ORIGINAL ARTICLE

A Comparison of Three Drug Combinations for Sedation during Middle Ear Surgeries under Local Anesthesia: A Multicentric Randomized Double Blind Study

Vikas Kumar¹, Jyotsna S. Paranjpe^{1*}, Shishir D. Gosavi², Ruta H. Kulkarni¹, Rahul S. Gosavi², Tanuja M. Kulkarni¹

¹Department of Anaesthesia, Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli-416416 (Maharashtra) India, ²Sanjeevan Medical Foundation, Miraj-416410 (Maharashtra) India

Abstract:

Background: During Middle Ear Surgeries (MES) done under Local Anesthesia (LA), patients may feel discomfort due to noise of suction, manipulation of instruments, positioning of head-neck and sometimes due to pain. A bloodless microscopic field is also essential to facilitate surgical exposure in MES. Various combinations of analgesics and sedatives have been tried to alleviate apprehension of the patients and improve microscopic field which may result into reduction in surgical time. In the present study, we have compared Dexmedetomedine (Dex) with Midazolam-Fentanyl (MF) and Pentazocine-Promethazine (PP) combinations for their sedoanalgesia, anxiolysis and other pharmacological effects when administered during MES, not lasting for more than 60 min. Material and Methods: Ninety American Society of American Society of Anesthesiologists (ASA) group I /II patients admitted in either of the three hospitals during May 2014 to January 2015 for MES under LA were randomly divided into three groups by an independent observer. Group D received intravenous bolus of Injection Dexmedetomidine 1 µg/ kg over 10 min. Group MF received Injection Midazolam 0.06 mg/ kg + Inj. Fentanyl 1 µg/ kg and Group PP received Injection Pentazocine 0.3 mg/kg + Injection Promethazine 0.5mg/kg given intravenously followed by LA before taking incision for the surgery. Need of a rescue sedoanalgesic dose of (Midazolam 0.01 mg/kg + Fentanyl 0.5 µg/kg) during the surgery was noted. All the patients received 500 ml of normal saline infusion

till the end of the surgery. All surgeries were finished within 60 min. Vital parameters and Ramsay Sedation Score (RSS) of the patients were noted from the time of administration of sedative till the end of the surgery. Patient and surgeon satisfaction scores were recorded immediately after the surgery. Drug combinations of three groups were compared for their effectiveness, adverse effects and satisfaction scores in given doses. Children, mentally unstable patients, uncooperative patients, patients requesting general anesthesia, patients with known sensitivity to local anesthetic drug Lignocaine, and allergy to study drugs, pregnant and lactating females were excluded from the study. Results: RSS were satisfactory in Group D and Group MF but not in Group PP. Percentage of patients requiring rescue sedoanalgesic dose of (Midazolam 0.01 mg/kg + Fentanyl 0.5 µg/kg) was the highest (20%) in Group PP. It was the least in Group D. Intraoperative heart rate and mean arterial pressure in Group D were significantly lower than the baseline values and the corresponding values in Group MF and Group PP. Incidence of postoperative nausea was higher in Group PP. One patient in Group D had significant bradycardia with hypotension while one patient in Group MF got desaturated needing Oxygen therapy. Statistically significant number of patients from Group D had bloodless microscopic field compared to Group MF and Group PP. Surgeon satisfaction scores which showed statistically significant correlation with type of microscopic field were better in Group D. Patient satisfaction scores were better in Group D than Group MF and Group PP.

Conclusion: Out of the sedoanalgesics tested, Dexmedetomidine was found to be the best drug for MES patients performed under local anaesthesia. It produced near bloodless microscopic surgical field with better surgeon and patient satisfaction.

Keywords: Dexmedetomidine, Fentanyl, Midazolam, Middle Ear Surgery, Pentazocine

Introduction:

Middle ear diseases affect patients of all ages. Common middle ear pathological conditions requiring surgery in adults include tympanoplasty (reconstructive surgery for the tympanic membrane or eardrum), stapedectomy or ossiculoplasty for otosclerosis, mastoidectomy for removal of infected air cells within the mastoid bone, and removal of cholesteoma [1].

