Original Research Article

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To Compare the Effectiveness of Non-Opioid Analgesics over Opioids in the Intraoperative Pain Management

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Abstract

The primary aim is to compare the effectiveness of non-opioid analgesics over opioids in the intraoperative pain management.

The secondary objective to compare the intraoperative hemodynamic variables, requirement of additional analgesia intraoperativelyand to assess the side effects in both groups.

The study was approved by the University's institutional ethics committee(Reg No. ECR 518/Inst/MH/2014/RR-17) and written informed consent was obtained from all subjects participating in the trial. The study was registered prior to patient enrollment at BHARATI VIDYAPEETH MEDICAL COLLEGE institutional ethics committee (REF: BVDUMC/IEC/51, Principal investigator: Dr. Ashish Nair, Date of registration:10th October 2017).

This prospective comparative study enrolled a sample of 60 patients undergoing ENT surgeries, with 30 in each group.Non-Opioid group receivedpreoperative Intravenous (IV) dexmedetomidine 1mcg/kg started as infusion 15 mins prior to induction followed by a Maintenance dose of 0.5mcg/kgand the Opioid group received IV fentanyl 1mcg/kg as bolus prior to induction and were supplemented with 0.5mcg/kg as and when required. Intraoperative haemodynamic variables and analgesic requirement were monitored and were observed postoperatively till the patient received rescue analgesia as IV paracetamol 1gm.

Results: The haemodynamic variables at different time interval after intubation was statistically more significant in the Non-Opioid group as compared to Opioid group. Additional analgesia requirement was higher in the Opioid group (26.67%) as compared to Non-Opioid group (10%). Patients in the Non-Opioid group were better sedated and more comfortable post-operatively.

Conclusion: Opioid free anaesthesia is a better alternative in maintaining intraoperative haemodynamic parameters and pain management as compared to the Opioid drugs.

Keywords: Opioid free anesthesia; Dexmedetomidine hydrochloride; Additional analgesia.

Introduction

Acute pain is an expected outcome in any surgical procedure and Opioids remain the mainstay for pain management.[1] Opioids are associated with many dose-related side effects such as nausea, vomiting, urinary retention, pruritis and sedation. The concept of *Opioid-Free Anaesthesia (OFA)* is based on the idea that haemodynamic stability and pain management can be attained without the use of opioids. The availability of novel, less cardiovascular suppressant anaesthetic drugs forms the foundation of the Opioid Free Anaesthesia "movement".[2] A recent study by Frauenknecht J,

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Kirkham KR, et al (2019) concluded that a single modality of Non-Opioid drugs when used were associated with a 20% reduction in post-operative nausea and vomiting and thus the patients had a better recovery period.[3] Alpha-2 agonists like Dexmedetomidine in the intra-operatively decreases the sympathetic tone with attenuation of the neuroendocrine and hemodynamic responses to anaesthesia and surgery, thus reducing the anaesthetic and opioid requirements and causes adequate sedation and analgesia.[4]

Thus, Alpha-2 agonists may offer new possibilities in the treatment of pain and may help to reduce intraoperative opioid requirements. Therefore, we decided to compare the effectiveness of dexmedetomidine over opioids in the intraoperative management of pain.

Methodology

This prospectiverandomized study was carried out on 60 patients of ASA Grade I/II between 18 to 50 years of age posted for all elective ENT surgery after getting approval from ethical committee and written inform consent. Patients on beta-blocker, comorbidities and chronic opioid treatment were excluded from the study.Patients was divided into 2 groups by simple randomization, Non-Opioid group and Opioid group (30 patients each). Study was conducted between October 2017 to September 2019.

Non-Opioid group receivedIV Dexmedetomidine 1mcg/kg started as infusion 15 mins prior to induction followed by a Maintenance dose of 0.5mcg/kg.

Opioid group receivedIV fentanyl 1mcg/kg as bolus prior to induction and were supplemented with 0.5mcg/kg as and when required.

