

Intravenous Sedation for Tympanoplasty - Comparison of I.V. Dexmedetomidine and Nalbuphine with I.V. Dexmedetomidine and Fentanyl

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Abstract

Introduction: Monitored Anaesthesia Care (MAC) involves administration of local anaesthesia (LA) with intravenous sedatives, anxiolytic and analgesic drugs with detailed monitoring of vital parameters. In tympanoplasty, reconstruction of tympanic membrane with or without ossicular reconstruction is done. To avoid pain, decrease bleeding IV sedation with local anaesthesia is preferred. In this study we compared the effects of Inj. Dexmedetomidine and Inj. Nalbuphine versus Inj. Dexmedetomidine and Inj. Fentanyl. **Aims and objectives:** 1. To compare the sedation effects and analgesic effects of Dexmedetomidine (1mcg/kg) / Nalbuphine (100 mcg/kg) and Dexmedetomidine (1mcg/kg) /Fentanyl (1mcg/kg) in I.V. sedation in Tympanoplasty. 2. To compare Heart rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Respiratory Rate, Oxygen Saturation (SpO₂) and Surgeon's Satisfaction Score. **Material and method:** 60 patients undergoing tympanoplasty surgery under MAC were randomly divided in two groups of 30 each according to chit block method in addition to Inj. Dexmedetomidine 1µgm/kg received either inj. Nalbuphine 100µgm/kg (Group N) or inj. Fentanyl 1µgm/kg (Group F) intravenously for sedation along with local anaesthesia during surgery. Ramsay sedation score (RSS), Visual analogue score (VAS), Heart rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean arterial pressure (MAP), Respiratory Rate (RR), Oxygen Saturation (SpO₂) were recorded after giving both the drugs at the interval of 2, 4, 6, 8, 10, 30, 60, 90, 120 minutes. **Result:** We observed that RSS score was more and VAS score was less in group N than group F. This indicates that sedation and analgesia was better in Dexmedetomidine with Nalbuphine group than Dexmedetomidine with Fentanyl group. Decrease in heart rate, Systolic Blood Pressure and Diastolic Blood Pressure, Mean Arterial Pressure was statistically significant in group N than group F. This indicates that Dexmedetomidine with Nalbuphine provides better cardiovascular stability. Rescue analgesic requirement was comparable in both groups. **Conclusion:** From this study, we concluded that, intravenous Inj. Dexmedetomidine with Inj. Nalbuphine provides better sedation and analgesia, good hemodynamic stability, good surgeon's satisfaction score without side effects. It also reduces the requirement of rescue sedation and analgesia as compared to Inj. Dexmedetomidine with Inj. Fentanyl in patients undergoing Tympanoplasty under local anaesthesia with monitored anaesthesia care. Thus Dexmedetomidine with Nalbuphine is a better alternative to Dexmedetomidine with Fentanyl as sedation for middle ear surgery.

Keywords: Tympanoplasty; Dexmedetomidine; Nalbuphine.

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Introduction

Monitored Anaesthesia Care (MAC) involves administration of local anaesthesia (LA) with

intravenous sedatives, anxiolytic and analgesic drugs with monitoring of vital parameters. Monitored anaesthesia care is indicated in various ENT surgeries in which an adequate sedation and analgesia are desirable for the comfort of both the

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patient and surgeon. It is cost-effective, causes less bleeding, allow to test hearing intra-operatively has faster recovery and can provide postoperative analgesia.

Tympanoplasty is superficial, less invasive surgery but patient may feel discomfort due to pain, noise of suction, middle ear instrumentation and head-neck position. Pain will lead to sympathetic stimulation, a restlessness, tachycardia, hypertension leading to increased bleeding in surgical field.

Many drugs have been used for sedation during surgery under local anaesthesia with MAC including Propofol, benzodiazepines and opioids. Midazolam is the most frequently used sedative and well tolerated when used in MAC. Alfa-2 adrenoreceptor agonists i.e. Clonidine and Dexmedetomidine have been recently used preoperatively for their sedation without respiratory depression [1], analgesic, and sympatholytic and cardiovascular stabilising effects with reduced anaesthetic requirements. It decreases sympathetic outflow and hence, it reduces bleeding significantly.

This study was undertaken to evaluate and compare the effects of inj. Dexmedetomidine and inj. Nalbuphine versus inj. Dexmedetomidine and Inj. Fentanyl with respect to sedation, analgesia and hemodynamic stability intraoperative in patients undergoing tympanoplasty under local anaesthesia with monitored anaesthesia care.

Aims & Objectives

To compare the efficacy of I.V. Dexmedetomidine with Nalbuphine versus I.V. Dexmedetomidine with Fentanyl during Tympanoplasty under Local Anaesthesia with Monitored Anaesthesia.

To study and compare the sedation and analgesic effect of Dexmedetomidine (1mcg/kg)/ Nalbuphine (100 mcg/kg) with Dexmedetomidine (1mcg/kg) / Fentanyl (1mcg/kg) in I.V. sedation for Tympanoplasty. Also to compare effect on Heart rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Respiratory Rate, Oxygen Saturation (SpO₂).