Middle Ear Surgeries (MES) can be performed under either local or general anesthesia. Many advantages have been reported with the local anesthetic techniques, such as less bleeding, costeffectiveness, early recovery, postoperative analgesia, and of great importance is the ability to test the hearing of the patient intraoperatively [2, 3]. Despite these advantages, most of MES are still done under general anesthesia due to special concerns; some are related to patients' anxiety which is augmented in some by their hearing loss, limiting their ability to cooperate. Other concerns are related to surgeon comfortability with the hypotensive general anesthetic techniques, and the fear of sudden patient movement during operation [1, 3]. The most common discomforts reported by the patients during MES under local anesthesia were anxiety caused by noise during surgery, dizziness, discomfort due to positioning of head and neck [2, 3].

Dexmedetomedine (Dex); is a highly selective -2 adrenoreceptor agonist, which possess both sedative and analgesic actions [4]. By attenuating sympathetic activity, it inhibits norepinephrine release and produces predictable, dose-dependent reduction in the arterial blood pressure and heart rate [5,6]; these effects prove advantageous in microsurgeries on middle ear in which even a small amount of blood will obscure the surgeons view. Review of literature suggests that Dex can be used to provide sedation, analgesia and bloodless field for MES under LA resulting into high surgeon and patient satisfaction [7, 8].

Promethazine counteracts nausea and vomiting caused by the opioid analgesic Pentazocine by virtue of its antihistaminic effects. Moreover it has a sedative effect [9].

It was designed this study to compare the efficacy of Dex to a time-tested combination of Midazolam - Fentanyl [7, 9, 10] and Pentazocine -Promethazine [9], to provide sedation and analgesia for MES (primary outcome).

The study was aimed to compare three groups under study for their efficacy to provide a nearbloodless microscopic surgical field, hemodynamic and respiratory effects, surgeon and patient satisfaction, and adverse effects, if any (secondary outcome).

Material and Methods:

This prospective multicentric randomized double blind study was undertaken after institutional ethical committee approval. Ninety patients admitted in any of the three hospitals in Group I or II as per classification of American Society of Anaesthesiologist during May 2014 to January 2015 for MES under LA who satisfied the inclusion criteria were randomly divided into three groups by an independent observer by a lottery method. All the patients were examined a day before surgery. They were counseled with regards to sedation, local anesthesia as well as the operative procedure. Data was recorded by a blinded observer and the drugs were prepared by an anesthesiologist who did not participate in patient management or data collection. Group D patients received injection Dexmedetomidine 1µg kg⁻¹, Group MF received injection Midazolam 0.06 mg kg⁻¹ plus injection Fentanyl 1µg kg⁻¹ and Group PP received injection Pentazocine 0.3mg kg⁻¹ plus injection Promethazine 0.5 mg kg⁻¹ from their respective loading syringes.

Children, mentally unstable patients, uncooperative patients, patients requesting general anesthesia, patients with known sensitivity to local anesthetic drug Lignocaine, allergy to study drugs, pregnant and lactating females were excluded from the study.

On arrival to the operation theatre, baseline vital parameters of the patient were recorded. All the patients received injection Glycopyrrolate 0.2 mg intravenously as a premedication. All the patients received a bolus of sedoanalgesic drug in the prefilled syringe administered by a blinded anesthesiologist.

From the onset of administration of a drug, level of sedation of the patients was assessed using RSS every ten minutes. If sedation score found was < 2, anytime during the surgery, a rescue sedoanalgesic dose of IV midazolam 0.01mg kg⁻¹ + Fentanyl 0.5µg/kg was administered. The need and frequency of rescue sedoanalgesic dose was recorded.

