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OPIOID SPARING & SUPPRESSION OF HEMODYNAMIC RESPONSE BY PREOPERATIVE MULTIMODAL NON-OPIOID ANALGESIC REGIME IN LAPAROSCOPIC SURGERIES UNDER GENERAL ANAESTHESIA: A PROSPECTIVE RANDOMIZED COMPARATIVE STUDY

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ABSTRACT: Background & Aims: Laparoscopic surgeries produces significant hemodynamic changes leading to increased opioid consumption. This study aims to assess the efficacy of a unique opioid free multimodal analgesia in the prevention of adverse hemodynamic changes during intubation and pneumoperitoneum in a patient undergoing laparoscopic surgery in comparison with standard opioid based anaesthesia. **Material & Methods:** Sixty patients undergoing elective laparoscopic surgery were randomly assigned into two groups Group OFA (Opioid Free Anaesthesia) received tablet pregabalin 150mg 1hour prior to induction. Intravenous ketorolac 30mg, magnesium sulphate 30 mg/kg, preservative free lidocaine 1.5mg/kg, dexamethasone 8mg was administered as an analgesic mixture in 100ml normal saline half an hour prior to induction. Dexmedetomidine 1mcg/kg diluted in 100ml saline was given over 10minutes prior to induction. Group OBA (Opioid Based Anaesthesia) received placebo tablet 1hour prior to induction,100ml normal saline half an hour prior to induction and 100 ml saline was given over 10minutes prior to induction. The primary outcome was to compare the efficacy of hemodynamic suppression to intubation and pneumoperitoneum. Other outcome parameters observed were perioperative analgesia, opioid sparing and adverse effects. **Results:** Significant suppression of heart rate and blood pressure following intubation and pneumoperitoneum by OFA multimodal regime was seen compared to Opioid based technique ($P < 0.05$) along with prolonged duration of postoperative analgesia (9.45+/-3.6 vs 4.03+/-1.6 hrs). **Conclusion:** Our unique non-opioid multimodal regime is a safe and effective method that provides significant suppression of stress responses induced during laparoscopic surgery.

INTRODUCTION: Laparoscopic surgeries are preferred in present days due to multiple benefits like better visualization of operating field, minimal surgical scar, lesser post-operative pain along with decreased length of hospital stay, reduced morbidity and mortality [1, 2].

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Laryngoscopy, intubation and pneumoperitoneum during laparoscopy are associated with increased hemodynamic response like tachycardia, hypertension, increased systemic and pulmonary vascular resistance which can predispose to cardiac ischemia [3-6].

Opioid analgesics are commonly used for perioperative pain relief and to suppress hemodynamic response to intubation and pneumoperitoneum. However, there is inadequate pain relief and hemodynamic suppression along with several side effects like dizziness, sedation,

nausea, constipation, vomiting, physical dependence, muscle rigidity, tolerance, respiratory depression and addiction. Multiple non-opioid analgesics like local anaesthetics, clonidine, dexmedetomidine, ketamine, gabapentin, magnesium sulphate, dexamethasone has been used individually and in varying combinations with acceptable results in maintaining antinociception, but suppression of hemodynamic response has variable results [7-17]. We hypothesised that use of non-opioid drugs with different targets in combination as part of a multimodal strategy may produce better suppression of hemodynamic response, better perioperative pain relief and can eliminate opioid related side effects along with enhanced recovery after surgery, with less potential for addiction. There are limited studies on multimodal non-opioid strategy for suppression of hemodynamic response to intubation and pneumoperitoneum in comparison with standard opioid regimen. This study aims not only to compare the effect of multimodal non-opioid therapy on the suppression of hemodynamic response to intubation and pneumoperitoneum but also to evaluate perioperative pain relief, opioid sparing effect, analgesic consumption and side effects if any.