Standard Anaesthesia Protocol was followed for all the patients. After attaching monitors and securing IV-line, IV Ondansetron 4mg and IV midazolam 1mg was given with ongoing IV crystalloids. In the Non-Opioid group, patients were given preoperative Intravenous (IV) Dexmedetomidine 1mcg/kg started as infusion 15 mins prior to induction inside the operation theatre as Loading dose while in the Opioid groupPatients received IV Fentanyl 1mcg/kg as bolus prior to induction.

All Patients were pre-oxygenated with 100% oxygen for 3 mins and were induced with Propofol 2mg/kg IV and were intubated under the effect of Succinylcholine 2mg/kg IV or Rocuronium 0.5mg/kg.The hemodynamic parameters like pulse rate, SBP, DBP and MAP were assessed as baseline record followed by at induction, after intubation and then at every 15 minutes till the end of surgery.

In the Non-Opioid group, the loading dose of Dexmedetomidine was followed by maintenance dose of 0.5mcg/kg via an infusion pump while in the Opioid group the patients were supplemented with 0.5mcg/kg as and when required. The patients were maintained on vecuronium and sevoflurane with adequate ventilatory settings.

In both the groups we assessed the percentage of inhalational agent required intraoperatively. In the Non-opioid group, patients were given additional analgesia as IV paracetamol 1gm as per requirement while in the Opioid group the patients were supplemented with Fentanyl 0.5 mcg/kg as additional analgesia.Dexmedetomidine infusions were stopped 30–45 mins prior to the reversal. Patient were reversed with neostigmine 0.05mg/kg + glycopyrrolate 0.01mg/kg IV.Patient were extubated after fulfilling all extubation criteria. Both groups were monitored intraoperatively and postoperatively till the patient received first dose of rescue analgesia for the occurrence of dose related side effects like nausea, vomiting, urinary retention, pruritis and sedation.

Statistical analysis was performed using SPSS ver. 20. Results were expressed as mean ± standard deviation, number and percentage (%). Data were analyzed normally distributed data were assessed using independent sample t test (for comparison of parameters among groups). Comparison was carried out using Chi-square ($\chi 2$) fisher exact test with a P value reported at 95% confidence level. P Value < 0.05 considered as statistically significant.

Results

There was no significant difference with respect to age, sex and weight (Table 1).

Table 1: Demographic characteristics of patients, operative data in studied groups.

Variable	Mean ± SD		P *	Statistical Significance
	Group B (n=26)	Group BD (n=26)		
Age(years)	36.83 ± 16.02	31.13 ± 8.20	0.0.088	NS
Sex				
Males	12(40)	10(33.3)	0.789	NS
Females	18(60)	20(66.7)		
Weight	60.80(13.89)	61.70(11.50)	0.786	NS

SD: Standard deviation, P* < 0.05 considered as statistically significant.

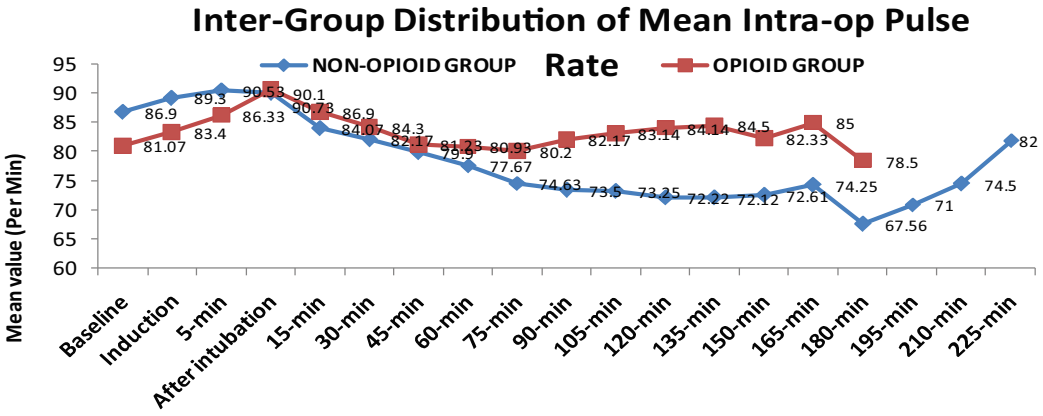
P*Value > 0.05 by independent sample t test.

