min	13.96+/-1.4	14.06+/- 1.79	0.81	22.36+/-1.4	24.6+/-2.15	0.0001
0.5 hour	13.56+/-1.57	13.9+/- 1.38	0.43	22.13+/1.59	24.2+/-1.73	0.0001
1 hour	12.7+/-1.4	13.37+/- 1.56	0.09	20.96+/-1.32	23.67+/-1.64	0.0001
2 hour	12.53+/-1.92	13.1+/- 1.28	0.5	20.83+/-1.16	23.63+/-1.54	0.0001
3 hour	12.2+/-1.6	12.4+/- 1.77	0.59	20.6+/-1.56	23.6+/-1.85	0.0001
4 hour	12.93+/-1.43	13.2+/- 1.02	0.40	23.3+/-1.9	25.2+/-1.18	0.0001
5 hour	13.1+/-1.02	13.6+/- 1.43	0.12	23.93+/-2.46	25.9+/-1.44	0.0001
6 hour	13.8+/-1.4	14.3+/- 1.97	0.26	25.6+/-1.69	27.2+/-1.69	0.0001
24 hour	7.66+/-1.12	7.77+/- 1.19	0.72	15.3+/-1.6	16.03+/-1.32	0.07

Table - 5: Time required for first rescue analgesic (hours) and total analgesic dose (mg diclofenac).

	RA -1 ST Dose	**RA –Total Dose**
Group R	8.23+/-0.511	95+/-33.3
Group B	7.59+/-0.52	112.5+/-38.4
P Value	0.0001	0.06

Figure - 4: Time for unassisted ambulation.



Discussion

Laparoscopic surgeries being minimally invasive surgeries are associated with a relatively minor surgical trauma. They also have evolved as day care surgeries owing to significantly reduced stress responses, postoperative pain and opioid requirements, improved postoperative pulmonary function, reduced overall morbidity resulting in rapid recovery, earlier ambulation thus a reduced risk of DVT and a rapid return to normal activities. Top priorities for successfully discharging patients of day care surgeries are the four A's: Alertness, Analgesia, Ambulation and Alimentation. Excessive pain, nausea and vomiting and fatigue will delay the discharge. The success of fast tracking depends on effective pain management by simple technique. Studies have shown that there has been underestimation of pain leading to under treatment especially in minimally invasive surgeries. About 30%-40%

of the patients discharged on a day care basis suffer from moderate to severe pain in first 24 to 48 hours, being significant enough to interfere with the sleep and daily functioning [4].

Optimal postoperative pain control should be effective, safe, produce minimal side effects and facilitate a rapid recovery. IPLAs have been used since the time as early as 1950. IPLA (intra-peritoneal local anaesthetics) has been used to reduce shoulder tip pain, overall pain, nausea and vomiting, and the time of hospital stay.

Postoperative pain in laparoscopic surgeries is multi-factorial in origin: somatic due to port site incisions, visceral due to pneumo-peritoneum causing stretching there by trauma to the vessels and nerve endings of peritoneum, local acidosis and Phrenic nerve irritation causing shoulder tip pain (It has been reported in 35-63% of cases in gynaecological laparoscopic surgeries due to insufflated carbon dioxide and therefore, multimodal therapy may be needed to optimize pain relief. Local anesthetic techniques are part of the multimodal approach to postoperative pain management.

The reason for choosing the Intra-peritoneal route is to block the visceral afferent signalling, and thereby potentially modifying visceral nociception and providing analgesia. The local anesthetic inhibits nociception by affecting nerve membrane associated proteins and by inhibiting the release and action of prostaglandins and other agents that sensitize or stimulate the nociceptors and contribute to inflammation. Also IP route reduces the opioid consumption significantly there by reducing their side effects. This is the rationale of comparing Ropivacaine and Bupivacaine in our study. Further no comparative data on Bupivacaine and Ropivacaine have been reported.

Alkhamesi, et al. [5] utilized a novel aerosolization system that has been proven to be successful in delivering intra-peritoneal local anesthetics to treat postoperative pain.

Patients in the therapeutic group had less pain at all measured time points compared to the control group and their PCA usage was less.

Tinatin Kakchekeeva, et al. [6] during their study with Pressurized intra-peritoneal aerosol chemotherapy (PIPAC) done in animal studies has shown that the macroscopic stain distribution throughout the entire peritoneal cavity was homogeneous in the abdominal cavity including the small bowel and anterior abdominal wall and hidden surfaces such as the inferior aspect of the liver and the hilum of the liver.

Frelich, et al. [7] in their study of intra-peritoneal aerosolization of Bupivacaine undergoing Robotic assisted laparoscopic pyeloplasty have concluded that it is a simple, effective and low-cost method to reduce postoperative pain in children undergoing laparoscopic pyeloplasty.