MATERIAL & METHODS: A prospective, double blinded, randomized, and comparative study was conducted after Institutional Ethical Committee approval (RRMCH-IEC/38/2023, 22/05/2023), Clinical Trial Registry-India (CTRI) registration (CTRI/2023/06/053847, 14/06/2023), and informed written consent of the patients explaining the drugs used, fascial plane blocks performed and their postoperative analgesic effect. 60 patients with normal BMI aged 18-65 years of either gender with American Society of Anaesthesiologists (ASA) I and II status undergoing elective laparoscopic surgeries under general anaesthesia were included in the study. Patients refusing to participate in the study, obese individuals, difficult airway, uncontrolled hypertension, diabetes, cardio-respiratory disorder, allergy to study drugs, neuro-psychiatric disorders, pregnant or lactating mothers, hepatic and renal dysfunction, alcoholics, patient on opioids, sedatives, beta-blockers were excluded from the study. Randomization was done using computer generated randomization software and group allocation was concealed by sealed opaque envelopes which was opened in the preoperative room. Randomization and preparation of the study drug was done by principal investigator. Patient and person administering the study drugs and assessing their outcome measures were blinded to group allocation. Administration and assessment was done by a second anaesthesiologist. Any adverse effects were reported to the principal investigator, blinding would be revealed and the patient would be appropriately treated and excluded from the study.

Group OFA (Opioid Free Anaesthesia): Received tablet pregabalin 150mg 1hour prior to induction. Intravenous ketorolac 30mg, magnesium sulphate 30 mg/kg, preservative free lidocaine 1.5mg/kg, dexamethasone 8mg were administered as an analgesic mixture in 100ml normal saline half an hour prior to induction. Dexmedetomidine 1mcg/kg diluted in 100ml saline was given over 10minutes prior to induction.

Group OBA (Opioid Based Anaesthesia): Received placebo tablet 1hour prior to induction. 100ml normal saline half an hour prior to induction. 100ml saline was given over 10minutes prior to induction.

General anaesthesia was administered with glycopyrrolate 5 mcg/kg, 2mcg/kg fentanyl diluted to 10ml in Group OBA and Group OFA received10ml normal saline. Patients were pre-oxygenated with 100% oxygen for 3 minutes and then induced with Injection propofol 30 mg over10s till loss of verbal response. Intubation by experienced anaesthetist using appropriate sized endotracheal tube was facilitated with 0.1 mg/kg vecuronium and anaesthesia maintenance was done using oxygen, air, isoflurane, and intermittent doses of vecuronium 0.02 mg/kg. Both groups received ultrasound-guided bilateral transversus abdominal plane (TAP) block with 20 ml of 0.125% bupivacaine injected bilaterally after completion of surgery. Patients were extubated after meeting the extubation criteria. Heart rate (HR) and blood pressure changes were noted before and after administration of study drug, immediately after induction, after intubation at 1,3 and 5minutes, post-pneumoperitoneum every 15 minutes till the end of surgery. Additional doses of fentanyl (25–50

mcg) and propofol (20–30 mg) were given if HR and SBP (Systolic Blood Pressure) increased more than 20%during surgery. Total consumption of fentanyl and propofol were noted. Depth of anaesthesia was monitored using Bi-spectral index monitor to maintain adequate depth of anaesthesia (40-60). Patients were transferred to post anaesthesia care unit to monitor postoperative pain, sedation, nausea and vomiting at 0, 1, 2, 4, 6, 8, 12, 16, 20, 24 hrs. Postoperative pain was assessed using a standard 10 cm linear VAS. When VAS score was more than or equal to 4, IV Paracetamol 1gm IV as rescue analgesia was given and the time of first rescue analgesic administered was recorded. Once the patient received first dose rescue analgesia, Intravenous (IV) paracetamol 1gm was given 8th hourly thereafter. If the VAS score was more than or equal to 4 or if patient demanded additional analgesia, IV tramadol 50mg was administered and the total number of doses were recorded in 24 hrs.