So, there was no significant difference with respect to age, sex and weight.

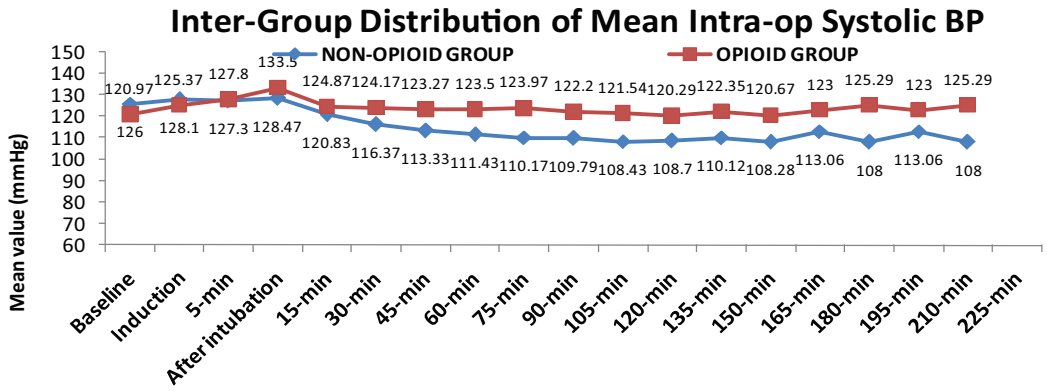
Inter-group comparison of mean intra-op pulse rateat different time intervals were statistically significantly lower at all times in the Non-Opioid group (Graph 1).

Furthermore, Mean Systolic Blood Pressure (Graph 2), Diastolic blood pressure (Graph 3) and

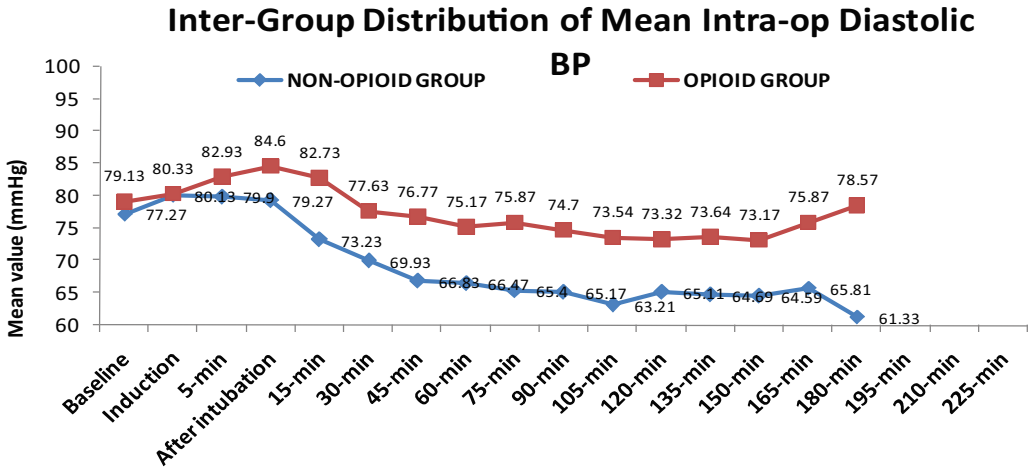
Graph 1: Inter-group comparison of mean intra-op pulse.