Material and Method

We conducted a Prospective, Randomized, double blind, clinical study after approval of institutional medical ethics committee and written informed consent was obtained from all patients participating in the study. 60 patients of ASA Grade I & II, age

between 18 - 60 years undergoing Tympanoplasty under local anaesthesia with 2% Lignocaine plus adrenaline 1:200000 and I.V. sedation with either Dexmedetomidine with Nalbuphine or Dexmedetomidine with Fentanyl. Patients were divided in two groups of 30 each allocated randomly by chit block method in two groups, Group N and Group F Group N received Inj. Dexmedetomidine 1 mcg/kg I.V. in 100 ml normal saline over 10 min followed by Inj. Nalbuphine 100 mcg/kg in 10 ml normal saline bolus over 5 min. Group F received Inj. Dexmedetomidine 1 mcg/kg I.V. in 100 ml normal saline over 10 min followed by Inj. Fentanyl 1 mcg/kg in 10 ml normal saline bolus over 5 min.

Standard monitoring including ECG, noninvasive BP and pulse oximetry were applied to patients and baseline vitals were recorded. I.V. line was secured with 20G cannula, antiemetic premedication drug i.e. Inj. Ondansetron 0.15 mg/kg I.V. was administered and I.V. Ringer Lactate solution 2ml/kg/hr was started. O₂ was administered with nasal cannula at a rate 4 lit/min. To maintain the double blind nature of study, anaesthesiologist who was not involved in study prepared the drug bolus to fixed volume. The anaesthesiologists conducting the case, surgeons and patients were blinded to group assignment.

Local anaesthesia was given by ENT surgeons using 6-7 ml of 2% Lignocaine with Adrenaline (1:2,00000) in the postauricular area to block greater auricular & lesser occipital nerves in the incisura terminalis while administration of intravenous drugs. Dose of Lignocaine with adrenaline should not exceed >5 mg/kg.

Ramsay sedation score (RSS), Visual analogue score (VAS), Heart rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean arterial pressure (MAP), Respiratory Rate (RR), Oxygen Saturation (SpO₂) were recorded after giving both the drugs at the interval of 2, 4, 6, 8, 10, 30, 60, 90, 120 min of surgery.

After completion of surgery patients were shifted to Post Anaesthesia Care Unit and I.V. Inj Diclofenac 1.5mg/kg was given for postoperative analgesia.

After the loading dose of the drug, Ramsay Sedation Score (RSS) was assessed with target sedation of RSS 3. If patient complains of pain, Inj Propofol 100-300mcg/kg I.V. bolus with Inj Fentanyl at 1 mcg/kg was given. If still patient complains of pain general anaesthesia was given and was excluded from the study.

Sedation score was analysed by Ramsay Sedation Scale (RSS) as follows-

Grade 1 Patient is anxious and agitated or restless, or both.

Grade 2 Patient is co-operative, oriented, and tranquil.

Grade 3 Patient responds to commands only.

Grade 4 Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.

Grade 5 Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus.

Grade 6 Patient exhibits no response.

Analgesia was assessed by Visual Analogue Scale (VAS) as one to ten where one is minimum pain while ten is severe pain.

Adverse effects namely Bradycardia, Hypotension, desaturation, nausea, vomiting, dry mouth or any other events during procedure were noted and treated accordingly.

Bradycardia was defined as pulse rate < 60 beats/min or <20% of baseline heart rate and was treated with I.V. Atropine Sulphate 0.01mg/kg. Hypotension was defined as Mean Arterial Pressure <60 mm of Hg or systolic blood pressure <20% of baseline level and was treated with fluid therapy and when this therapy was inadequate then I.V. Mephenteramine 6mg in incremental doses was administered if required.

Desaturation was defined as SpO₂ < 90% and was treated by increasing O₂ flow at a rate 6 lit/min via Hudson's Face mask or bag mask ventilation if required. Bradypnea (respiratory rate is less than 8

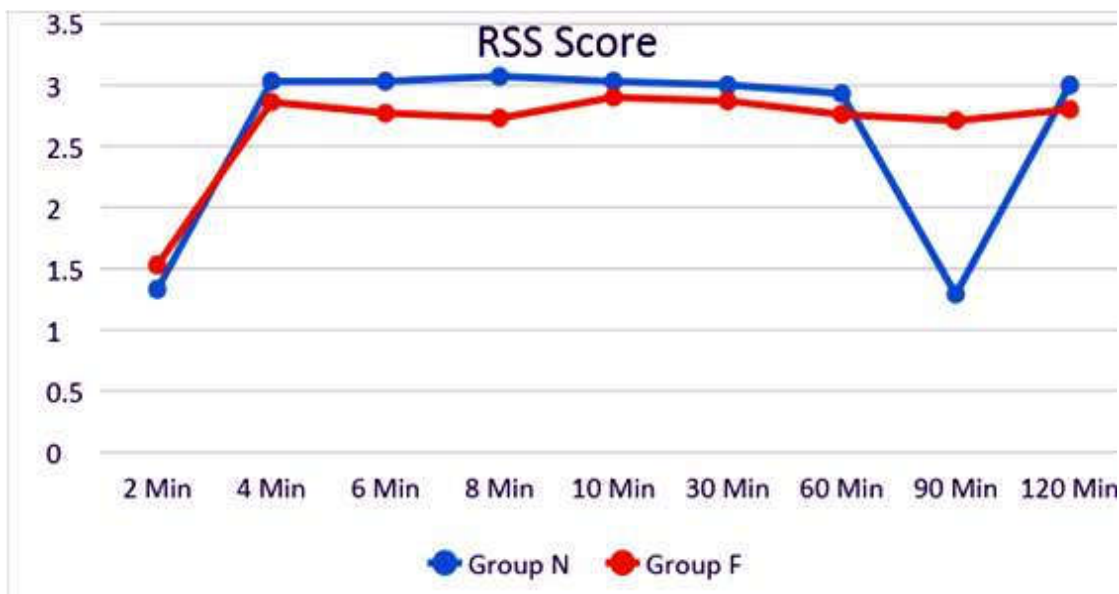
per min) was treated with assisting or supporting the ventilation on mask.