Sample size: Pilot study was conducted. Sample size was estimated by using mean HR at 5 minutes following intubation. To detect at least 20% of difference in HR amongst study groups at 95% confidence interval, 90% power, sample size of 26 was obtained. Assuming 10% dropout, we recruited 30 patients in each group.

$$\text{Sample size (N)} = 2SD^2 (Z_{\alpha/2} + Z_{\beta})^2 / d^2$$

SD – Standard deviation = from previous studies or pilot study

$Z_{\alpha}/2 = Z0.05/2 = Z0.025 = 1.96$ (From Z table) at type 1error of 5%

$Z_{\beta} = Z0.20 = 0.842$ (From Z table) at 80% power

d = effect size = difference between mean values

Statistical Analysis Method: Data was entered into Microsoft excel data sheet and analysed using SPSS 22 version software (IBM SPSS Statistics, Somers NY, USA). Categorical data was represented in the form of Frequencies and proportions and continuous data as mean and standard deviation. Chi-square test or Fischer's exact test was used as test of significance for Categorical data and Student t test for Quantitative data. Independent t test was used to compare mean between two groups or Mann Whitney U test was used to compare median when Independent t test showed to be invalid or distribution was skewed. Paired t test was used for paired data before and after intervention or surgery or anaesthesia or Wilcoxon Signed rank test would be the test of significance for paired data such as before and after surgery for quantitative data with skewed distribution. p value <0.05 was considered as statistically significant.

RESULTS: Study was adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines. Patient Recruitment is illustrated in Consort flow diagram **Fig. 1.**

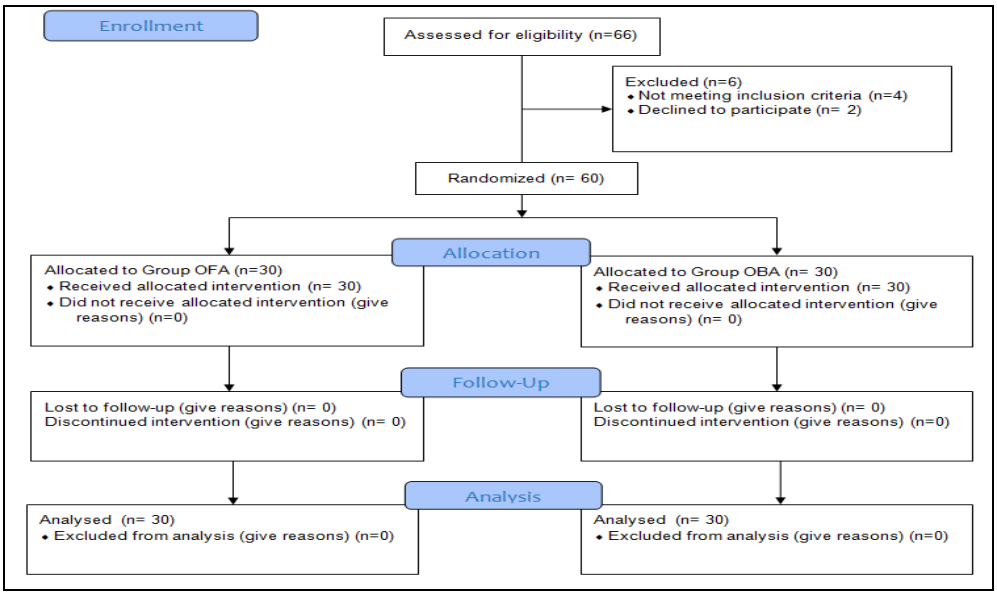

FIG. 1: CONSORT FLOW DIAGRAM

Demographic profile was comparable in both the groups **Table 1.** Heart rate post-intubation and post-pneumoperitoneum was significantly better controlled in group OFA compared to group OBA **Table 3.**

TABLE 1: DEMOGRAPHIC PROFILE OF THE PATIENTS IN BOTH GROUPS

Variables	Group OFA (n= 30)	Group OBA (n= 30)
Age (yr), Mean (SD)	40.33 (12.073)	40.07 (13.133)
Gender (n) (%)		
Male	11 (36.7%)	12 (40.0%)
Female	19 (63.3%)	18 (60.0%)
ASA grade		
1	11	17
2	19	13
BMI (mean) (SD)	21.1 (2.59)	20.6 (3.01)