Zanetta, et al. [8] in their study using intra-peritoneal nebulization of Bupivacaine in children undergoing robotic assisted laparoscopic reconstructive surgery concluded that plasma levels of Bupivacaine were lower probably due to reduced systemic absorption thus improved safety.

Kaufmann, et al. [2] in their randomized controlled study of evaluating pain relief by continuous intra-peritoneal nebulization of Ropivacaine in gynaecological laparoscopic surgeries found that it didn't improve patient's outcomes in terms of intra-operative and postoperative pain along with consumption of analgesics that indicated a further research.

The results of these studies formed the basis for the present study, where the effects of intra-peritoneal nebulization of Ropivacaine 0.75% (4ML/ 30 MG) with Bupivacaine 0.5% (4ML /20 mg) for laparoscopic surgeries have been compared using the nebulizer available in our setting.

VAS scores – static and dynamic

The finding of this study is that, in comparison with the patients belonging to Bupivacaine group, the patients of Ropivacaine group experienced statistically significantly reduced dynamic VAS scores in first 6 hours ($p < 0.05$) and not statistically significant at 24 hours ($p > 0.05$). Static VAS scores were however not statistically significant over 24 hours.

Ingelmo, et al. [9] in their RCT comparing Ropivacaine nebulization versus Normal Saline for postoperative analgesia in laparoscopic cholecystectomy also obtained similar results with 33% reduction in dynamic VAS scores.

Alkhamesi, et al. [5] in their study on patients undergoing laparoscopic Roux En Y gastric bypass using Bupivacaine aerosolization technique to reduce postoperative pain have found that mean pain scores over 24 hours were not statistically significant (p=0.52). This may be due to their use of PCA regularly even if they had no pain.

Kaufman, et al. [2] in their randomized study for pain relief by continuous intra- peritoneal nebulization of Ropivacaine during gynaecological laparoscopic surgeries observed that no significant difference existed between the groups in postoperative Visual Analog Scale scores including visceral, abdominal wall, and shoulder pain during rest and during cough at the different time frames.

This might be due to use of Fentanyl for every 20% rise in MAP intra-operatively and Diclofenac per rectal after induction which might have masked early pain. Also sample size of 40 may not have been adequate to effectively evaluate the results. Also, the duration of surgery haven't been mentioned in the study.

Time for first requirement of rescue analgesic

Time for first requirement of rescue analgesic is also less in Ropivacaine group when compared to Bupivacaine group of patients (8.23+/-0.5(R) Vs 7.59+/-0.52(B)) and it was found to be statistically significant (p=0.0001).

Solankhi Rekha, et al. [10] in their study comparing intra-peritoneal instillation versus nebulization for laparoscopic surgeries for postoperative pain relief using Ropivacaine plus morphine in either groups found that the requirement for first rescue analgesic was 17.57+/- 0.02 hours.

It is almost twice that compared to present study which might have been due to addition of morphine and a larger dose of the drug 100 mg against 30 mg used in the present study.

Dolphine Betton, et al. [11] in their study observed that the pharmacokinetic profile of Ropivacaine nebulization is similar to direct intra-peritoneal instillation but with a lower absorption rate, resulting in prolonged duration of analgesia.

Total analgesic consumed

Also there was reduction in total analgesic consumed over 24 hours though not quite statistically Significant (p=0.06). Ingelmo, et al. [9] found that the morphine requirements were reduced by 41% in Ropivacaine nebulization group.

Zanetta, et al. [8] in their study using Bupivacaine nebulization for postoperative pain relief in children undergoing robotic assisted laparoscopic urological reconstructive procedures have concluded that total opioid requirement reduced by half when compared to historical controls.

Kaufmann, et al. [2] found that with Ropivacaine nebulization there was no reduction in total analgesic requirements (p=0.52) over 24 hours. The use of per rectal Diclofenac immediately after induction might have had pre-emptive analgesic effect. Also Inj. Fentanyl 1 mcg/kg for every 20% rise in MAP might have had accumulative effect.

Time of unassisted ambulation

Time of unassisted ambulation were similar (12.8+/-0.61(R) vs. 13.16+/-0.6(B), p=0.519). Catenacci, et al. [12] concluded that Ropivacaine nebulization resulted in early mobility Post-operatively and time taken for unassisted ambulation was 12+/-6 hours. Ingelmo, et al. [9] observed that Ropivacaine nebulization was associated with early mobility (10-12 hours vs. 18 hours i.e. 44% reduction in time required for early ambulation in comparison with Saline controls). Marata Somaini, et al. [13] found that patients after receiving Ropivacaine nebulization could walk without assistance within 12 hours of awakening.

Shoulder tip pain

None of the patients belonging to either group complained of shoulder tip pain in this study. Ingelmo, et al. [9] observed that there was no incidence of shoulder tip pain in Ropivacaine nebulization group as compared to Normal Saline control 100% reduction in shoulder tip pain.