Data was expressed as Mean + Standard Deviation (SD). Demographic data and complications were analyzed using Chi-square test and haemodynamic variables were analyzed using paired and unpaired 't' test. 'p' value less than 0.05 was considered statistically significant.

Result

In our study we observed that both groups were comparable as per age, sex, weight and ASA grade is considered. RSS was more in group N than group F. (Graph 1) There was statistically significant difference between RSS among the two groups at 6, 8 and 90 min duration during the surgical time with p value <0.05. The difference was not statistically significant at the end of 2 min, 4 min, 10 min, 30 min, 60 min and 120 min with p value > 0.05. This indicates that sedation was better in Dexmedetomidine with Nalbuphine group than Dexmedetomidine with Fentanyl group.

VAS was less in group N than group F. The difference was statistically significant. The VAS score was higher in Group F than group N at 6, 8, 10, 30, 60, 90, 120 min. This indicates that Dexmedetomidine with Nalbuphine provided better analgesia than Dexmedetomidine with Fentanyl. One patient from group N while three patients from group F required rescue sedation. Additional analgesic requirement



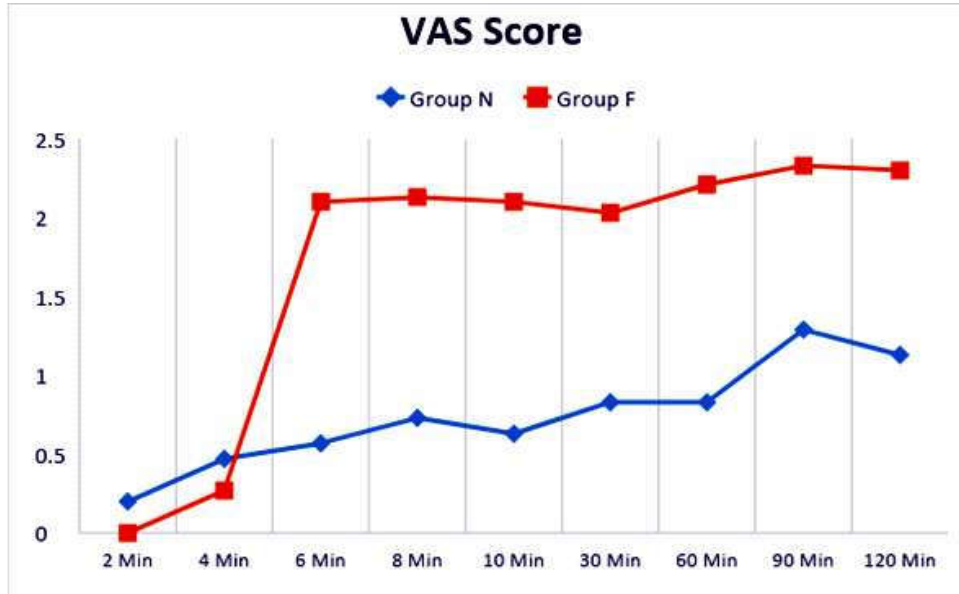
Graph 1: RSS Score among Two Groups

was not statistically significant. Three patients from group N while seven patients from group F required rescue analgesia. (Graph 2).