ENT surgeon administered LA using 2% Lignocaine with adrenaline (1:2, 00,000). Surgery was commenced after confirming adequate analgesia. Intraoperatively Heart Rate (HR), Mean Arterial Blood Pressure (MABP), respiratory rate and SPO₂ were recorded every 5 min during the surgery.

Patient Characteristics	Group D (n=30)	Group MF (n=30)	Group PP (n=30)
Age (year)	37 +/-17	38+/-12	33+/-11
Weight (kg)	55+/-4	58+/-7	54+/-5
Sex			
Male (n)	18	17	14
Female (n)	12	13	16
Type of surgery			
Mastoidectomy	6	6	3
Tympanoplasty	19	21	20
Stapedectomy	5	3	7
Operating hospital			
BVDUMCH	4	4	4
Ashviniprasad	18	15	17
Purohit	8	11	9

 Table 1: Demographic Characteristics, Types of Surgeries and Hospital Wise Distribution

 of the Patients

Patient characteristics (Mean+/- SD), BVDUMC:-Bharati Vidyapeeth University Medical College and Hospital

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All the patients received 500 ml of normal saline infusion till the end of the surgery. All surgeries were finished within 60 min.

Adverse events like tachy /bradycardia, hyper/ hypotension (deviation of HR, MAP >20% of baseline), bradypnea (RR <8 breaths/min), desaturation (SpO₂ < 90%), nausea, vomiting, dry mouth or any other event during or within two hours after the procedure were noted. Bradycardia was treated with intravenous Atropine sulphate 0.01mg kg⁻¹, hypotension with fluid resuscitation and if needed, intravenous ephedrine hydrochloride 5 mg in incremental doses was administered. Desaturation was treated by administration of O₂ by mask up to 6 liters / min.

At the end of the surgery, the surgical field was graded in terms of bleeding by the surgeon blinded to the study drug, using the scale developed by Boezaart [11, 12]. Percentage of a favorable quality of surgical field (score Grade I) was 80% (24 patients), 20% (6 patients) and 13.33% (4 patients) in Group D, Group MF and Group PP respectively.

Assessment of surgeon as well as patient satisfaction scores was based on 4 point Likert scale.

The primary end point of our study was the patient satisfaction score using 4 point Likert scale. Efficacy of the sedation technique was defined as the ability to complete the surgery without any rescue sedatives and analgesics. Safety of the technique was determined based on the frequency of analgesia/sedation-related intra or postoperative adverse events.

Statistical analysis:

Power analysis was based on the results of a previous study. Sample size calculation was based on a population standard deviation of 1.1 with 80% power and 5% alpha error. Hemodynamic data was evaluated using unpaired t test for intergroup and paired t-test for within group comparisons. Data not normally distributed was compared using Mann Whitney U test. Categorical data was analyzed using Chi square test. *P* value less than 0.05 was considered as significant.

Table 2: Intraoperative and Postoperative Adverse Effects			
Parameters	Group D (N=30)	Group MF (N=30)	Group PP (N=30)
Desaturation	0	1	0
Bradypnea	0	0	0
Hypotension	1	0	0
Hypertension	0	0	0
Bradycardia	1	0	0
Nausea	1	2	3
Vomiting	0	0	0
Dry mouth	2	0	0
Other	0	0	0

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Grade	Group D (N=30)	Group MF (N=30)	Group PP (N=30)
Grade 0	-	-	-
Grade 1	24	6	4
Grade 2	6	21	22
Grade 3	0	3	4
Grade 4	-	-	_
Grade 5	_	-	_

Table 3: Boezaart Grading Scale forScoring of Surgical Field Bleeding

0: No bleeding (cadaveric conditions)

1: Slight bleeding—no suctioning required

2: Slight bleeding—occasional suctioning required

3: Slight bleeding—frequent suctioning required. Bleeding threatens surgical field a few seconds after suction is removed

4: Moderate bleeding—frequent suctioning required. Bleeding threatens surgical field directly after suction is removed

