ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Comparison of nalbuphine and propofol verses pentazocine and promethazine in tympanoplasty surgeries under monitored anesthesia care

Deepali Valecha[1], Monika Gandhi[2], Ravi Barde[3], Arpit Agrawal[4], Kishore Kumar Arora[5]

[1,3]Assistant Professor, [2,5]Professor, [4]Senior Resident, Department of Anaesthesiology, M.G.M Medical College, Indore, Madhya Pradesh, India

Submission: 20-04-2022 Revision: 28-07-2022 Publication: 01-09-2022

ABSTRACT

Background: A middle ear surgery (tympanoplasty), is done under various modes of anaesthesia such as local anaesthesia (LA), general anaesthesia (GA) or sedation with local anaesthesia (MAC). It is usually performed under MAC providing advantages of rapid onset, allowing hearing test intraoperatively and early mobilization of the patient. **Aims and Objectives:** The aim of this study was to compare effectiveness of nalbuphine and propofol with pentazocine and promethazine combination for intraoperative sedation under monitored anesthesia care for tympanoplasty under local anesthesia (LA). **Materials and Methods:** A total 60 patients undergoing tympanoplasty under LA divided in to two groups randomly to receive either IV nalbuphine (50 mcg/kg) and propofol 750 mcgs/kg in 10 min followed by a maintenance infusion at the rate of 25 mcg/kg/min. Group N or pentazocine 0.6 mg/Kg and Inj. Promethazine 0.5 mg/kg IV diluted in 10 ml normal saline over 10 min followed by 25 mcg/kg/min infusion of normal saline (Group P). Sedation was titrated to Ramsay Sedation Score (RSS) of 3. Vital parameters such as HR, BP, SpO_2, RSS, visual analog scale score (VAS), requirement of rescue analgesics, mean bleeding score, and surgeon satisfaction score (Likert Scale) were recorded and analyzed. **Results:** RSS was higher and VAS score was lower in Group N at 30, 60, 90, and 120 min ($P<0.05$) that mean bleeding score was lower in Group N as compare to Group P which was statistically significant. **Conclusion:** Nalbuphine and propofol combination are superior to pentazocine and promethazine combination in terms of producing better analgesia, sedation with batter surgical field.

Key words: Monitored anesthesia care; Nalbuphine; Pentazocine; Promethazine; Propofol; Sedation; Tympanoplasty

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v13i9.44543

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Perforation of the tympanic membrane is one of the most common conditions encountered in the ENT outpatient department. Tympanoplasty is a surgical repair of the tympanic membrane, commonly performed under local anesthesia, general anesthesia, or monitored anesthesia care (MAC).[1] Less bleeding, cost-effectiveness, early recovery, and assessment of on-table hearing during tympanoplasty are advantages of using local anesthesia (LA). Patient's anxiety caused by noise during surgery, dizziness, and discomfort due to positioning of head and neck, etc., are the most common disadvantages of LA during Tympanoplasty.[1-3] These problems can easily be overcome by administering appropriate sedatives as monitored anesthesia care. The most important elements of MAC are sedation, analgesia, and control of anxiety.[4] Judicious use of MAC can bring inhibition

Address for Correspondence:
Dr. Arpit Agrawal, Senior Resident, Department of Anaesthesiology, M.G.M Medical College, Indore - 452 001, Madhya Pradesh, India.
Mobile: +919479888123. **E-mail:** arpitagrawal878@gmail.com