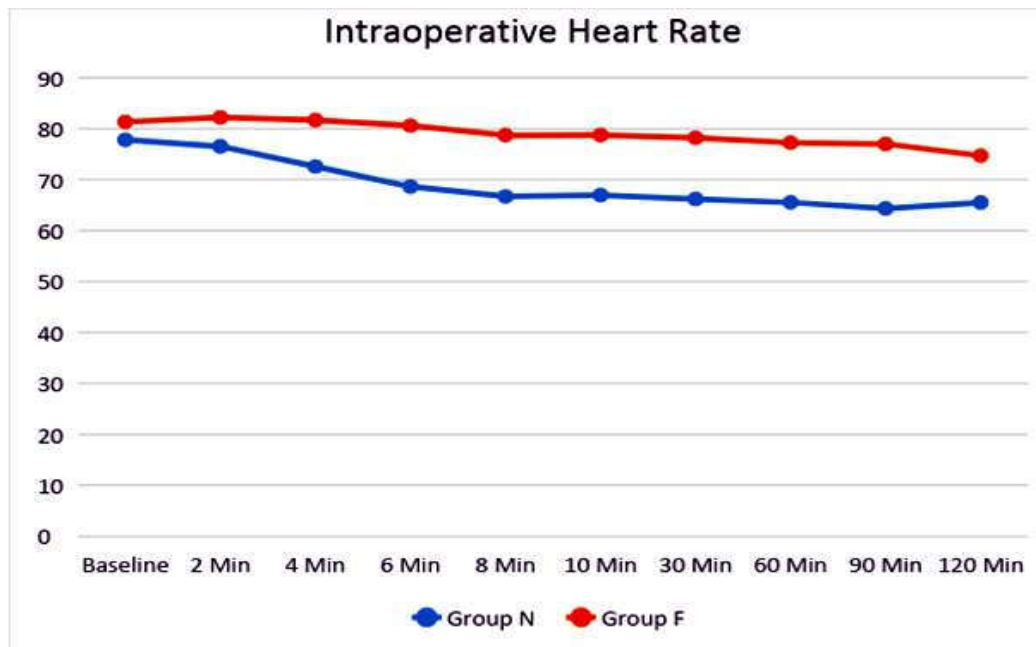
Decrease in heart rate was statistically significant in group N than group F. In Group N baseline mean HR was 77.8 ± 7.74 /min while in Group F baseline mean HR was 81.33 ± 11.34 /min. Both the groups were comparable at baseline HR ($p=0.164$). In group N, HR decreased to 72.57 ± 6.33 /min at the end of 4 min and was continued till the

end of surgery with statistically significant difference ($p = 0.001$). In group F the mean HR did not decrease significantly. This indicates that Dexmedetomidine with Nalbuphine provides better cardiovascular stability. (Graph 3).

In Group N, the baseline means SBP was 117.8 ± 10.78 mm Hg and In Group F, mean SBP was 121.33 ± 10.4 mm Hg, which were comparable ($p= 0.201$) in both groups. In group N at 4 min SBP decreased to 112.2 ± 11.4 mm Hg. The difference was statistically



Graph 2: VAS Score among Two Groups

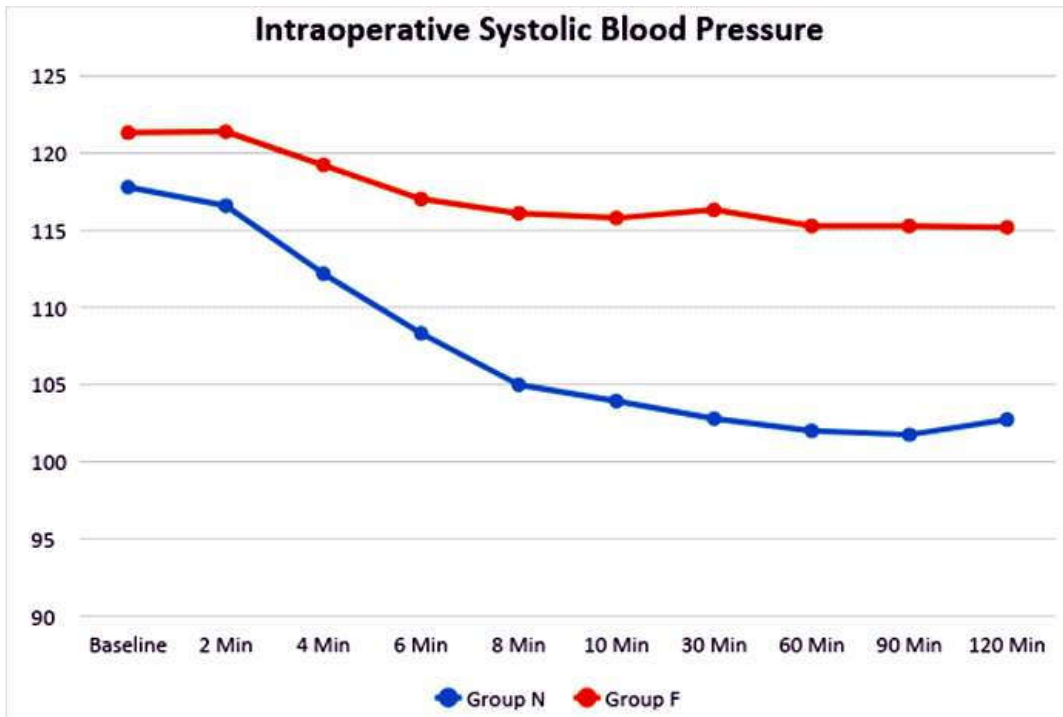


Graph 3: Intraoperative mean heart rate (HR in beats/min)