5: Severe bleeding—constant suctioning required. Bleeding appears faster than can be removed by suction; surgical field severely threatened and surgery usually not possible

 Table 4: Surgeon Satisfaction Scores

Grade	Group D (N=30)	Group MF (N=30)	Group PP (N=30)
Excellent	21	14	11
Good	7	11	12
Average	2	3	6
Bad	0	2	1

Table 5: Patients Satisfaction Score

Grade	Group D (N=30)	Group MF (N=30)	Group PP (N=30)
Excellent	19	13	11
Good	8	11	9
Average	2	3	9
Bad	0	3	1

Results:

The patient characteristics and surgical data were comparable between the three groups. No major adverse events were observed in this study. Group D patients had significant fall in heart rate (> 20% of baseline) from 25 min after administration of study drug till the end of surgery. Group D also had significant fall in MABP (>20% of baseline) from 15 min after administration of study drug.

One patient in Group D developed hypotension and bradycardia which was successfully treated with intravenous atropine 0.6 mg and intravenous ephedrine 6 mg. Respiratory rate and SpO_2 were comparable and within normal limits in all the groups. There was an episode of desaturation in MF group which was treated with nasal insufflations of Oxygen.

Ramsay Sedation Score (RSS): 1. anxious and agitated or restless, or both, 2. cooperative, oriented, and calm, 3. responsive to commands only, 4. exhibiting brisk response to light glabellar tap or loud auditory stimulus, 5. exhibiting a sluggish response to light glabellar tap or loud auditory stimulus, 6. unresponsive.

Most of the patients reached RSS of 3 within 10 min of administration of study drug. During surgery, one patient in Group D required rescue sedoanalgesic dose in contrast to two patients in Group MF and 6 patients in Group PP. No patient in any group had RSS >3 at any point during surgery. Immediately upon arrival into the recovery room, all the patients were able to obey commands. At the end of 30 min most of them reached RSS of < 2. Time until needed for postoperative analgesic was comparable in all the groups. Average surgeon and patients' satisfaction scores were higher in Group D than Group MF and Group PP. Two patients in Group D had dryness of mouth in contrast to none in Group MF and Group PP.



D: Dexmedetomedine, MF: Midazolam-Fentanyl, PP: Pentazocine-Promethazine, MAP: Mean Arterial Pressure. X axis – Time in minutes from administration of the study drug upto end of surgery Y axis – Variation in MABPs over the operative period



Fig. 1: Comparison of Intraoperative Mean Arterial Blood Pressure Values

D: Dexmedetomedine, MF: Midazolam-Fentanyl, PP: Pentazocine-Promethazine, HR: Heart Rate. X axis –Time in minutes from administration of the study drug upto end of surgery Y axis – Variation in heart rates over the operative period

Fig. 2: Comparison of Intraoperative Heart Rates



X axis – Time in minutes from administration of the study drug upto end of surgery Y axis – Variation in sedation scores over the operative period

Fig. 3: Sedation Score in Three Groups at Various Specified Timings

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Discussion:

Middle-ear surgeries pose a different set of challenges for the patient, surgeon and anesthesiologist. Sympathetic stimulation and movements of an anxious patient cause increased bleeding and disturb the fine microscopic nature of the surgery which may even lead to graft failure. The advantages of local anesthesia include possibility of testing of hearing intraoperatively, less bleeding, immediately detecting complications and a truncated postsurgical emergence [1, 7]. Good patient selection, preoperative counseling and use of appropriate sedation are important factors for success of surgery under LA [13]. The patient needs to be informed prior to infiltration of LA that he will be able to feel manipulation of tissues and the noise of instruments, but there will be no pain [3]. The ability to deliver safe, effective and moderate sedation is crucial to the ability to perform MES under LA. A sedative drug should have a quick onset of action, provide rapid and clear-headed recovery, and be easy to administer and monitor.

