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Original Research Article

Evaluating the efficacy and safety of simple combination of analgesics with and without low dose opioid for perioperative analgesia, hemodynamic and recovery profile in various surgeries posted under general anaesthesia: a prospective randomised controlled study

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ABSTRACT

Background: Multimodal analgesia is an emerging technique.It has been consistently demonstrated to minimise opioid consumption, related side effects and vital component of enhanced recovery after surgery pathways. The current study presents use of combination of readily available medication as a part of multimodal analgesia. Balanced anaesthesia with multimodal analgesia is harmonious use of combination of agents to produce desired effects with minimal side effects of individual agents.
Methods: This study was done in a tertiary health care centre, Government General Hospital, Kakinada over a duration of two months from August 2022 to September 2022. 60 adult patients of either sex of physical status ASA grade 1and 2 undergoing elective surgery under general anaesthesia were randomly allocated into Group A and Group B of 30 patients. Group 1: received Inj. Lignocaine+Inj. Paracetamol+Inj. Magnesium sulphate+Inj. Fentanyl. Group 2:received Inj. Lignocaine+Inj. Paracetamol+Inj. Magnesium sulphate+Normal saline (control group) as premedication for perioperative analgesia.
Results: All patients were hemodynamically stable for first 30 minutes period of observation in Group A compared to Group B. There is clinically and statistically significant difference in the duration of analgesia in Group A compared to Group B. There is no statistically significant difference in the Numerical Rating Scale (NRS) for pain in both the groups.
Conclusions: This study concluded that simple analgesia combination of multimodal analgesia regimen comprising of Inj. Lignocaine, Inj. Paracetamol and Inj. Magnesium sulphate produces safe and effective analgesia with good recovery profiles and no adverse opioid related side effects for ASA 1 and 2 patients posted under general anaesthesia.

Keywords: Multimodal analgesia, Minimal opioid, Recovery profiles

INTRODUCTION

The best characterised clinical strategies include the use of multimodal analgesia (MMA) and enhanced recovery after surgery (ERAS) initiatives to provide standardise care and improve outcomes while providing satisfactory Perioperative pain control.[1] Opioids which are being routinely used as the part of a balanced anaesthesia are known to have lots of side effects such as respiratory depression, postoperative nausea and vomiting (PONV), pruritus, difficulty in voiding and ileus. These side effects prolong the patient's hospital stay.[2] MMA has been

consistently demonstrated to minimise opioid consumption and related side effects and is considered a vital component of ERAS pathway as proved in various studies.[3] Opioid free anaesthesia (OFA) is a technique in which no intraoperative opioid is administered via any route including systemic, neuraxial or tissue infiltration.[4] This technique relies on combination of non-opioid agents and adjuncts including Propofol, Dexmedetomidine, Lignocaine, Magnesium sulphate and Ketamine to produce anaesthesia, sympatholysis and analgesia.[5] In contrast to OFA. Traditional anesthetic protocols rely on intraoperative opioids to achieve these 3 important surgical conditions. Hence in this study the aim is to compare different combination of analgesics, opioid versus opioid free combination as a part of multimodal analgesia for patients posted for various surgeries under general anaesthesia.[6]

Aim and objectives

Aim of current study was to determine the efficacy and safety of combination of intravenous IV Lignocaine, Paracetamol, Magnesium sulphate and low dose fentanyl compared with intravenous IV Lignocaine, Paracetamol, Magnesium sulphate and Normal saline. Primary objective of the study is to assess the duration of analgesia. Secondary objectives of the study are to compare the hemodynamic variations and recovery profile.

METHODS

The comparative study was conducted over a period of 2 months from August 2022 to September 2022 among 60 patients who belong to ASA 1 and 2, aged between 30 to 55 years scheduled for elective surgeries posted under general anaesthesia of duration between 50 to 90 minutes in Government general hospital, Rangaraya medical college, Kakinada. After obtaining institutional ethics committee approval and informed written consent from the patients, this study population is allocated into two groups of 30 each. Sample size was estimated based on the previous clinical study taking into consideration alpha value of 0.05, beta error of 80% and margin of error 5%. Total number of subjects included 60 patients based on the above. Blinding: The anesthesiologist who is involved in abstraction and collection of data for clinical assessment is blinded to statistical analysis and vice-versa.

Inclusion criteria

Total of 60 patients who belonged to ASA 1 and 2, aged between 30-55 years either gender, BMI>25 kg/m2 scheduled for elective surgeries scheduled under general anaesthesia of duration of surgery between 50-90 mins were included.