of movement by the patient during surgical procedure, but the patient still can respond to verbal commands as required for the surgical stage of operation. An ideal sedative agent for MAC should have a rapid onset of action, high clearance, easy titration, less cardiovascular, and respiratory depression.[5] During MAC, a wide variety of inhaled and intravenous (IV) drugs have been used including, benzodiazepines, barbiturates ketamine, propofol, opioid and non-opioid analgesics, alpha agonists, and nitrous oxide.[6,7] Combination of drugs produces synergistic effects with the advantage of reduced doses of each drug and hence their side effects. Since then many combinations of drugs such as promethazine and midazolam,[3] midazolam and fentanyl,[1] dexmedetomidine and midazolam,[8] fortwin and phenergan and midazolam,[9] dexmedetomidine and fentanyl versus dexmedetomidine and nalbuphine,[10] etc., for MAC under sedation were tried. Each one of them had their set of adverse effects. Recent studies have shown promising results with propofol in combination with other drugs such as nalbuphine. Nalbuphine a phenethrene opioid is μ receptor antagonist and κ, δ receptor agonist (dose of 50–250 mcgs/kg I.V). Its onset of action is 2–3 min. It provides analgesia and sedation without respiratory depression (ceiling effect).[11] Propofol is a selective modulator of GABA A receptors. It is a sedative-hypnotic agent with rapid onset of action with short and clear-headed recovery. If given in the doses of 25–100 mcgs/kg/min, it causes conscious sedation. It also has antiemetic properties.[12] Pentazocine is an agonist at the κ-receptors and weak σ-receptor agonist produces analgesia. Nausea vomiting caused by pentazocine can be counteracted by the sedative drug promethazine (antagonist of histamine H1, post-synaptic mesolimbic dopamine, alpha-adrenergic, muscarinic, and NMDA receptors), so combination can be used in MAC.[13]

Hence, we want to explore the effectiveness of propofol-nalbuphine combination and pentazocine-promethazine combination in tympanoplasty surgeries scheduled under MAC.

Aims and objectives

The aim of this study was to compare the effectiveness of nalbuphine and propofol with pentazocine and promethazine combination in terms of sedation, analgesia, and surgical field.

MATERIALS AND METHODS

It is a prospective, randomized, and comparative double-blind study. This study was conducted in the Department of Anesthesiology, M.G.M Medical College and M.Y Hospital, Indore after approval by the Institutional Ethics and Scientific Review Committee. Written informed consent was taken from all the patients after explaining the procedure, its associated risks and side effects. Sixty adult patients (30 in each group) between 18 and 60 years of age belonging to the American Society of Anesthesiologists (ASA) physical status I or II, of either sex, who were admitted for elective tympanoplasty under local anesthesia, were recruited for the study. Patients with known allergy or hypersensitivity to local anesthetics and study drugs, pregnant or lactating women, patients on sedative medication, hepatorenal, and cardiorespiratory comorbidities were excluded from our study. Randomization was done by the chit method. The patients were counseled in detail about sedation, LA, and operative procedure. All the patients underwent pre-anesthetic checkups including a detailed history, general, and systemic examination and investigations. The visual analog scale (VAS) (0–10), where 0 indicated no pain, while ten indicated maximum pain, was explained to the patients. Preoperatively, patients were advised to remain nil by mouth for at least 8 h. The patient was shifted to the operation theater after confirming nil by mouth and consent. All baseline vital parameters, heart rate (HR), SBP, DBP, mean arterial pressure (MAP), and SpO_2, were recorded by a multipara monitor. Ringer lactate solution was started after IV access was secured. All the patients were given oxygenate 2 L/min through nasal cannula. Ondansetron 0.08 mg/kg and inj. Glycopyrrolate 0.004 mg/kg IV was given to all patients as premedications. Infusion pumps and I.V. sets were covered with Aluminium foils to blind an investigator. Drugs were given according to group allocation. Group N received IV nalbuphine (50 mcg/kg) and propofol 750 mcgs/kg in 10 min followed by a maintenance infusion at the rate of 25 mcg/kg/min Group P received pentazocine 0.6 mg/Kg and Inj. Promethazine 0.5 mg/kg IV diluted in 10 ml normal saline over 10 min followed by 25 mcg/kg/min infusion of normal saline. After Ramsay Sedation Score (RSS) of 3 and VAS score ≤3 was achieved. 2% Lignocaine and Adrenaline (1:100,000) were used for the Infiltration of operative field. Surgery was commenced after confirmation of the adequate analgesia. Patient's response to LA infiltration was evaluated for pain and body movement. The pain was recorded on 10 point VAS. Vital parameters were recorded intraoperatively every 2 min during loading dose of study drugs and at 10 min intervals till the end of surgery. At, every 10, 30, 60, 90, and 120 min sedation level was assessed by RSS, if RSS <3 IV midazolam 0.01 mg/kg was administered in either group. VAS was used for intraoperative pain evaluation. LA infiltration at the surgical site and rescue IV fentanyl 1 mg/kg were used for inadequate analgesia.