Monitored Anaesthesia Care (MAC) is the terminology used for sedation given along with the local anesthesia for short procedures [9]. Oversedation leading to respiratory depression is an important mechanism of patient injuries during MAC [10, 14]. A dose-dependent relationship exists with a sedative induced reduction in ventilator response to hypercarbia. The doses of Dexmeditomedine [7], Midazolam - Fentanyl [7, 10] and Pentazocaine - Promethazine [9] were chosen based on previous studies. The doses of Midazolam 0.06 mg kg $^{-1}$ [7, 15] and Promethazine 0.5mg kg-1 [9] are comparable to Dexmedetomidine $1 \mu g k g^{-1}$ in terms of sedation. We aimed to compare equisedative doses which were targeted to a predefined end point of moderate sedation/analgesia (conscious sedation) which corresponds to RSS [2-3]. The literature suggests that combining a sedative with an opioid provides effective moderate sedation [8].

Dexmedetomidine has both sedative and analgesic properties and has been extensively studied as a single agent for various procedures performed under MAC [5-7, 13, 15-27].

In the present study, in addition to comparable respiratory rates there was no evidence of bradypnea in any group. Dexmedetomidine is unique in that it does not cause respiratory depression [6, 21 - 23] because its effects are not mediated by the gamma aminobutyric (GABA) system. [28-29].

The reported incidence of Postoperative Nausea Vomiting (PONV) after MES is quite high (62-80%) which is less with intravenous anesthetics than use of volatile agents [1, 4]. The reduced incidence of PONV in the present study (6.6%) than that reported in literature could be due to antiemetic properties of Dex [13, 18] and Promethazine [9]. There are several studies which have detected reduced incidence of PONV after Midazolam premedication, mechanism of action postulated is via the action on chemoreceptor trigger zone [30]. The fact is yet not widely accepted due to lack of the confirmative evidence by large multicentric ramdomised control trials RCTs.

The lower HR and MABP in Group D in comparison to the other two groups could be explained by the decreased sympathetic activity caused by Dex by virtue of its -2 agonist effect [22, 25]. These results suggest that Dexmeditomedine has clinical advantage over Midazolam in providing a better operative field for microscopic surgery [7].

For bloodless operative field, physical and pharmacological techniques are used: a Head up tilt by 15-20 degrees, avoidance of venous obstruction, normocapnoea, reduction in BP. Use of clear plastic drapes reduce feeling of claustrophobia and a forced air device can be used to provide room air ventilation [1]. Controlled hypotension is defined as a drug induced reduction of SBP upto 80 mm Hg and MAP to 50 mm of Hg. Pharmacological agents used for controlled hypotension include inhalational anesthetics, vasodilators, [11] blockers, [26] -2 agonists [26], opioids [26] and magnesium sulphate. The danger of this technique is that it can cause tissue hypoxia by reducing microcirculatory autoregulation of vital organs. To avoid the complication, a close blood pressure monitoring, preferably with an arterial line is recommended [1, 11, 26].

In the present study, surgeon satisfaction scores were significantly better with Dexmeditomedine. They correlated well with the visibility of the surgical field. Durmus *et al.* [27] have evaluated this property of Dex for providing controlled hypotension in general anesthesia for tympanoplasty cases and concluded that it is a useful adjuvant to decrease bleeding when a bloodless surgical field is required. Reduction in intraoperative patient movements and surgical time are also contributory factors.

Lesser number of patients receiving Dexmeditomedine demanded rescue analgesics as compared to the Midazolam-Fentanyl and Pentazocine -Phenargan group, could be attributable to the quality of sedation and analgesia [17, 31]. Reduced sense of PONV also contributed to the better patient satisfaction scores [5, 13, 19, 21]. Review of literature suggests that maintenance dose of Dex is 0.2 - 1 mcg/kg/hr is needed for surgeries requiring more than 60 min [5, 7, 19, 25]. GA is recommended in uncooperative patients, in children, in patients with known hypersensitivity to LAs or when LA is unsuitable due to length of surgery (>4h) [3].