Exclusion criteria

Exclusion criteria for current study were; refusal to give consent, ASA status >3, BMI >35 kg/m2, Chronic history of opioid usage and Patients having convulsions, meningitis and infections.

Procedure

All the 60 patients were thoroughly evaluated for Pre-Anesthetic Check Up, necessary investigations done and optimised for the elective surgery. Patients were then shifted to operation theatre and baseline vitals were recorded after connecting standard monitors. All patients received Inj. Glycopyrrolate (40 mcg/kg) IV, Inj. Ondansetron (0.1mg /kg) IV, Inj. Midazolam (0.05mg/kg) IV as premedication. Then the following infusions were given over 20 minutes with 2 litres /min O2 during premedication and was increased to 12 litres /minute during induction. Group A: was assigned to receive IV Lignocaine (1.5 mg/kg), Inj. Paracetamol (1gm) IV, Inj. Magnesium sulphate (40-52 mg/kg) IV and low dose fentanyl (1 mcg/kg) IV. Group B: was assigned to receive IV Lignocaine (1.5 mg/kg), Inj. Paracetamol (1gm) IV, Inj. Magnesium sulphate (40-52 mg/kg) IV and normal saline IV (5 cc). Patients of both the groups were induced according to standard GA protocol comprising of Inj, Propofol (1.5-2 mg/kg), Inj. vecuronium (0.1 mg/kg) and intubated with appropriate size ET tube. During maintenance of Anaesthesia hemodynamics (Heart rate (HR)and mean arterial pressures (MAP) were recorded throughout out the surgical procedure. At the end of the surgery all patients were reversed with standard reversal protocol Inj. Neostigmine (0.05 mg/kg) IV and glycopyrrolate (40 mcg/kg) IV. After reversal all the patients were shifted to recovery area where they were monitored for 1hr before being shifted into wards.

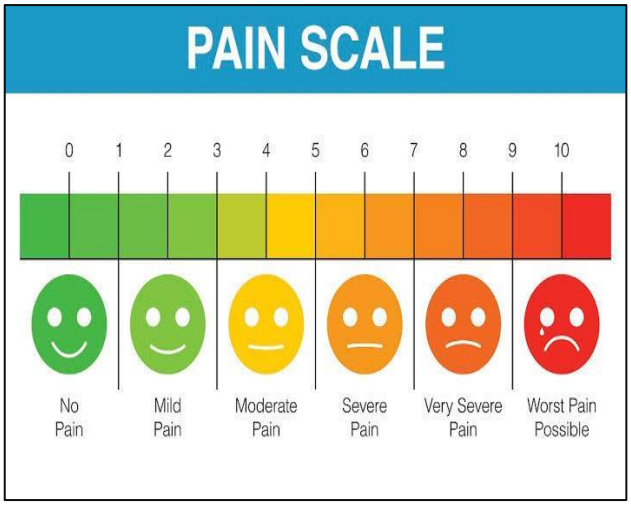

Figure 1: Numerical rating scale for assessment of pain.

Statistical analysis

Data were compiled, analysed using SPSS version 20 and presented as mean, standard deviation (SD), percentage, student t-test, Chi square test and Mann-Whitney's test. The p value was considered significant as if $p<0.05$.

RESULTS

A total of 60 patients were enrolled for the study of 30 patients in each group. All patients completed the study with no dropouts. In respect to demographic data, in both the groups Age, weight and duration of surgery were comparable (Table 1).

Table 1: Demography, age, weight, duration of surgery.

Parameters	N	Min	Max	Mean	SD
Age	60	30	55	49.32	±9.4
weight	60	50	84	68.91	±12.6
Duration of surgery (min)	60	60	120	84.2	±8.62

The percentage distribution of either gender was shown in (Table 2). Regarding ASA status, patients belonging to ASA grades 1and 2 were taken for study. Their percentage distribution was shown in (Table 3).

Table 2: Demographic distribution.

Sex	N	%
Male	32	53.3
Female	28	46.6

Table 3: ASA grading.

ASA	N	%
1	42	70
2	18	30

Table 4: Intraoperative mean HR.

Time (minutes)	Group A	Group B	P value
0	78.19±12.43	75.7±16.04	0.421
5	86.71±11.13	100.6±24.5	0.003
10	81.67±11.69	100.6±24.9	0.001
15	80.19±15.84	96.76±12.08	0.02
20	75.57±15.25	91.57±12.05	<0.001
25	72.76±11.1	81.33±16.60	0.04
30	71.67±12.55	86.67±18.717	0.02
45	71.24±10.44	79.38±15.03	0.51
60	70.48±9.616	76.76±13.6	0.476
75	74.45±12.1	76.18±9.8	0.72
90	79.51±14.4	81.21±7.8	0.34
120	80.21±9.2	98.24±6.9	0.001

It was observed that intraoperative mean heart rate was comparatively stable for the first 30 mins in group A compared to group B (control group) and was statistically significant since p value is <0.05 (Table 4). The mean arterial pressures (MAP) were also stable among group A during the intraoperative period and was statistically significant since p value is <0.05 (Table 5).