Approximately 15 min before the end of surgery, maintenance infusion was discontinued at the time of closure. All adverse events such as bradycardia (HR<45 beats/min), hypotension (MAP<50 mmHg sustained for >10 min), respiratory depression (respiratory rate <10 bpm), oxygen desaturation, (SpO_2<90%), nausea, or vomiting were recorded. Bradycardia was managed with IV Atropine and IV fluids or Inj. Mephenteramine is used for the management of Hypotension. The surgical field was graded in terms of bleeding by the blinded surgeon using the scale developed by Boezaart at the end of surgery.[14,15] The Likert scale was used for the assessment of surgeon's satisfaction. Patients were shifted to post-anesthesia care unit and monitored for hemodynamic parameters, analgesia, and adverse events if any within 2 h after completion of surgery. Patients were observed for 24 h postoperatively. All data were recorded in a structured case record form.

Statistical analysis

The data were initially entered into the Microsoft Excel from the customized pro forma for analysis. SPSS software was used for calculating P values. A comparison of means between the two groups was done using the Chi-square test. Descriptive statistics were presented in the form of numbers and percentages. P<0.05 was taken as a statistically significant Unpaired t-test and the Chi-square test was used for categorical values as data expressed in number of patients or ratio (age, sex, weight, height, HR, MAP, SpO_2, and adverse effects). Mann–Whitney U-test and Freidman test are used for numerical values as data expressed in mean and standard deviation (Sedation scores at various intervals intraoperatively, pain score at various intervals intraoperatively, post-operative sedation, and pain scores).

Table 1: Demographic profile in the groups

Demographic variables	N Group	P Group	P-values
Age (years)	37.27	37.77	0.868
Sex (F/M)	17/13	16/14	0.785
Weight (kg)	60.27	64.3	0.258
Height (cm)	161.3	162.1	0.724
ASAI/II	13/17	14/16	0.896
Mean duration of surgery (min)	71.33	73.23	0.849

Table 2: Comparison of hemodynamic parameters among the two groups (mean)

Group P	PR (bpm)		MAP (mmhg)	
	At 10 min	At 20 min	At 10 min	At 20 min
N Group	70.22±10.23	78.73±11.32	64.23±7.74	69.22±2.69
P Group	90.76±11.21	91.63±10.92	84.65±9.61	79.66±7.84
P value	<0.0001	<0.0001	<0.0001	<0.0001

RESULTS

Basic profile of study participants is shown in Table 1. Both the groups had no statistically significant difference in respect to mean age, sex, weight, height, and mean duration of surgery. There were total 13 participants of ASA I and 17 participants of ASA II in group N were as in group P, there were total 14 participants of ASA I and 16 participants of ASA II. Table 2 shows comparison of hemodynamic parameters by means of HR and MAP among the two groups were recorded at 0, 10, 20, 30, 45, 60, 90, and 120 min. HR and MAP were well maintained in both the groups. However, it was observed that HR and MAP were lower side at 10 and 20 min in Group N and the difference was statistically significant. RSS shows in table 3 and it was used to measure intraoperative sedation. Mean RSS in Group N were 3.29 ±0.861, 3.19 ± 0.406, 3.21 ± 0.679, 3.23 ± 0.376, and 3.09 ± 0.523 at 10, 30, 60, 90, and 120 min, respectively. While in Group P the RSS were 3.41 ± 0.707, 2.79 ± 0.504, 2.79 ± 0.616, 2.74 ± 0.467, and 2.79 ± 0.630 at 10, 30, 60, 90, and 120 min, respectively. RSS was higher in Group N as compare to group P at 30, 60, 90, and 120 min and the difference was statistically significant. Mean VAS for pain shows in table 4. Mean VAS in Group N was 1.57 ± 0.641, 1.62 ± 0.665, 1.52 ± 0.522, and 1.53 ± 0.601 at 30, 60, 90, and 120 min, respectively. While in Group P the VAS were 3.19 ± 0.521, 2.98 ± 0.495, 2.48 ± 0.694, and 2.56 ± 0.378 at 30, 60, 90, and 120 min, respectively. VAS was lower in Group N as compare to group P at 30, 60, 90, and 120 min and the difference was statistically significant. Requirement of rescue analgesic and rescue sedative was high with P group as compared to N group (statistically significant), as shown in Table 5. Boezaart bleeding score is shown in Table 6 and it was lower in Group N (1.57 ± 0.19) as compare to Group P (2.11 ± 0.36) and the difference was found to be statistically significant. The patient satisfaction score is shown in Table 7 and it was comparable in both the groups.