The effects of Dex on the cardiovascular system may be beneficial in high-risk patients [24, 25] for which further studies need to be carried out on cardiac patients.

A possible limitation of this study could be that amnesia scoring and cognitive function testing for psychomotor impairment was not done as early discharge of the patients was not a concern of this study. Midazolam has a potent anterograde amnesic effect and Dexmeditomedine also results in memory impairment [4, 7, 17, 20].

Conclusion:

Based on RSS, surgeon and patient satisfaction scores, Dexmedetomidine, Midazolam-Fentanyl or Pentazocine-Promethazine provided adequate analgesia and sedation in adult patients undergoing middle ear surgery under local anesthesia. Dexmedetomidine was found to be the best drug out of the sedo-analgesics tested. It produced near bloodless microscopic surgical field with better surgeon and patient satisfaction.

References

- 1. Liang S, Irwin MG. Review of anesthesia for middle ear surgery. *Anesthesiol Clin* 2010; 28:519-28.
- 2. Yung MW. Local anaesthesia in middle ear surgery: Survey of patients and surgeons. *Clin Otolaryngol Allied Sci* 1996; 21:404-8.
- Sarmento KM, Jr, Tomita S. Retroauricular tympanoplasty and tympanomastoidectomy under local anesthesia and sedation. *Acta Otolaryngol* 2009; 129:726-8.
- 4. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of smalldose dexmedetomidine infusions. *Anesth Analg* 2000; 90:699-705.
- 5. Candiotti KA, Bergese SD, Bokesch PM, Feldman MA, Wisemandle W, Bekker AY. Monitored anesthesia care with dexmedetomidine: A prospective, randomized, double-blind, multicenter trial. *Anesth Analg* 2010; 110:47-56.
- 6. Paris A, Tonner PH. Dexmedetomidine in anaesthesia. *Curr Opin Anaesthesiol* 2005; 18:412-8.
- Parikh DA, Kolli SN, Karnik HS, Lele SS, 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; 29:173-8.

- American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by nonanesthesiologists. *Anesthesiology* 2002; 96:1004-17.
- 9. Sanjekar DA Comparative Study between Fentanyl -Midazolam With Pentazocine - Promethazine For Conscious Sedation During Cardiac Catheterization. *The Internet Journal of Anesthesiology* 2006;12(2).
- Bailey PL, Pace NL, Ashburn MA, Moll JW, East KA, Stanley TH. Frequent hypoxemia and apnea after sedation with Midazolam and fentanyl. *Anesthesiology* 1990; 73:826–30.
- 11. Mishra A, Singh RB, Choubey S, Tripathi RK, Sarkar A. A comparison between nitroprusside and nitroglycerine for hypotensive anesthesia in ear, nose, and throat surgeries: A double-blind randomized study. *Med J DY Patil Univ* 2015; 8:182-8.
- Hasani V, Alimian M, Farhadi M, Zaman B, Mohseni M. Surgeon Satisfaction During Endoscopic Management of Cerebrospinal Fluid Rhinorrhea: A Comparison Between Propofol-Remifentanil and Isoflurane-Remifentanil Anesthesia. J Minim Invasive Surg Sci 2012; 1: 62-6.
- Dogan R, Erbek S, Gonencer HH, Erbek HS, Isbilen C, Arslan G. Comparison of local anaesthesia with Dexmedetomidine sedation and general anaesthesia during septoplasty. *Eur J Anaesthesiol* 2010; 27: 960–4.
- 14. Bhananker SM, Posner KL, Cheney FW, Caplan RA, Lee LA, Domino KB. Injury and liability associated with monitored anesthesia care: a closed claims analysis. Anesthesiology 2006; 104:228-34.
- 15. Eren G, Cukurova Z, Demir G, Hergunsel O, Kozanhan B, Emir NS. Comparison of Dexmedetomidine and three different doses of Midazolam in preoperative sedation. *J Anaesthesiol Clin Pharmacol* 2011; 27:367–72.
- 16. Abdalla MIM, Mansouri FA, Bener A. Dexmedetomidine during local anesthesia. *J Anesth* 2006; 20:54-6.
- 17. Cheung CW, Ying CL, Chiu WK, Wong GT, Ng KF, Irwin MG. A comparison of Dexmedetomidine and Midazolam for sedation in third molar surgery. *Anaesthesia* 2007; 62:1132-8.
- Demiraran Y, Korkut E, Tamer A, Yorulmaz I, Kocaman B, Sezen G, *et al.* The comparison of Dexmedetomidine and Midazolam used for sedation of patients during upper endoscopy: A prospective, randomized study. *Can J Gastroenterol* 2007; 21:25-9.
- 19. Goksu S, Arik H, Demiryurek S, Mumbuc S, Oner U, Demiryurek AT. Effects of Dexmedetomidine infusion