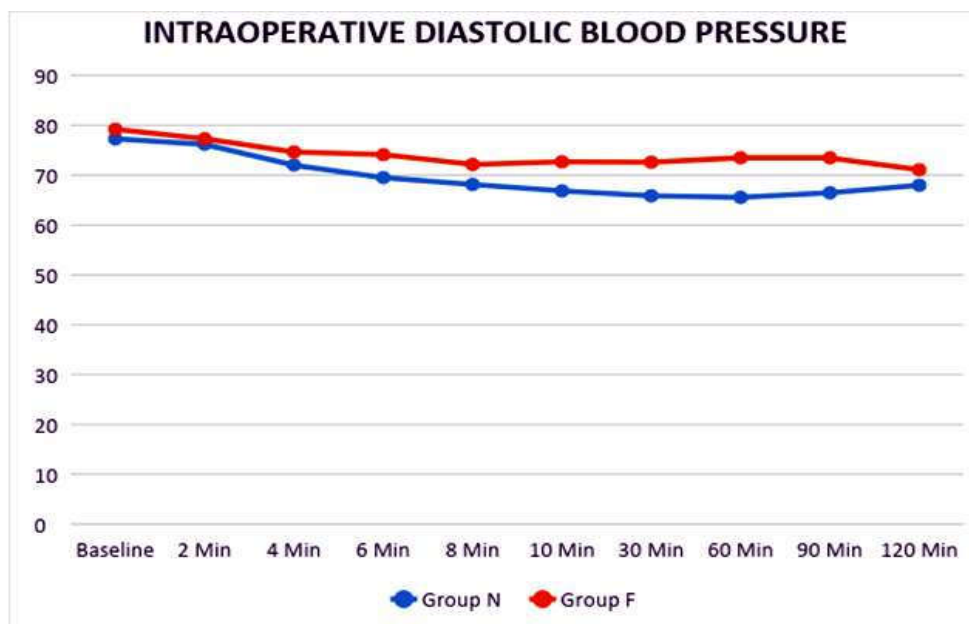
significant ($p = 0.001$). In group F there was no any significant reduction at 4 min but 6 mins onwards it was significantly reduced ($p=0.001$) till end of surgery. Decrease in Systolic Blood Pressure and Diastolic Blood Pressure, Mean Arterial Pressure were statistically significant in group N than group F. This indicates that Dexmedetomidine with Nalbuphine provides better cardiovascular stability (Graph 4,5 and 6).

Oxygen saturation and RR were maintained within normal limits in both the groups. They were comparable in both the groups and hence statistically not significant. No significant side effects were noted in both the groups. It was not statistically significant.

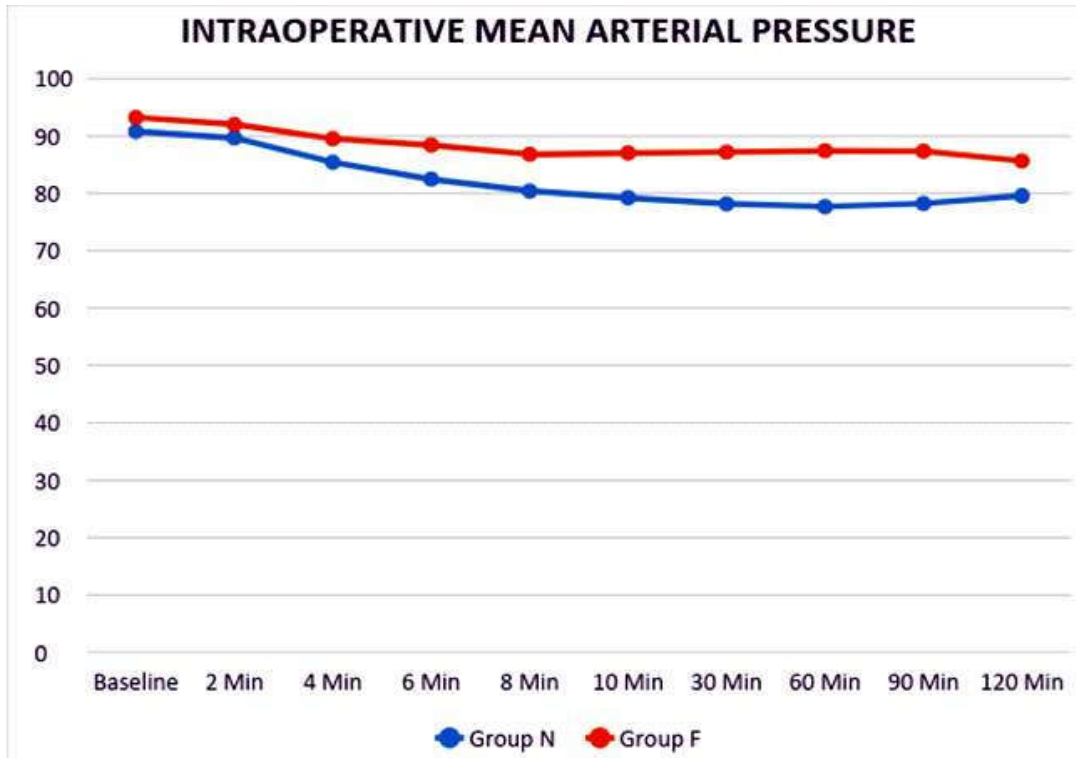
Additional sedation requirement was not statistically significant (Graph 7).