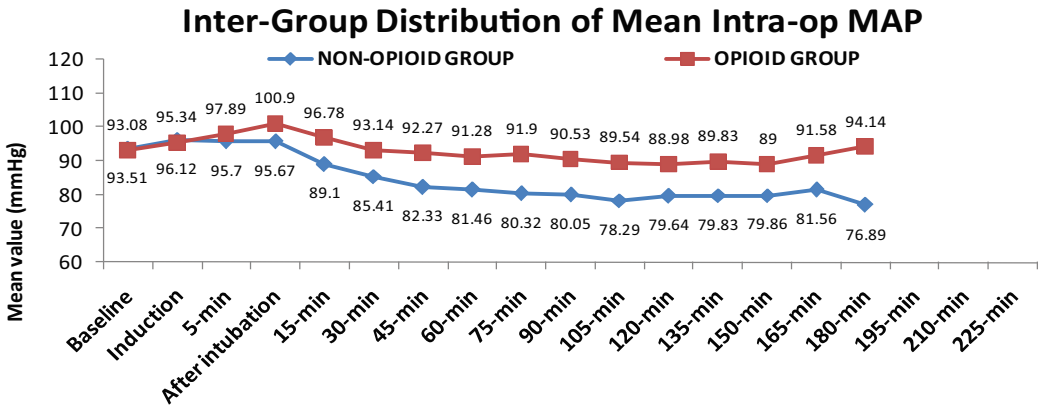
Graph 2: Inter-group comparison of mean intra-op SBP.



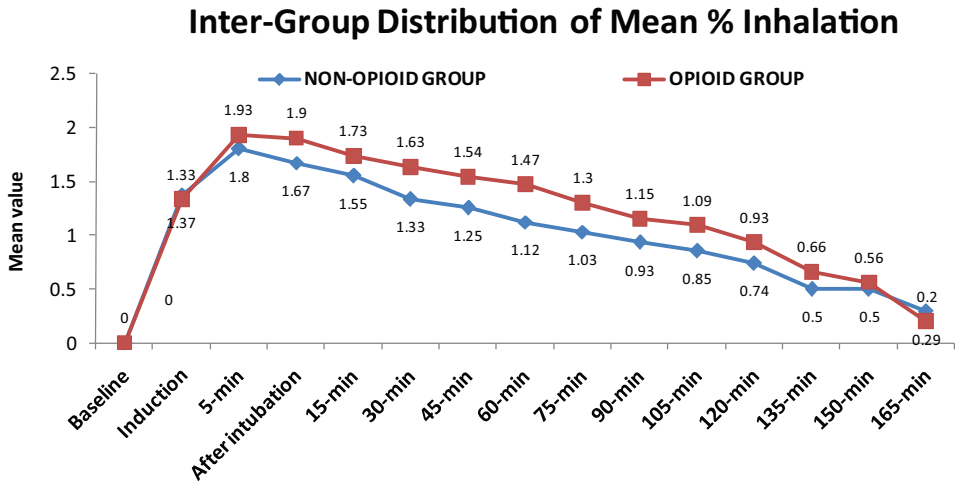
Graph 3: Inter-group comparison of mean intra-op DBP.



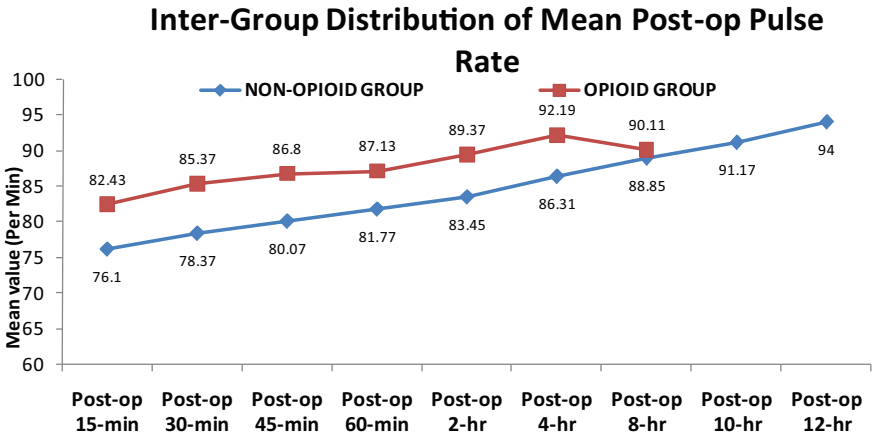
Graph 4: Inter-group comparison of mean intra-op MAP.