TABLE 2: VARIOUS SURGERIES PERFORMED DURING THE STUDY

		Group			
		Group OFA		Group OA	
		Count	%	Count	%
Surgery	Diagnostic laparoscopy	0	0.0%	4	13.3%
	IPOM (Intraperitoneal On lay Mesh repair)	1	3.3%	5	16.7%
	Lap appendectomy	3	10.0%	4	13.3%
	Lap cholecystectomy	19	63.3%	17	56.7%
	Lap hernia mesh repair	7	23.3%	0	0.0%

TABLE 3: COMPARISON OF HEART RATE AMONG BOTH THE GROUPS

	Group				P value
	Group OFA		Group OA		
	Mean	SD	Mean	SD	
Baseline HR	84.37	9.03	81.63	8.00	0.220
After administration of study drug HR	79.80	10.51	82.57	6.78	0.230
Induction HR	77.03	10.69	81.33	8.18	0.085
Intubation HR	85.40	11.98	96.07	6.96	0.000
Post Intubation HR 3m	83.30	10.32	94.57	7.02	0.000
Post Intubation HR 5 m	78.67	9.78	94.23	6.00	0.000
Pneumoperitoneum	78.50	8.36	94.37	6.26	0.000
HR 15	76.03	7.44	88.10	6.01	0.000
HR30	75.67	8.15	85.20	5.71	0.000
HR 45	74.63	7.66	83.77	4.88	0.000
HR 1h	75.90	7.95	83.23	5.49	0.000
HR 1h15mins	74.97	7.48	83.03	6.06	0.000
HR 1h30mins	75.87	7.74	82.53	5.55	0.000
HR 1h 45m	75.83	8.07	82.20	5.20	0.001
HR 2h	75.72	7.54	81.73	4.19	0.000
HR 2h 15m	74.35	8.59	82.74	3.96	0.000
HR 2h 30m	76.18	8.68	83.33	3.72	0.008

SBP and DBP changes were controlled significantly in group OFA at all the time after intubation and pneumoperitoneum compared to group OBA. There was no incidence of hypotension or bradycardia in both the groups **Table 4** and **Table 5**. None of the patients required rescue analgesia (intravenous Fentanyl) in the intraoperative period in OFA group whereas 6 patients in group OBA required additional boluses of fentanyl for suppression of blood pressure during the course of surgery **Table 6.**

TABLE 4: COMPARISON OF SYSTOLIC BLOOD PRESSURE (SBP) AMONG BOTH THE GROUPS

	Group				P value
	Group OFA		Group OA		
	Mean	SD	Mean	SD	

SBP baseline	124.40	13.08	123.67	6.39	0.784
SBP after administration of study drug	121.47	11.22	123.10	5.87	0.483
SBP induction	112.23	12.63	117.90	8.90	0.049
SBP intubation	126.63	12.26	136.40	6.04	0.000
SBP intubation 3m	122.57	10.11	134.37	6.02	0.000
SBP intubation 5m	120.33	9.03	131.43	6.24	0.000
SBP Pneumoperitoneum	121.23	7.12	130.83	6.92	0.000
SBP 5 m	118.97	8.62	126.93	6.10	0.000
SBP15min	117.57	6.71	124.67	5.52	0.000
SBP30m	118.03	7.14	124.57	3.53	0.000
SBP 45m	117.43	7.24	123.37	3.37	0.000
SBP 1h	117.47	6.36	122.43	3.27	0.000
SBP 1H 15m	118.23	6.55	122.80	4.36	0.002
SBP 1H 30m	117.47	6.47	121.43	3.45	0.004
SBP 1h45m	119.53	5.78	122.47	4.35	0.030
SBP 2h	120.93	5.05	122.47	3.69	0.185
SBP 2h 15m	121.85	5.12	124.04	4.39	0.130
SBP 2h30m	120.36	6.76	124.25	3.00	0.052