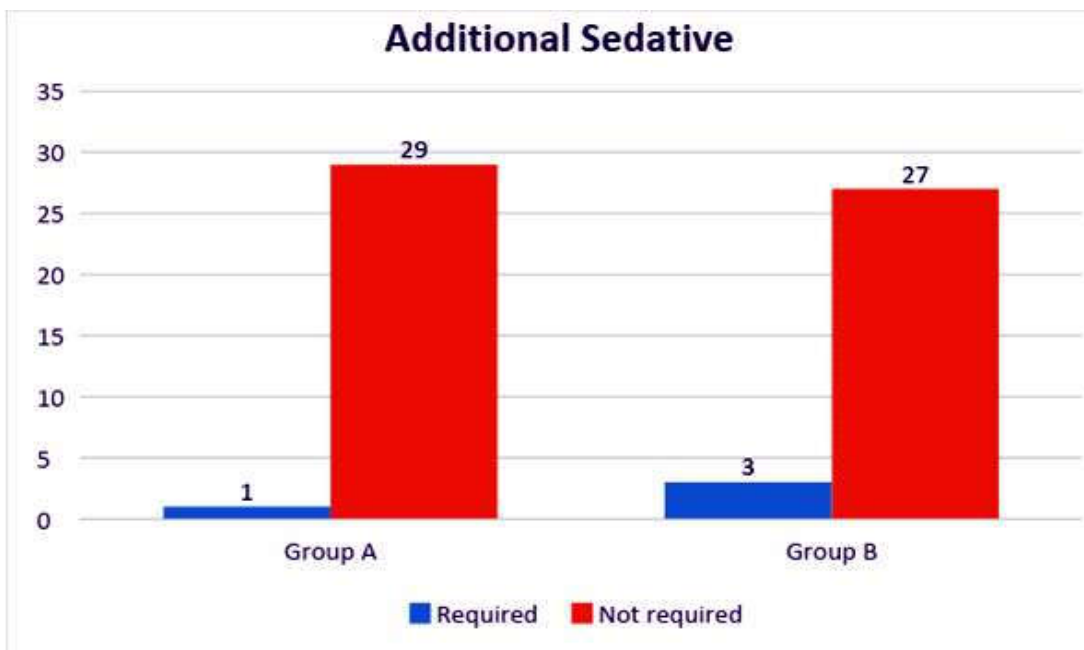
Graph 4: Intraoperative systolic blood pressure (SBP in mmHg)



Graph 5: Intraoperative diastolic blood pressure (DBP in mmHg)



Graph 6: Intraoperative mean arterial pressure (MAP in mmHg)



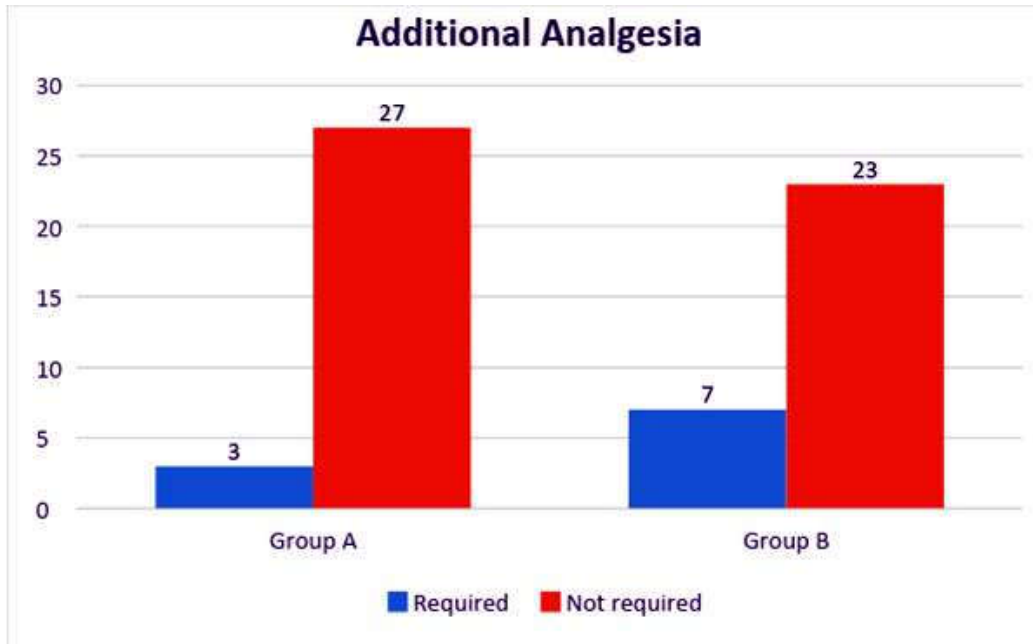
Graph 7: Distribution according to Additional Sedative

Additional analgesia in both the groups was not statistically significant (Graph 8).