Graph 5: Inter-group comparison of mean % inhalation.



Graph 6: Inter-group comparison of mean post-op pulse rate.



Mean Arterial Pressure (Graph 4) among the cases studied is significantly higher in Opioid group compared to Non-Opioid group (P-value <0.05 for all).

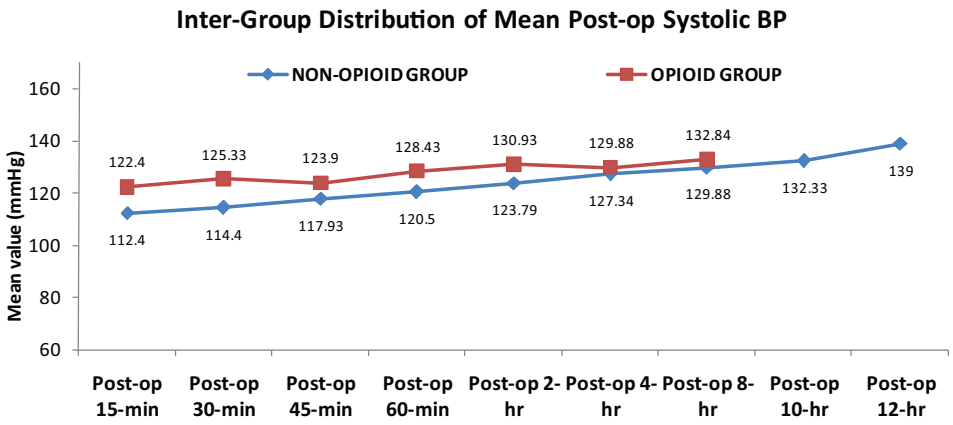
Distribution of mean % inhalational requirement among the cases studied is significantly higher in Opioid Group compared to Non-Opioid Group (P-value <0.05 for all). (Graph 5).

Table 2: Inter-group comparison of intraoperative analgesic requirement.

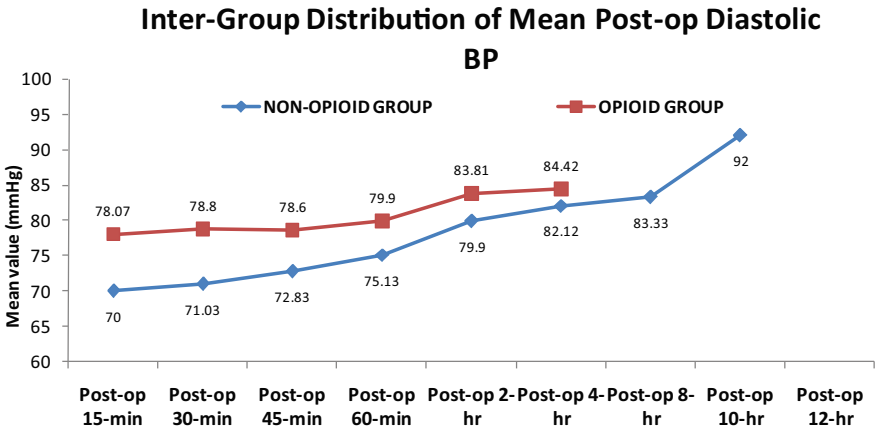
	Non-Opioid Group	Opioid Group
Rescue Analgesia	3(10%)	8(26.67%)
No Rescue Analgesia	27(90%)	22(73.33%)
Total Patients	30(100%)	30(100%)