DISCUSSION

MAC is being widely used for performing different ENT surgeries. The basic principle is to supplement sedation along with LA so that less bleeding during surgery occurs, hearing can be tested intraoperatively and any immediate complications can be detected early and managed accordingly.[4,6,7] Different drugs are used for MAC, but no standard regimen can be designed which can be fitted to all patients. The primary aim of this study was to compare the effectiveness of nalbuphine and propofol with pentazocine and promethazine

Table 3 : Comparison of intraoperative mean sedation score in both the groups at various time intervals

Parameters (Ramsay sedation score)	Total number of cases in each group	Group N Mean value±S.D.)	Group P (Mean value±S.D.)	P value
RSS 10 min	30	3.29±0.861	3.41±0.707	0.557
RSS 30 min	30	3.19±0.406	2.79±0.504	0.001
RSS 60 min	30	3.21±0.679	2.79±0.616	0.014
RSS 90 min	13 (Group N) 14 (Group P)	3.23±0.376	2.74±0.467	<0.001
RSS 120 min	2 (Group N) 3 (Group P)	3.09±0.523	2.79±0.630	0.044

Table 4: Comparison of intraoperative mean VAS score in both the groups at various time intervals

Parameters (VAS)	Total number of cases in each group	Group N (Mean value±S.D.)	Group P (Mean value±S.D.)	P value
VAS 10 min	30	2.17±0.674	2.37±0.568	0.218
VAS 30 min	30	1.57±0.641	3.19±0.521	<0.001
VAS 60 min	30	1.62±0.665	2.98±0.495	<0001
VAS 90 min	13 (Group D) 14 (Group P)	1.52±0.522	2.48±0.694	<0.0001
VAS 120 min	2 (Group D) 3 (Group P)	1.53±0.601	2.56±0.378	<0.0001

VAS: Visual Analog Scale

Table 5: Comparison of requirement of rescue sedative and rescue analgesia in both the groups

Parameter	Groups	n/30	%	P-value
Rescue sedative required	N	2/30	6	<0.05
	P	4/30	12	
Rescue analgesia required	N	3/30	10	<0.05
	P	6/30	20	

Table 6: Bleeding scores at the end of the surgery in both the groups

Parameters	Total number of cases in each group	Group N (Mean value±S.D.)	Group P (Mean value±S.D.)	P value
Boezaart bleeding score	30	1.57±0.19	2.29±0.36	<0.001

Table 7: Comparison of mean patient satisfaction scores in both the groups

Parameters	Total number of cases in each Group	Group N (Mean value±S.D.)	Group P (Mean value±S.D.)	P value
Patient satisfaction Score	30	3.43±0.22	3.29±0.32	0.053

combination for MAC with LA. Group N received IV nalbuphine (50 mcg/kg) and propofol 750 mcgs/kg in 10 min followed by a maintenance infusion at the rate of 25 mcg/kg/min. The dose of propofol 0.75 mg/kg was chosen based on a recent study by Verma et al.,[16] and Nallam et al. [17]