TABLE 5: COMPARISON OF DIASTOLIC BLOOD PRESSURE (DBP) AMONG BOTH THE GROUPS

	Group				P value
	Group OFA		Group OA		
	Mean	SD	Mean	SD	
DBP Baseline	82.70	9.55	81.60	6.88	0.611
DBP after administration of study drug	78.77	9.10	81.17	5.83	0.229
DBP Induction	74.53	6.98	78.03	6.94	0.056
DBP intubation	84.80	7.59	91.07	3.42	0.000
DBP intubation 3m	79.50	7.64	89.97	3.99	0.000
DBP intubation 5m	77.30	6.75	86.77	4.45	0.000
DBP Pneumoperitoneum	78.83	5.24	86.20	4.16	0.000
DBP 5 m	77.87	4.63	83.07	5.41	0.000
DBP15min	77.23	3.49	81.80	3.81	0.000
DBP 30m	77.27	3.59	81.20	3.75	0.000
DBP 45m	76.30	4.05	80.80	2.85	0.000
DBP 1h	76.80	3.94	80.37	4.17	0.001
DBP 1H 15m	76.27	4.25	80.23	4.58	0.001
DBP 1H 30m	76.87	4.47	80.47	3.67	0.001
DBP 1h45m	77.50	3.54	80.73	3.18	0.000
DBP 2h	78.63	2.99	81.93	3.97	0.001
DBP 2h 15m	79.90	4.42	81.40	3.50	0.211
DBP 2h30m	78.73	2.72	82.37	3.36	0.006

TABLE 6: RESCUE FENTANYL REQUIRED IN BOTH THE GROUPS

		Group			
		Group OFA		Group OA	
		Count	%	Count	%
Consumption of fentanyl	20 mcg	0	0.0%	5	16.7%
	40 mcg	0	0.0%	1	3.3%
	Nil	30	100.0%	24	80.0%

Patients in group OFA had better pain relief post operatively for initial 8hrs as assessed by VAS scores. Patients in group OFA had prolonged duration of analgesia compared to group OBA (*P* value = <0.001).

TABLE 7: COMPARISON OF POST-OPERATIVE VISUAL ANALOGUE SCALE (VAS) SCORES AMONG BOTH THE GROUPS

	Group						P value
	Group OFA			Group OA			
	Mean	SD	Median	Mean	SD	Median	
VAS Bassline	.17	.46	0	1.67	.61	2	0.000

VAS 1 h	.57	.68	0	2.00	.79	2	0.000
VAS 2 h	1.07	.74	1	3.10	1.16	3	0.000
VAS 4 h	1.87	1.25	2	3.73	1.60	3	0.000
VAS 6 h	2.10	1.03	2	3.33	1.79	3	0.002
VAS 8 h	3.40	1.89	3	4.13	1.93	3	0.142
VAS 12 h	3.03	1.77	3	3.80	1.67	3	0.090
VAS 16 h	2.03	1.54	2	2.43	1.14	2	0.257
VAS 24 h	.80	.71	1	1.80	.61	2	0.000

TABLE 8: POST-OPERATIVE DURATION OF ANALGESIA

Group Statistics					
	Group	**N**	**Mean**	**SD**	**P value**
First rescue analgesia (hrs)	Group OFA	29	9.45	3.621	<0.001*
	Group OA	30	4.03	1.671	

Few patients experienced nausea and vomiting in OBA group. No other complications in any of the patients **Table 9.**

TABLE 9: POST-OPERATIVE COMPLICATIONS IN BOTH THE GROUPS

		Group			
		Group OFA		**Group OA**	
		Count	**Column N %**	**Count**	**Column N %**
Complications	Nil	30	100.0%	25	83.3%
	Nausea	0	0.0%	4	13.3%
	Vomiting	0	0.0%	1	3.3%

DISCUSSION: This study evaluated the effect of OFA on the haemodynamic suppression, opioid sparing effect, perioperative pain relief in patients undergoing laparoscopic surgery. We found that patients who received OFA had a better suppression of haemodynamic response to laryngoscopy and pneumoperitoneum without requirement of rescue opioids than those who received opioid-based anaesthesia with fentanyl. Furthermore, better perioperative pain relief, prolonged duration of analgesia, without any adverse effects confirm that OFA is a safe and easy technique in laparoscopic surgeries.