in patients undergoing functional endoscopic sinus surgery under local anaesthesia. *Eur J Anaesthesiol* 2008; 25:22-8.

- Busick T, Kussman M, Scheidt T, Tobias JD. Preliminary experience with dexmedetomidine for monitored anesthesia care during ENT surgical procedures. *Am J Ther* 2008; 15:520-7.
- 21. Taghinia AH, Shapiro FE, Slavin SA. Dexmedetomidine in aesthetic facial surgery: Improving anesthetic safety and efficacy. *Plast Reconstr Surg* 2008; 121:269-76.
- 22. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. *Drugs* 2000; 59:263–8.
- 23. Kamibayashi T, Maze M. Clinical uses of alpha2adrenergic agonists. *Anesthesiology* 2000; 93:1345-9.
- 24. McCutcheon CA, Orme RM, Scott DA, Davies MJ, McGlade DP. Comparison of Dexmedetomidine versus conventional therapy for sedation and hemodynamic control during carotid endarterectomy performed under regional anesthesia. *Anesth Analg* 2006; 102:668-75.
- Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous Dexmedetomidine in humans. II. Hemodynamic changes. *Anesthesiology* 1992; 77:1134–42.
- Turan G, Dincer E, Ozgultekin A, Uslu C, Ormanci F, Akgun N. Comparison of Dexmedetomidine, Remifentanil and Esmolol in Controlled Hypotensive Anaesthesia. *The Internet Journal of Anesthesiology* 2008; 17(2).
- Durmus M, But AK, Dogan Z, Yucel A, Miman MC, Ersoy MO. Effect of dexmedetomidine on bleeding during tympanoplasty or septorhinoplasty. *Eur J Anaesthesiol* 2007; 24:447-53.
- Kumari I, Naithni U, Bedi V, Gupta S, Gupta R, Bhuie. Comparison of clonidine versus midazolam in monitored anesthesia care during ENT surgery– A prospective, double blind, randomized clinical study. *Anaesth Pain & Intensive Care* 2012; 16(2): 157-164
- 29. Gerlach AT, Dasta JF. Dexmedetomidine: An updated review. *Ann Pharmacother* 2007; 41:245-52.
- Jung JS, Park JS, Kim SO, Lim DG, Park SS, Kwak KH, Cho JD, Jeon YH. Prophylactic antiemetic effect of midazolam after middle ear surgery. *Otolaryngol Head Neck Surg* 2009; 141:797.
- Alhashemi JA. Dexmedetomidine vs. Midazolam for monitored anaesthesia care during cataract surgery. *Br JAnaesth* 2006; 96:722-6.

*Author for Correspondence: Dr. Jyotsna S. Paranjpe, 'Dhanvantari, 36, Ekata colony, Market Yard, Sangli-416416 (Maharashtra) India Email: san_jyotsna@yahoo.co.in Cell: 9423268066, 8275471160