The intraoperative requirement of additional analgesia was less (10%) in the Non-Opioid group as compared to the Opioid group (26.67%). (Table 2)

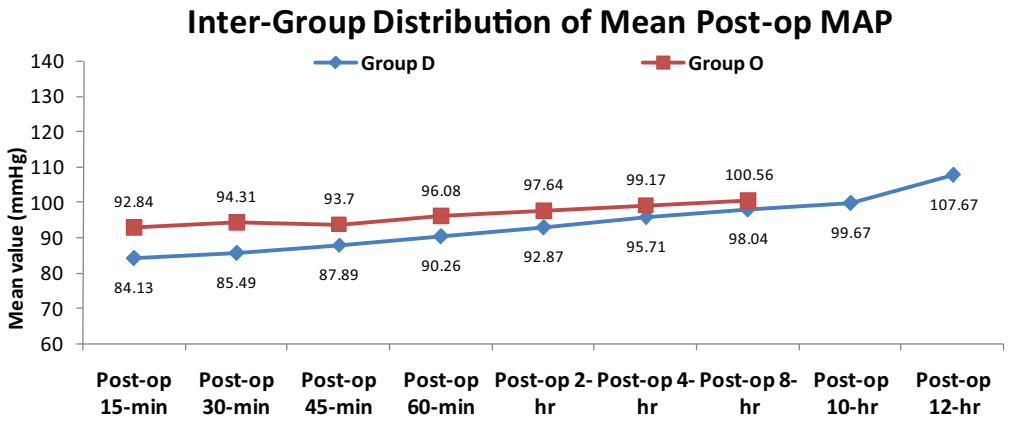
Graph 7: Inter-group comparison of mean post-op SBP.



Graph 8: Inter-group comparison of mean post-op DBP.



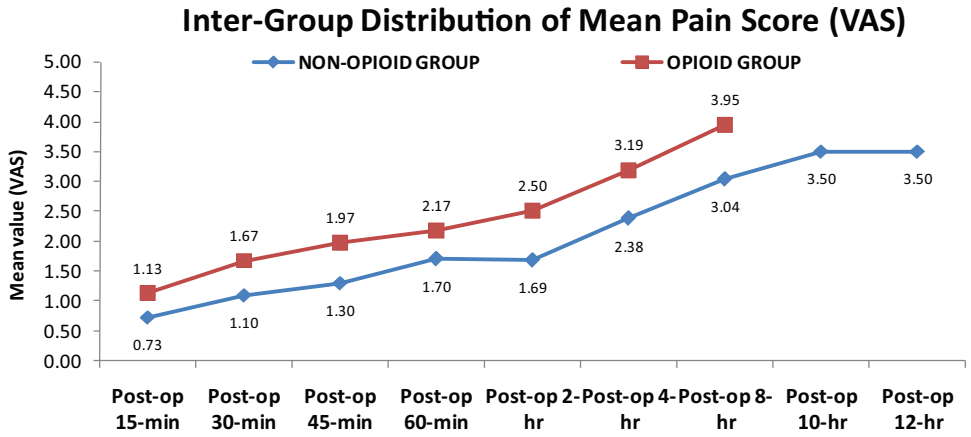
Graph 9: Inter-group comparison of mean post-op MAP.