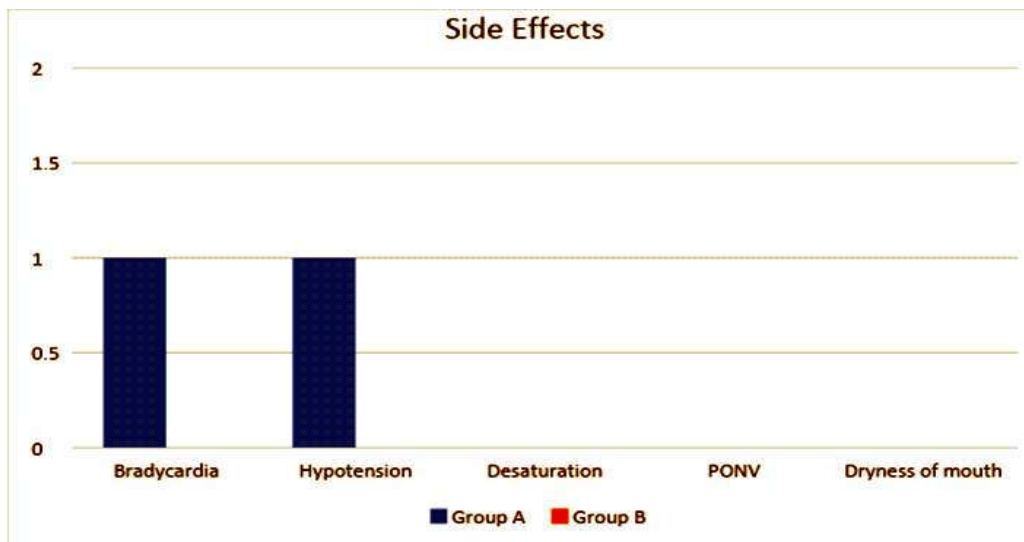
No significant side effects were noted in the two group (Graph 9).

Discussion

Monitored anaesthesia care (MAC) involves administration of local anaesthesia with



Graph 8: Distribution according to Additional Analgesia



Graph 9: Distribution according to Side Effects

intravenous sedatives, anxiolytic and analgesic drugs with monitoring of vital parameters. It is indicated in middle ear surgery in which an adequate sedation and analgesia are desirable for the comfort and safety of patient [2]. Conscious sedation is defined as a state of altered or reduced consciousness in which the patient is able to maintain his vitals [3,4].

During tympanoplasty pain may lead to restless patient with sympathetic stimulation, tachycardia, hypertension and increased bleeding. Intraoperative bleeding may lead to prolongation of surgery and

graft rejection. Hence, it is important to have a bloodless surgical field. Several drugs have been used for sedation during surgery under local anaesthesia with monitored anaesthesia care including Propofol, Benzodiazepines and Opioids. However, Propofol may cause deep sedation, disorientation and unconsciousness [3], Benzodiazepines may result in confusion, particularly in elderly and opioids are associated with postoperative nausea and vomiting, increased risk of respiratory depression [5].

Combining opioid with Dexmedetomidine have synergistic effect and better intra-operative

sedation, analgesia, hemodynamic stability and better surgeon's satisfaction score [6]. Combination of two drugs from the beginning of procedure allows the use of lower dose of each agent and thus decreases its undesired effects [7]. Synergism of Dexmedetomidine with other opioids decreases the need of complementary opioid analgesics [8]. Dexmedetomidine and Morphine combination significantly enhances analgesic effect of Morphine, reduces PCA Morphine requirements and coexisting Morphine induced nausea without causing bradycardia or hypotension, sedation, respiratory depression [8].

Alka Kewalramani, S.S. Jaitawat et al. compared Dexmedetomidine with Dexmedetomidine and Butorphanol as an adjuvant I.V. for MAC in Tympanoplasty and myringoplasty. They noted that RSS was better in Dexmedetomidine with Butorphanol group which proves that Dexmedetomidine along with opioid provides better sedation [6] which was our observation too. Kazim Karaaslan, Fahrettin Yilmaz, et al. noted that amount of PCA administered rescue analgesic Tramadol was higher in patients who used Midazolam than in patients who received Dexmedetomidine [10]. This shows that Dexmedetomidine has opioid sparing action too and decreases the requirement of other analgesics.

In our study we observed that intraoperative RSS was better in group N Dexmedetomidine with Nalbuphine than group F Dexmedetomidine with Fentanyl at 6, 8 and 90mins. Only one patient from group N required Inj. propofol as rescue sedation and three patients from group F required Inj. Propofol, lower vas score in group N than in group F with less requirement of rescue analgesic in group N, Similar result was noted by Mahmoud Hassan Mohamed, Karim Youssef Kamal Hakim, et al. who compared I.V. Dexmedetomidine and Nalbuphine with Midazolam and Nalbuphine in ear surgeries under MAC. They observed that RSS was better in Dexmedetomidine with Nalbuphine, rescue analgesic requirement in Dexmedetomidine with Nalbuphine was 34% while it is 60% in Midazolam with Nalbuphine group. Also they noticed significant hypotension and bradycardia in patients of Dexmedetomidine with Nalbuphine group than Dexmedetomidine with Fentanyl group [11]. There was no statistically significant difference between the 2 groups as regards respiratory rate, saturation when they compared Dexmedetomidine and Nalbuphine with Midazolam and Nalbuphine [11].