Table 5: Intraoperative mean MAP.

Time (minutes)	Group A	Group B	P value
0	93.2±7.5	95.9±7.7	0.117
5	101.8±6.6	103.1±7.2	0.403
10	94.7±7.5	96.4±7.5	0.327
15	91.2±6.6	92.7±7.7	0.368
20	88.6±6.9	91.1±6.9	0.116
25	87.3±6.8	90.8±5.8	0.014
30	86.4±7.2	90.2±6.3	0.014
45	88.2±4.3	90.0±5.3	0.001
60	86.7±5.3	89.9±4.3	0.005
75	88.7±3.9	90.6±3.6	0.032
90	89.2±5.6	90±4.0	0.199
120	88.6±7.1	90.1±6.9	0.115

Table 6: Duration of Analgesia (Time to 1st request Analgesia).

Time (minutes)	Group A	Group B	P value
Time of 1st analgesic	65±8.27	45±6.72	0.004

Table 7: Maximum numerical rating scale.

Post operative time interval	Of group NRS score	O group NRS score	P value
1sthr	0	0	0.986
2ndhr	2.5	2.4	0.09
3rdhr	3.5	3.5	0.782
4thhr	3.8	4	0.52
5thhr	4	4	0.873
6thhr	1	0	0.23
9thhr	2	1.6	0.486
12thhr	4.5	4.3	0.637
18thhr	5.1	5	0.743
24thhr	7.6	7.4	0.061

Table 8: Emergence and recovery profile.

Emergency and recovery characteristics	Group A	Group B	P value
Emergence delirium	2	3	0.07
PONV	4	1	0.03
Bradycardia	1	0	0.784
Hypotension	1	0	0.73
Desaturation	0	0	-
Shivering	0	2	0.26
Adverse reactions	0	0	-
Recovery time (min)	7.18	6.5	

The time for first request analgesia was higher in group A i.e., 65±8.27 mins and in group B it is 45±6.72 mins. The time for first request analgesia was compared to be statistically significant as the p value <0.05 (Table 6). Numerical rating scale (NRS) between group A and group B was found to be statistically insignificant as the p value

>0.05. This indicates that opioid free analgesia regimen also provided effective and comparable analgesia compared to opioid combination group (Table 7) (Figure 1). The incidence of postoperative nausea and vomiting (PONV) was compared to higher in group A compared to group B and was considered to be statistically significant as p value 0.03. The remaining postoperative complications and recovery time were comparable and considered to be statistically insignificant (Table 8). This study was conducted in patients posted for elective surgeries under general anaesthesia including laparoscopic Appendicectomy, laparoscopic Cholecystectomy, Umblical hernia repair and Epigastric hernia repair. The percentage of various surgeries shown (Figure 2).

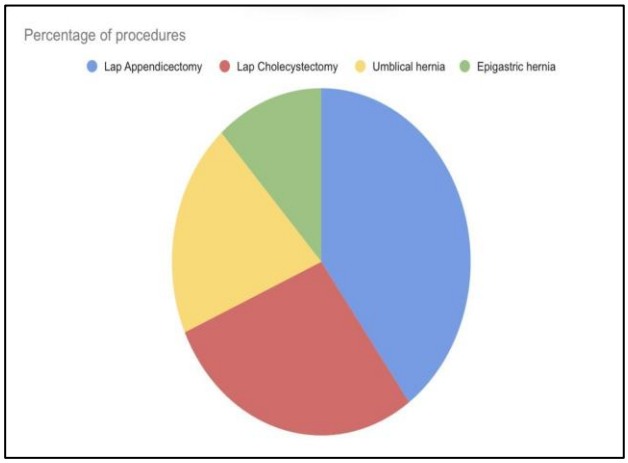

Figure 2: Percentage of procedures performed.