In recent days, opioids are used sparingly to prevent opioid related adverse effects which influence patient outcomes and cost, all of which can be achieved by using non-opioid analgesics. Initially opioid free multimodal analgesia was used for postoperative pain relief and to minimize adverse effects from individual agents, of late, its use has been extended to the entire perioperative period to improve haemodynamic stability, recovery, along with reducing the opioid requirements [18-21]. Although OFA is used in various surgeries with variable results, there is still controversy about the choice of agents [22]. In our study, we used a combination of easily available medications in combination as pre-emptive analgesia at different phases prior to induction of anaesthesia. Drugs which we included were gabapentin, ketorolac, dexamethasone, lidocaine, magnesium sulphate and dexmedetomidine within their dose limits without adverse events proving that the combination and dosage is highly effective and safe.

Dexmedetomidine is an alpha-2 agonist with analgesic action that causes far less hypotension than clonidine. Blood pressure transiently rises following dexmedetomidine administration followed by a drop to ten percent below baseline values. Unlike opioids it is not associated with significant respiratory depression, Postoperative nausea vomiting (PONV), pruritus, constipation, ileus or delirium. It can reduce intraoperative opioid administration by more than 50%. In laparoscopic surgeries, it has been found to provide adequate analgesia when used as the sole analgesic. It has been shown to provide better heart rate control post intubation than fentanyl when used for intravenous induction [23, 24, 25].

Intravenous Iidocaine: Lidocaine is an amino-amide local anesthetic that has a profound analgesic effect and has been shown to significantly reduce opioid requirements and side effects. The loading dose is 1-2 mg/kg followed by

an infusion of 1-2 mg/kg/hr. The rate should be reduced by 50% every 6 hours. In abdominal operations lignocaine reduced ileus, PONV, and has been shown to be of similar efficacy to epidural administration of local anesthetic. This may be an effective neuroprotective agent to prevent early post-operative cognitive dysfunction. It is also effective for neuropathic pain [23, 24].

Magnesium Sulphate: Magnesium (Mg) produces analgesic action by regulating calcium flux into the cell and acting as an NMDA receptor antagonist. It also suppresses neuropathic pain. This has been shown to reduce the need for post-operative opioids and improve post-operative pain scores. The loading dose is 30-50 mg/kg and may be followed up by an intravenous infusion of 10 mg/kg/hr [23, 24]. Ketorolac is a non-steroidal anti-inflammatory drug with significant analgesic action. Single dose systemic ketorolac is an effective adjunct in multimodal regimens to reduce postoperative pain [26].

Gabapentin/Pregabalin: Gabapentinoids are derivatives of the inhibitory neurotransmitter gamma aminobutyric acid (GABA). Both gabapentin 300 mg PO (PER ORAL) and pregabalin 150 mg PO are effective analgesics that are effective in neuropathic pain. Their use leads to lower pain scores, reduced opioid consumption and opioid related side effects [23].

In the current study, significant suppression of heart rate and blood pressure following intubation and pneumoperitoneum was seen in all patients of OFA group whereas haemodynamic parameters remained stable in 80% of the patients. In a study conducted by Ramanarayanan Ragupathy *et al* [16] who aimed at comparing anaesthetic doses of lidocaine, magnesium and paracetamol in combination with fascial plane block for post-operative pain relief in laparoscopic surgeries on 60 patients, they found inadequate hemodynamic suppression. This shows that our non-opioid multi-modal regimen had better haemodynamic stability. *Mefkur Bakan et al* [17]conducted a study using opioid-free anesthesia with dexmedetomidine, lidocaine, and propofol infusions (Group DL) or opioid-based anesthesia with remifentanil, and propofol infusions (Group RF) in laparoscopic cholecystectomy surgery and concluded that opioid-free TIVA with dexmedetomidine, lidocaine and propofol infusions is associated with lower fentanyl requirements. Also, maximum-NRS, rescue analgesic need and ondansetron use was significantly lower in the opioid-free group in the first postoperative day. Similar to the above study, our results show that in OFA group, total analgesic consumption was less, and none required opioid as rescue analgesia in intraoperative period, whereas in the conventional opioid group 6 patients required rescue fentanyl. 26 patients in group OBA required tramadol 50 mg secondary to paracetamol as they had a higher VAS score whereas only 4 patients required second rescue analgesic in group OFA. It follows that a multimodal analgesic approach will eliminate the need for opioids in the perioperative period. TAP block was used in both the groups as a multimodal approach which contributed to the prolonged duration of analgesia in OFA group.