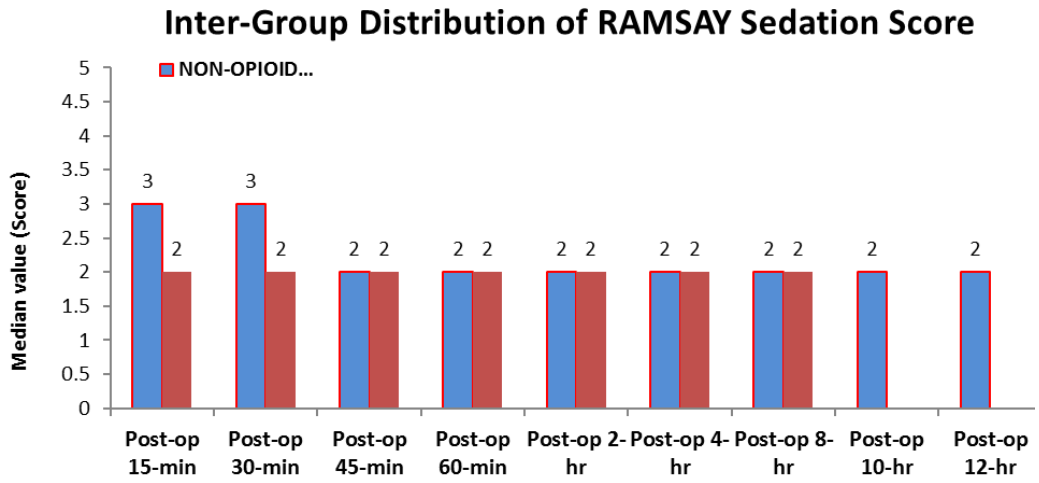
Distribution of mean Pulse rate(Graph 6), SBP (Graph 7), DBP (Graph 8) and MAP (Graph 9) in the post-operative period among the cases studied are significantly higher in Opioid Group compared to Non-Opioid Group.The mean post-operative haemodynamic variables in the Non-Opioid group After 30 min post-operatively till 4 hours post-operatively were lower and statistically significant with p value <0.05 for all.

Distribution of mean pain score (VAS) among the cases studied is significantly higher in Opioid Group compared to Non-Opioid Group (P-value <0.001 for all) (Graph 10). The analgesic effect of Dexmedetomidine lasted longer till 8-10 hours before their VAS score became more than 3 and they were given rescue analgesia. Demographic data was analyzed which was comparable with respect to sedation scores of patients in both the groups as

Graph 10: Inter-group comparison of mean pain score (VAS).



Graph 11: Inter-group comparison of RAMSAY SEDATION SCORE.



shown in Graph 11. The Ramsay Sedation scores in both the groups were statistically not significant (p value >0.05) in the post-operative period.

Discussion

Peri-operative opioid administration has long been one of the three pillars of 'balanced anaesthesia'. Pain management is an important aspect for haemodynamic stability and the patient's outcome in the postoperative period. Opioids have always been considered effective in pain management as they suppress or block ascending nociceptive stimuli thus reducing the requirement of higher doses of anaesthetic drugs. Use of Opioids has always been associated with dose-related adverse effects such as nausea, vomiting, urinary retention, itching, and sedation. Lyons P. J et al (2015) published a review article where he evaluated the concept of opioid-induced hyperalgesia after acutefentanyl exposure.[1] The concept of Opioid-free Anaesthesia (OFA) has been discussed by many authors recently and this is based on the idea that haemodynamic stability can be attained by avoiding Opioid use. OFA with a Non-Opioid drug like dexmedetomidine significantly attenuates postoperative pain and reduces Opioid requirements without causing respiratory depression.

Our Primary Objective was to compare the haemodynamic variables in both the groups. There are several studies comparing the efficacy of Opioid Free Anaesthesia (OFA) over Opioids in anaesthesia and pain management. There are various schools of thought on the risk versus benefits of Opioid Free Anaesthesia. In a Meta-Analysis by Gupta K et al (2013)[5] and Shareef SM et al (2016)[6], it was observed that when Dexmedetomidine was used before induction, it attenuated the haemodynamic response to pneumoperitoneum during laparoscopic surgeries as compared to Fentanyl.