DISCUSSION

Opioids have been the gold standard traditional medication for Perioperative pain control until recently.[7] As a part of balanced anaesthesia regimen opioids have been used to alleviate perioperative pain with the advent of availability of various non-opioid analgesics with different mechanisms of action and also raising concerns regarding the adverse effects of opioids, the usage of analgesics like Lignocaine etc, Paracetamol, Diclofenac, Ketamine, Dexmedetomidine etc have been used in the recent years.[8] Various studies have been published highlighting the importance of opioid-free analgesia in general anaesthesia owing to improved postoperative complication rate when compared to opioid based general anaesthesia regimens.[9] In the present study simple combination of analgesics versus simple combination of analgesics with low dose opioid compared in surgeries posted under general anaesthesia. This study demonstrated that Group A (IV Lignocaine (1.5 mg/kg), Inj. Paracetamol (1gm) IV, Inj. Magnesium sulphate (40-52 mg/kg) IV and low dose fentanyl (1 mcg/kg) IV) and Group B-control group (IV Lignocaine (1.5 mg/kg), Inj. Paracetamol (1gm) IV, Inj. Magnesium sulphate (40-52 mg/kg) IV and normal saline IV 5cc) had effective perioperative analgesia and were comparable in recovery profiles. The concept of multimodal analgesia incorporating various analgesics with different mechanisms of actions provided adequate analgesia for cases under GA.[10] In this study Group A (opioid combination group) had showed stable hemodynamic parameters in the first 30 mins compared to Group B (opioid-free combination group). Khan IA and Singh SK conducted a case series on 70 patients with simple and readily available opioid free analgesia regimen with IV Lignocaine, IV Paracetamol, IV Magnesium sulphate and IV Diclofenac sodium and concluded that this opioid free analgesia regimen provided safe and effective analgesia while maintaining stable hemodynamics and minimal complications like PONV and shivering.[11] The observations of this study correlates with the observations of our study where Group B (control group) also showed that there are minimal complications like PONV and shivering while there is effective analgesia. The present study showed that there is clinically and statistically significant difference in the duration of analgesia in Group A compared to Group B. Patuents in Group A had increased duration of analgesia by 20-25 mins only. But there is no significant difference in the numerical rating scale (NRS) for pain in the both groups indicating that opioid free analgesic regimen also provided effective and comparable analgesia compared to the opioid combination group. Saudi et al compared opioid free general anaesthesia to traditional balanced general anaesthesia regarding achievement of enhanced recovery in laparoscopic bariatric surgeries and concluded that opioid free anaesthesia regimen has better profile than traditional balanced anaesthesia regimen with opioid with regard to postoperative pain scores but they have a relative increase in time to extubation and time to reach an aldrete score of 9.[12] The present study is comparable to above study with regard to effective analgesia and pain scores. In the present study only low dose fentanyl is used contrasting to the above study where full dose of fentanyl bolus and infusions are used. In the present study, recovery times are comparable between both the groups contrary to the above study where there is a relative increase in recovery times. The difference in the recovery times is due to the use of potent analgesics like dexmedetomidine and ketamine in the OFA regimen in Saudi et al study. Unlike several studies which incorporated alpha 2 agonists and ketamine as a part of OFA regimen, the present study is done with simply available analgesia medication like Lignocaine, Paracetamol and Magnesium sulphate which provide multimodal analgesia while alleviating all the side effects related to the potent drugs like Dexmedetomidine and Ketamine.[13] Hence recovery times were comparable in both Group A and Group B in this study. Suandika et al studied the impact of opioid free anaesthesia on nausea, vomiting and pain treatment in the perioperative period and concluded that opioid-free group did not demonstrate significant results in lowering pain in the postoperative period compared to opioid group and also linked to less nausea and vomiting after surgery.[14] The above observations are similar to the observations of the present study with respect to analgesia duration and side-effects. In the present study Group A had longer duration of analgesia compared to opioid free group (Group B) had

significantly less incidence of PONV compared to Group A. Overall this study demonstrated that simple analgesia combination with low dose opioid regimen and simple analgesia combination regimen administered for general anaesthesia cases for multimodal analgesia provided comparable and effective perioperative analgesia, though the duration of postoperative analgesia is slightly higher and intraoperative hemodynamics are stable in opioid based regimen. However simple analgesic combination (without opioid) produced significantly less incidence of PONV.

Limitations

Limitations of current study were; Small sample size and single centre study.

CONCLUSION

Hence it can be concluded that simple analgesic combination of multimodal analgesia regimen comprising of Lignocaine, Paracetamol and Magnesium sulphate produces safe and effective analgesia with good recovery profiles and no adverse opioid related side-effects for ASA 1 and 2 patients posted under General anaesthesia compared to addition of low dose Fentanyl (1 mcg/kg).

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Ethical approval: The study was approved by the Institutional Ethics Committee

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