Several studies using various regimens have been done for opioid-free anaesthesia. An RCT showed that using propofol, dexmedetomidine and lignocaine infusions for laparoscopic cholecystectomy was associated with lower VAS scores, reduced analgesic consumption and reduced incidence of post-operative nausea and vomiting[17]. In this study, none of the patients in OFA group experienced significant adverse effects of opioids in the post-operative period like nausea, vomiting and respiratory depression.

Limitations of this Study: Recovery profile and time of discharge were not noted. Further randomized controlled trials would be required to explore the benefits of this regime on other surgeries and study of other parameters could make it more comprehensive.

CONCLUSION: This opioid free multimodal analgesia along with TAP block in laparoscopic surgeries produces significant haemodynamic suppression to intubation and pneumoperitoneum along with opioid sparing effect, better postoperative pain relief with lower VAS scores, increased duration of analgesia as compared to the standard conventional opioid anaesthesia.

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REFERENCES:

1. Rao LN: A clinical study of dexmedetomidine for maintenance during general anaesthesia for laparoscopic surgeries. Int J Med Sci Clin Invent 2015; 2: 681-7.
2. Srivastava VK, Agrawal S, Gautam SK, Ahmed M, Sharma S and Kumar R: Comparative evaluation of esmolol and dexmedetomidine for attenuation of sympathomimetic response to laryngoscopy and intubation in neurosurgical patients. Journal of Anaesthesiology Clinical Pharmacology 2015; 31(2): 186-90.
3. Chraemmer-Jørgensen B, Hertel S, Strøm J, Høilund-Carlsen PF and Bjerre-Jepsen K: Catecholamine response to laryngoscopy and intubation. The influence of three different drug combinations commonly used for induction of anaesthesia. Anaesthesia 1992; 47(9): 750-6.
4. Manne GR, Upadhyay MR and Swadia VN: Effects of low dose dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy. Indian Journal of Anaesthesia 2014; 58(6): 726.
5. O'leary E, Hubbard K, Tormey W and Cunningham AJ: Laparoscopic cholecystectomy: haemodynamic and neuroendocrine responses after pneumoperitoneum and changes in position. British Journal of Anaesthesia 1996; 76(5): 640-4.
6. Bhattacharjee DP, Nayek SK, Dawn S, Bandopadhyay G and Gupta K: Effects of dexmedetomidine on haemodynamics in patients undergoing laparoscopic cholecystectomy-A comparative study. Journal of Anaesthesiology Clinical Pharmacology 2010; 26(1): 45-8.
7. Victory RA, Gajraj NM, Pace NA, Ostman LP and White PF: Nebulized bupivacaine attenuates the heart rate response following tracheal intubation. Journal of Clinical Anesthesia 1995; 7(1): 9-13.
8. Singh H, Vichitvejpaisal P, Gaines GY and White PF: Comparative effects of lidocaine, esmolol, and nitroglycerin in modifying the hemodynamic response to laryngoscopy and intubation. Journal of Clinical Anesthesia 1995; 7(1): 5-8.
9. Inada E, Cullen DJ, Nemeskal AR and Teplick R: Effect of labetalol or lidocaine on the hemodynamic response to intubation: a controlled randomized double-blind study. Journal of Clinical Anesthesia 1989; 1(3): 207-13.
10. Ghignone M, Quintin L, Duke PC, Kehler CH and Calvillo O: Effects of clonidine on narcotic requirements and hemodynamic response during induction of fentanyl anesthesia and endotracheal intubation. Anesthesiology 1986; 64(1): 36-42.