Solanki Rekha, et al. [10] found that the incidence of shoulder tip pain was zero in Ropivacaine nebulization group.

Instillation of local anaesthetics in the supine position might prevent its flow over the celiac plexus and Phrenic nerve endings whereas nebulization provides uniform distribution giving better results.

Volume and dose nebulised in present study: In the present study volume nebulised was 4 ml corresponding to 30 mg of Ropivacaine 0.75% and 20 mg of Bupivacaine 0.5%.

Marta Somaini [13], Ingelmo, et al. [9] used 30 mg 1% 3 ml Ropivacaine in their studies conducted on patients undergoing laparoscopic gynaecological surgeries and laparoscopic cholecystectomies respectively and obtained statistically significant pain relief after surgery.

Labaille, et al. [14] used intra-peritoneal Ropivacaine during laparoscopic cholecystectomy in the dose of 100 mg and 300 mg and found reduction in postoperative pain. However, they did not find any statistically significant difference in visceral pain scores, time to first rescue morphine in PACU, total consumption of morphine and incidence of PONV. Smaller dosage provided similar analgesia with significantly smaller plasma concentrations than the larger dosage.

Hemodynamic parameters

Intra-operatively there were statistically significant differences in SBP and MAP of both the groups at 15 and 30 min post nebulization and at extubation. Diastolic blood pressure was not significantly difference. Postoperatively there was no significant difference between MAP of both the groups at any of times measured.

Kaufman, et al. [2] in their study found that no significant differences existed between the groups during surgery and at the recovery department in terms of mean arterial blood pressure (p= 0.42) or heart rate (p=0.60). Events of insufficient analgesia as expressed by a 20% elevation in MAP were less frequent in the study group than in the control group only at the time interval between 15 and 30 minutes from beginning of surgery (5% vs. 40%, p= .02). This difference was not found regarding heart rate.

Solankhi Rekha, et al. [10] observed that there was no significant difference in hemodynamic changes in intra-operative as well as postoperative periods between instillation and nebulization groups.

Signs of toxicity

Signs of toxicity such as arrhythmias, hypotension, delayed awakening were not noted in any of the two groups in the present study.

There is no record of clinical signs of local anaesthetic systemic toxicity amongst all the previous studies.

Post-operative nausea and vomiting: There were no significant differences in the proportion of patients with PONV (p value= 0.54).

In the study by Solankhi Rekha, et al. [10] the incidence of PONV was, none presented with nausea and 2 out of 30 in nebulization group presented with vomiting. It would have been probably due to more emetogenic potential of Tramadol when compared to morphine given postoperatively.

A study by Goldstein, et al. [15] comparing instillation of Bupivacaine with that of Ropivacaine at the sub-diaphragmatic and surgical sites showed that 20 ml of 0.75% Ropivacaine provided significantly better analgesia than 20 ml of 0.5% Bupivacaine in gynaecologic laparoscopy. Both local anaesthetics were equally effective in prevention of PONV.

Nebulization system

The nebulization system (NUNEB PRO) is a piston compression type nebulizer generating particles of 0.5-5 microns with airflow of around 8 Lit/min. To avoid accidents due to air insufflation harmonic scalpel was used in the intra-operative period.

Zimmer and colleagues [16] used the Insuflow device, which is a hot evaporation- based nebulizer. It is not surprising that these authors did not observe any analgesic benefits from nebulising Bupivacaine 0.5% (10 ml), because hot evaporation enables only evaporation of the solvent (e.g. water) and not of the solute (e.g. local anesthetic), thus making the device inefficient in delivering the local anaesthetic into the peritoneal cavity. This suggests that studies evaluating the effects of peritoneal nebulization should use a device suitable to deliver the local anaesthetic.

One of the limitations of the nebulization technique is that the small droplets size creates a "foggy" environment, which may interfere with the surgeon's vision. In the present study fogging was not a limiting problem mentioned by the surgeon. Low volume of the drug was used intentionally to reduce the fogging effect and also reduce the time required for nebulization.

Conclusion

From the present study, it is concluded that both Bupivacaine and Ropivacaine are safe and similarly efficacious in reducing postoperative pain following intra-peritoneal nebulization in laparoscopic surgeries and Ropivacaine nebulization significantly reduced dynamic VAS scores over 24 hours. Prolonged duration of analgesia was noted with Ropivacaine nebulization. Total analgesic required over 24 hours was less with Ropivacaine use. Ropivacaine group could ambulate early. No signs of local anaesthetic allergy and toxicity were observed. Thus the local anesthetic spread uniformly throughout the peritoneal cavity as well as to the most remote parts of the peritoneum may be beneficial to improve pain relief after Laparoscopic procedures.

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