In the intra-operative period, mean pulse rate (Graph 1) was better controlled in the Non-Opioid group as compared to the Opioid group from 90 minutes onwards which was statistically significant (p value = 0.001) till 180 mins.In our study we observed that in the Non-Opioid group patients

had better control over intraoperative SBP (GRAPH 2), DBP (Graph 3) and MAP (Graph 4) which was observed from 30 minutes onwards till 180 minutes, which was statistically significant with a p value= 0.001. These parameters were comparable to the study conducted by Patel CR et al (2012), who found lesser increase in SBP (6% vs 23%), DBP (7% Vs 20%) after using Dexmedetomidine 1 mcg/kg as compared to fentanyl 2 mcg/kg when given as loading dose prior to induction.[7]

Intraoperatively, we observed that the percentage of Sevoflurane required in the Non-Opioid group was less (0.6–1%) intraoperatively from 30mins onwards and is statistically significant (p value <0.05) as compared to the Opioid Group (1.5–2%) (GRAPH 5). This finding was comparable to a study conducted by Na Young Kim, So Yeon Kim et al where Intraoperative Dexmedetomidine 1 mcg/kg bolus, followed by 0.1 mcg/kg/h infusion in paediatric patients. They observed significant reduction in anaesthetic requirements and also less incidence of delayed recovery.[8]

Our Second Objective, where we observed the Intraoperative requirement of additionalanalgesiain both the group The NON-OPIOID group showed only 2 cases (10%) where additional analgesia was required and Injection Paracetamol 1gm IV was given as per protocol. In the OPIOID group, we observed that 8 cases (26.67%) required additional doses of Injection Fentanyl (0.5mcg/kg) (Table 2). These findings were comparable to a study conducted by Tang C, Xia Z et al (2017) where they described the analgesic efficacy of Dexmedetomidine as an adjuvant for perioperative acute pain treatment.[9]

In the Post-operative period,all the patients were observed post-operatively every 15 minutes for 2 hours and there after every 2 hourly up to 8 hours post-operatively. The Mean distribution of the haemodynamic parameters among the cases studied in both the groups and we observed that these parameters were better controlled in the Non-Opioid Group and the values were statistically significant (p value = 0.001) (Graph 6–9) These findings are comparable to Monaz Abdulrahman Ali et al (2013) who observed that Dexmedetomidine had better haemodynamic control and also decreased the postoperative pain without affecting the length of stay in post anaesthesia care unit.[10]

We found that duration of postoperative analgesia was higher in the Non-Opioid group as compared to Opioid group with a p value = 0.001 and was statistically significant (Graph 10) Our findings were consistent with that of Feld JM et al (2006) who reported that Dexmedetomidine provided both stable perioperative hemodynamic and postoperative analgesia, thus reducing the use of supplementary analgesic as compared to Fentanyl.[11] The analgesic effect of Dexmedetomidine lasted longer till 8–10 hours before their VAS score became more than 3 and they were given rescue analgesia.

Our Third Objective was to monitor the dose related complications like Post-operative sedation in both the groups. Graph 11 shows the inter-group comparison of Ramsay sedation scores of patients in both the groups. In our study, we found that patients who received Dexmedetomidine were better sedated with a Ramsay sedation score of 3 in the initial 15–30 minutes and were more comfortable post operatively than those patients who received Fentanyl. Our findings are in agreement with Patel CR et al (2012) who concluded that Dexmedetomidine (1 mcg/kg) shows significant sedation with a Ramsay sedation score of 3 at two hours postoperatively as compared to Fentanyl (2 mcg/kg).[7] Other dose related complications such as nausea and vomiting, pruritis, urine retention and delayed emergence were not observed in any patients of both the groups in our study. This is probably because the procedures were short and we did not require higher doses of Fentanyl were not required intraoperatively.

Our study concludes that Non-Opioid drugs like dexmedetomidine are a better alternative than Opioid drugs intraoperative haemodynamic stability and pain management.

However, the limitation of our study is the type of surgery we have chosen i.e. ENT surgeries and for the duration of the study, limited sample size was used.

Conclusion

We can conclude from our study we can conclude that Non-Opioid drugs like Dexmedetomidine are abetter anaestheticalternative to Opioid drugs in terms of intraoperative haemodynamic stability and pain management.

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