Srinivasa Rao Nallam et al. (2017) compared I.V. (Dexmedetomidine and Nalbuphine) with

(Propofol and Nalbuphine) in patients undergoing middle ear surgeries. He also observed that Dexmedetomidine with Nalbuphine provides better sedation and analgesia as we observed in this study [7]. Also they observed that there is decrease in HR and MAP in Dexmedetomidine and Nalbuphine group with bradycardia in 36% patients while only in 6% patients who received Propofol with Nalbuphine and 16 patients from Dexmedetomidine with Nalbuphine group and 7 patients from Propofol with Nalbuphine group had hypotension.

Dr Gauri M Panjabi et al. compared I.V. Nalbuphine with I.V. Fentanyl for postoperative analgesia in patients undergoing short surgical procedure under general anaesthesia. She observed that Nalbuphine provides better analgesia than Fentanyl with less respiratory depression in Nalbuphine than Fentanyl group [12]. In our study we also observed that Dexmedetomidine with Nalbuphine provides better quality of analgesia than Dexmedetomidine with Fentanyl. T.F.L. in et al. compared I.V. Dexmedetomidine with Morphine versus I.V. Morphine in patients undergoing total abdominal hysterectomy. Decreased in heart rate and MAP seen in Dexmedetomidine with Morphine group. Thus Dexmedetomidine with opioid causes more reduction in HR and MAP than Dexmedetomidine [9]. This shows that Dexmedetomidine provides controlled hypotension with surgical field. In our study Dexmedetomidine was used in both the groups so effect on pulse rate and blood pressure were comparable in both groups.

S. Goksu, H. Arik, et al. conducted a study for FESS surgery under LA with sedation divided in two groups placebo (NS infusion) and Dexmedetomidine (bolus followed by infusion). They observed that postoperative nausea and vomiting rates were significantly lower in the Dexmedetomidine group [13]. According to Parikh DA et al. 7 patients from Dexmedetomidine group showed dry mouth. More incidence of side effects seen may be due to infusion of Dexmedetomidine along with the bolus dose [14].

Dexmedetomidine is the most selective central α_2 adrenoceptor agonist, providing dose-dependent sedation, analgesia, sympatholysis and anxiolysis without respiratory depression. The sedative effect is rapid, stable and keep patient arousable. Sedation and analgesic property of Dexmedetomidine is attributed to stimulation of α_2 adrenoceptor in Locus ceruleus in brain and modulation of transmission nociceptive signal in CNS and

spinal level [6]. Due to sympatholytic effect it attenuates the stress response to surgery.

It has opioid sparing effect which provides hemodynamic stability in intra and postoperative period. Hypotension and bradycardia have been observed in studies done earlier with Dexmedetomidine. These effects are known to be related to the dose, route of administration, and infusion rate (in intravenous administrations) [10,15,16,17,18]. It does not cause respiratory depression because its effects are not mediated by the Y aminobutyric system [14].

Reports of its use state that alpha-2 agonist effect is more specific but not alpha-1 effect (200:1 for clonidine & 1600:1 for Dexmedetomidine), on administration of low and moderate doses and slow rates of infusion [11]. Consequently, peripheral vasoconstriction and hypertension would not be expected in these instances. Dexmedetomidine causes controlled hypotension & thus provides better surgical (bloodless) field for microscopic surgery compared with other drugs like Midazolam, Propofol.

Nalbuphine is a synthetic opioid which acts as an agonist at kappa receptors and an antagonist at mu receptors. It has analgesic potency equivalent to that of Morphine. When administered with mu agonist opioid analgesics (Morphine, Fentanyl) it may partially reverse or block opioid induced respiratory depression from mu agonist analgesic. Its onset of action is within 2-3 mins after I.V. administration and plasma half-life is 5 hours. Thus Nalbuphine has short duration of action and rapid clearance than other opioids and less side effects like over sedation, pruritus, respiratory depression and urinary retention.

Fentanyl is mu opioid agonist. Its analgesic property is 75-125 times more than Morphine. After I.V. administration, onset of action is within 1-2 mins and duration of action is 60 mins. Due to stimulation of central nucleus, there is decrease in heart rate which is dependent on dose and speed of injection. Fall in BP is due to decreased SVR through centrally mediated reduction in sympathetic tone. It causes dose dependent respiratory depression.

As Nalbuphine is not subject to the restriction of the Misuse of drugs act it is available freely [12].

Infusion of Dexmedetomidine gives better results in aspects of sedation, analgesia, rescue sedation & analgesia drug requirement compared to bolus dose but patients may have more side effects. Limitation of our study is that we used Dexmedetomidine as bolus dose only and even though BIS monitoring is more reliable parameter than RSS for monitoring

sedation we used RSS due to unavailability of BIS. So it needs to be studied further by use of infusion of Dexmedetomidine along with BIS monitoring.

Conclusion

From this study, we concluded that, intravenous Inj. Dexmedetomidine with Inj. Nalbuphine provides better sedation and analgesia, good hemodynamic stability, good surgeon's satisfaction score without side effects. It also reduces the requirement of rescue sedation and analgesia as compared to Inj. Dexmedetomidine with Inj. Fentanyl in patients undergoing Tympanoplasty under local anaesthesia with monitored anaesthesia care. Thus Dexmedetomidine with Nalbuphine is a better alternative to Dexmedetomidine with Fentanyl as sedation for middle ear surgery.

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