11. Charuluxananan S, Kyokong O, Somboonviboon W, Balmongkon B and Chaisomboonpan S: Nicardipine versus lidocaine for attenuating the cardiovascular response to endotracheal intubation. Journal of Anesthesia 2000; 14(2): 77-81.
12. Kutlesic MS, Kutlesic RM and Mostic-Ilic T: Attenuation of cardiovascular stress response to endotracheal intubation by the use of remifentanil in patients undergoing Cesarean delivery. Journal of Anesthesia 2016; 30(2): 274-83.
13. Min JH, Chai HS, Kim YH, Chae YK, Choi SS, Lee A and Choi YS: Attenuation of hemodynamic responses to laryngoscopy and tracheal intubation during rapid sequence induction: remifentanil *vs*. lidocaine with esmolol. Minerva Anestesiolica 2010; 76(3): 188-92.
14. Bohringer C, Astorga C and Liu H: The Benefits of Opioid Free Anesthesia and the Precautions Necessary When Employing It. Translational Perioperative and Pain Medicine 2020; 7(1): 152-157.
15. Suvarna Kaniyil and Christopher Haley: Opioid-Free Anaesthesia.
16. Anaesthesia Tutorial of the Week 461 — Opioid-Free Anaesthesia (14 December 2021).
17. Ragupathy R, Prabhu SCG, Thiyagarajan D and Anto V: Opioid-free anaesthesia for laparoscopic surgeries - A prospective non-randomised study in a tertiary care hospital. Indian Journal of Anaesthesia 2022; 66(3): 207-212.
18. Bakan M, Umutoglu T, Topuz U, Uysal H, Bayram M and Kadioglu H: Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: A prospective, randomized, double-blinded study. Brazilian Journal of Anesthesiolog. 2015; 65: 191–199.
19. Alexander JC, Patel B, Joshi GP: Perioperative use of opioids: Current controversies and concerns. Best Practise and Research: Clinical Anaesthesiology 2019; 33: 341–51.
20. Kehlet H and Dahl JB: The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. Anesthesia Analgesia 1993; 77: 1048–56
21. Gustafsson UO, Scott MJ, Hubner M, Nygren J, Demartines N, Francis N, Rockall TA, Young-Fadok TM, Hill AG, Soop M, de Boer HD, Urman RD, Chang GJ, Fichera A, Kessler H, Grass F, Whang EE, Fawcett WJ, Carli F, Lobo DN, Rollins KE, Balfour A, Baldini G, Riedel B and Ljungqvist O: Guidelines for perioperative care in elective colorectal surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations 2018. World J Surg 2019; 43: 659–95.
22. Koepke EJ, Manning EL, Miller TE, Ganesh A, Williams DGA and Manning MW: The rising tide of opioid use and abuse: The role of the anesthesiologist. Perioperative Medicine 2018; 7: 16.
23. Shanthanna H, Ladha KS, Kehlet H and Joshi GP: Perioperative opioid administration. Anesthesiology 2021; 134(4): 645–659.
24. Min JH, Chai HS and Kim YH: Attenuation of hemodynamic responses to laryngoscopy and tracheal intubation during rapid sequence induction: remifentanil vs Minerva Anestesiolica 2010; 76(3): 188-192.
25. Christian Bohringer, MD, Carlos Astorga, MD, Hong Liu, MD and FASE: The Benefits of Opioid Free Anesthesia and the Precautions Necessary When Employing It. Translational Perioperative and Pain Medicine 2020; 7(1): 152–157.
26. Laha A, Ghosh S and Sarkar S: Attenuation of sympathoadrenal responses and anaesthetic requirement by dexmedetomidine. Anaesth Essays and Researches 2013; 7: 65–70
27. De Oliveira GS, Agarwal D and Benzon HT: Perioperative single dose ketorolac to prevent postoperative pain: a meta-analysis of randomized trials. Anesthesia & Analgesia 2012; 114(2): 424-33.

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