On analyzing cardiovascular parameters in both study groups, there is a statistically significant difference (P<0.05) between the two groups, HR and MAP maintained at a lower side in Group N than in Group P. Findings can be explained easily by the property of propofol to reduce sympathetic activity in the body when it combines with nalbuphine. Nalbuphine and propofol combination helps in producing controlled hypotension which can be contributing factor to producing significantly more bloodless field at the operative site and less intraoperative bleeding in Group N as compared to Group P (P<0.05). These findings are also conquering with results of a similar study by Solanki et al.[18] Stable hemodynamics, controlled hypotension, and decreased bleeding could be responsible for a better surgical field in Group N in our study. Intraoperative VAS pain score was lower in Group N than in Group P.

propofol has no analgesic property but with combination of nalbuphine, it gives better a VAS score than pentazocine and promethazine combination (Fang et al., and Ghali et al.).[19,20] Intraoperative RSS was higher in Group N than in Group P. The findings can be explained easily by the property of propofol to reduce sympathetic activity in the body when it combines with nalbuphine (Ghali et al.).[20]

Although this study has compared the nalbuphine and propofol versus pentazocine and promethazine in MAC, with LA, the study was single centered. Therefore, variations in genetic, racial, and other factors could not be analyzed. Larger studies evaluating these aspects are required in the future for enhancing the quality of MAC for the betterment of patients.

Limitations of the study

A possible limitation of the study was that we assessed sedation by Ramsay Sedation Score while BIS monitoring is ideal for assessing sedation. Also due to small sample size, study findings cannot be generalized.

CONCLUSION

Our study demonstrates that nalbuphine and propofol combination has better sedation, analgesia, stable hemodynamics, and lesser bleeding under MAC as compared to pentazocine and promethazine combination in tympanoplasty surgery.

ACKNOWLEDGMENT

We are thankful to MGM Medical College and M.Y. Hospital Indore and also thankful to all individuals who participated in this study

REFERENCES

1. Parikh DA, Kolli SN, Karnik HS, Lele SS and Tendolkar BA. A prospective randomized double-blind study comparing dexmedetomidine vs. combination of midazolam-fentanyl for tympanoplasty surgery under monitored anesthesia care. J Anaesthesiol Clin Pharmacol. 2013;29(2):173-178.
   https://doi.org/10.4103/0970-9185.111671
2. El-Begermy MA, El-Begermy MM, Rabie AN, Ezzat AE and Sheesh AA. Use of local anesthesia in ear surgery: Technique, modifications, advantages, and limitations over 30 years' experience. Egypt J Otolaryngol. 2016;32:161-169.
   https://doi.org/10.4103/1012-5574.186541
3. Sarmento KM Jr. and Tomita S. Retroauricular tympanoplasty and tympanomastoidectomy under local anesthesia and sedation. Acta Otolaryngol. 2009;129(7):726-728.
   https://doi.org/10.1080/00016480802398996
4. Ghisi D, Fanelli A, Tosi M, Nuzzi M and Fanelli G. Monitored anesthesia care. Minerva Anestesiol. 2005;71:533-538.
5. Das S and Ghosh S. Monitored anesthesia care: An overview. J Anaesthesiol Clin Pharmacol. 2015;31(1):27-29.
   https://doi.org/10.4103/0970-9185.150525
6. Gan TJ. Pharmacokinetic and pharmacodynamic characteristics of medications used for moderate sedation. Clin Pharmacokinet. 2006;45(9):855-869.
   https://doi.org/10.2165/00003088-200645090-00001
7. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology. 2002;96(4):1004-1017.
   https://doi.org/10.1097/00000542-200204000-00031
8. Abdellatif AA, Elkabarity RH and Abd Elhamid Hamdy T. Dexmedetomedine vs midazolam sedation in middle ear surgery under local anesthesia: Effect on surgical field and patient satisfaction. Egypt J Anaesth. 2012;28(2):117-123.
   https://doi.org/10.1016/j.egja.2011.12.004
9. Sen J and Sen B. A comparative study on monitored anesthesia care. Anesth Essays Res. 2014;8(3):313-318.
   https://doi.org/10.4103/0259-1162.143121
10. Mane A and Kulkarni J. Intravenous sedation for tympanoplasty comparison of I.V. dexmedetomidine and nalbuphine with I.V. Dexmedetomidine and fentanyl. Indian J Anesth Analg. 2018;5(11):1791-1800.
    https://doi.org/10.21088/ijaa.2349.8471.51118.3
11. Flood P, Rathmell JP and Shafer S. Stoeltings Pharmacology and Physiology in Anaesthetic Practice. 5th ed. London: John Butterworth; 2014. p. 194.
12. Stoeltings Pharmacology and Physiology in Anaesthetic Practise. 5th ed. Philadelphia, Pennsylvania: Lippincott Williams and Wilkins; 2014. p. 162.
13. Sanjekar DA. Comparative study between fentanyl-medazolam with pentazocine-promethazine for conscious sedation during cardiac catheterization. Int J Anaethesiol. 2006;12(2): p. 1-4.
    https://doi.org/10.5580/d8a
14. Reves JG, Glass PS, Lubarsky DA, McEvoy MD and Ruiz RM. Intravenous Anesthetics. In: Miller RD, editor. Miller's Anaethesia. 7th ed. Amsterdam, Netherlands: Elsevier, Churchill Livingstone; 2009. p. 723-727.
15. Mahfouz AK and Ghali AM. Combined use of remifentanil and propofol to limit patient movement during retinal detachment surgery under local anesthesia. Saudi J Anaesth. 2010;4(3):147-151.
    https://doi.org/10.4103/1658-354x.71570
16. Verma R, Gupta R, Bhatia VK, Bogra J and Agarwal SP. Dexmedetomidine and propofol for monitored anesthesia care in the middle ear surgery. Indian J Otol. 2014;20(2):70-74.
    https://doi.org/10.4103/0971-7749.131872
17. Nallam SR, Chiruvella S and Reddy A. Monitored anaesthesia care comparison of nalbuphine/dexmedetomidine versus nalbuphine/propofol for middle ear surgeries: A double-blind randomised trial. Indian J Anaesth. 2017;61(1):61-67.
    https://doi.org/10.4103/0019-5049.198403
18. Solanki U, Patel D and Gupta S. Comparison of dexmedetomidine vs. pentazocine promethazine for tympanoplasty under MAC: A randomized double blind study. Indian J Anesth Analg. 2018;5(11):1933-1940.
    https://doi.org/10.21088/ijaa.2349.8471.51118.24
19. Fang P, Qian J, Ding J, Pan X, Su H and Liu X. Comparison of analgesic effects between nalbuphine and sufentanil in

first-trimester surgical abortion: A randomized, double-blind, controlled trial. Pain Ther. 2022;11(1):121-132.
https://doi.org/10.1007/s40122-021-00334-0

20. Ghali A, Mahfouz AK, Ihanamäki T and El Btarny AM. Dexmedetomidine versus propofol for sedation in patients undergoing vitreoretinal surgery under sub-Tenon's anesthesia. Saudi J Anaesth. 2011;5(1):36-41.
https://doi.org/10.4103/1658-354x.76506

Authors Contribution:
DV- Concept and design of the study, aims and objectives; **AA**- Prepared the first Draft of manuscript, arranged all the references, developing consent form and this is his own dissertation work; **MG**- Contribute regarding conception or design of study, data collection, interpreted the results and manuscript preparation; **RB**- Coordination, statistical analysis and interpretation and revision of manuscript; **KKA**- concept and coordination of the overall study.

Work attributed to:
M.G.M Medical College, Indore - 452 001, Madhya Pradesh, India.

Orcid ID:
Dr. Deepali Valecha - https://orcid.org/0000-0002-7813-6720
Dr. Monika Gandhi - https://orcid.org/0000-0002-3637-830X
Dr. Arpit Agrawal - https://orcid.org/0000-0002-4455-4115
Dr. Ravi Barde - https://orcid.org/0000-0002-0736-0207
Dr. Kishore Kumar Arora - http://orcid.org/0000-0002-7376-4322

Source of Support: Nil, **Conflict of Interest:** None declared.