

Comparative Evaluation of IV Dexmedetomidine versus Dexmedetomidine with Butorphanol as an Adjuvant for Monitored Anaesthesia Care in Tympanoplasty and Myringoplasty: A Prospective, Controlled, Randomized, Double Blind Study

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Abstract

Background and Aims: It is a common practice to perform procedures like Tympanoplasty and Myringoplasty under Monitored Anaesthesia care (MAC). The recently introduced selective α_2 agonist dexmedetomidine, known for its opioid sparing effect along with sedative, analgesic hypotensive and anaesthetic properties with minimal respiratory depression has been used as a sole agent to provide MAC in various surgical interventions. The present study is aimed to evaluate the role of Dexmedetomidine as a sole sedoanalgesic agent and compare the efficacy of adding an adjuvant like Butorphanol to Dexmedetomidine.

Material & Methods: 60 patients of either sex, aged 18-20 years, ASA grade I&II were randomized into two groups(D and BD) of 30 patients each for microscopic ear surgery under Local Anaesthesia(LA) with MAC. Group D received inj. Dexmedetomidine 1 mcg/kg iv loading dose while Group BD received inj. Dexmedetomidine 1 mcg/kg iv loading dose along with inj. Butorphanol 0.02 mg/kg. Both groups received an infusion of inj. Dexmedetomidine @ 0.2 mcg/kg/hr. All patients were assessed for intraoperative haemodynamic changes, SpO₂, respiratory rate, Ramsay sedation score(RSS), and visual analogue scale(VAS).Rescue doses of sedatives, analgesics, satisfaction scores(Patients and Surgeons) were compared in both the groups. Data was analyzed using chi-square and t-test. *p* value <0.05 was considered significant.

Results: Mean Heart Rate (HR) and Mean Arterial Pressure (MAP) were significantly decreased from baseline in group BD as compared to group D (*p*<0.001). RSS, in group BD was significantly higher as compared to group D throughout the surgery. Rescue sedation was given in 3 patients in group BD while in group D, 9 patients required additional sedation (*p*<0.01).Rescue analgesic with iv fentanyl was administered in 27 patients and 6 patients respectively in groups D and BD.Patient and surgeon satisfaction scores were also significantly higher in group BD vs group D (*p*<0.001)

Conclusion: A combination of Dexmedetomidine with Butorphanol as an adjuvant for Monitored Anaesthesia Care in microscopic ear surgery was found to provide superior sedoanalgesia.

Key Words: Monitored Anaesthesia Care, Dexmedetomidine, Butorphanol, Middle ear surgery.

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-4994.2016.00023.8

Introduction

Tympanoplasty and Myringoplasty procedures in adults are performed either under local anaesthesia along with monitored anaesthesia care or under general anaesthesia. Operations conducted under LA prove to be cost effective with early postoperative recovery. Despite these advantages, General Anaesthesia is generally preferred due to special concerns like patients anxiety and complaints of discomfort due to noise of suction, manipulation of instruments, lateral position of head and neck and side effects like dizziness and nausea. Surgeons are also wary of sudden head movement by the patient during surgery. To minimize these adverse events several drugs have been used for

sedation during surgery if done under LA with Monitored Anaesthesia Care(MAC)including Propofol, benzodiazepines and opioids.¹These drugs have its own limitations because of side effects like delayed recovery, respiratory depression and dose related haemodynamic instability.

Dexmedetomidine is increasingly being used for MAC because of analgesia, cooperative sedation, opioid sparing effect and anaesthetic properties².It is a highly selective alpha 2 agonist, exhibiting sympatholytic activity. It inhibits norepinephrine release and produces predictable dose dependent reduction in arterial blood pressure and heart rate.These effects prove advantageous in middle ear surgeries for providing bloodless field³.Thus Dexmedetomidine with its short half-life, enabling titration to effect via iv infusion, rapid recovery avoiding hangover effects is considered a sedoanalgesic drug of choice for MAC⁴. However rescue analgesic doses are still required if it is used as a sole agent in surgery conducted under MAC. So we planned to add an adjuvant like Butorphanol tartarate which is a highly effective opioid agonist antagonist analgesic.⁵ The primary aim of our study was

to evaluate the role of Dexmedetomidine as a sole sedoanalgesic agent for middle ear surgery and compare the efficacy of Butorphanol as an adjuvant to Dexmedetomidine. The secondary aim of the study was to compare the haemodynamic parameters between the two groups, requirement of rescue analgesics and sedatives along with satisfaction scores among surgeons and patients.

Material and Methods

This prospective, controlled, randomized, double blind study was conducted after institutional ethics committee approval and written informed consent from patients. Patients with ASA grades I–II, age group 18–60 years, scheduled for Tympanoplasty and Myringoplasty under MAC were included in the study. Exclusion criteria included the patients less than 18 years and more than 60 years of age, patients with known hypersensitivity to study drugs, presence of cardio pulmonary, hepatic and renal diseases, hypertensive patients, B MI >26kgs/m² and patients with history of hypnosedatives.

Before surgery, all the patients were counselled with regard to sedation, Local anaesthesia, operative procedure and Visual Analogue Score(VAS) 0–10(where 0 indicates no pain and 10 corresponds to maximum pain).

On arrival in the operating room, routine monitors were applied to the patients for baseline values of Heart rate, Blood pressure, MAP and SpO₂. Patients were randomly allocated into two groups, of 30 patients each, with the help of computer generated table of random numbers.

All patients were premedicated by inj glycopyrrolate 10mcg/kg bw and inj. ondansetron 0.1mg/kg iv 10 minutes prior to surgery. Simultaneously Ringer lactate solution was started at the rate of 2ml/kg. The drugs were prepared by an anaesthesiologist who did not participate in patients management and data collection. All data were recorded by a blinded observer. The patients were assigned into two groups according to the following protocol:

Group D: Patients were given inj. Dexmedetomidine 0.1mcg/kg bw iv as a loading dose over 10 minutes followed by 10 ml Normal Saline(NS).

Group BD: Patients were given inj Dexmedetomidine 0.1mcg/kg as a loading dose over 10 minutes followed by inj Butorphanol 0.02mg/kg bw diluted in 10 ml NS.

In both groups, an infusion of inj. Dexmedetomidine @0.2mcg/kg /hr was started after giving loading dose using an infusion pump(L&T SP102). Infusion of Dexmedetomidine was prepared by diluting 1ml of 100mcg/ml of Dexmedetomidine with 49ml of 0.9%NS to produce a strength of 2mcg/ml.

The surgeons were asked to administer Local Aesthetic (1:200000) only after the initial bolus dose

and infusion had been started. All patients were administered O₂ @3 lit/min via nasal prongs.

The level of sedation was assessed by Ramsay Sedation Score (RSS-1= Agitated and restless; 2= Cooperative, tranquil; 3=Response to verbal command while sleeping; 4= Brisk response to glabellar tap or loud voice; 5= Sluggish response to glabellar tap or loud voice; 6= No response to glabellar tap or loud voice.) and intraoperative pain intensity was evaluated by Visual Analogue Scale(VAS) from the end of giving loading dose of inj. Dexmedetomidine. The target end point of sedation was aimed at maintaining a RSS was 3 throughout the surgery.

Intraoperatively patients vital parameters like Heart Rate(HR), Systolic BP, Diastolic BP, Mean arterial pressure(MAP), SpO₂, Respiratory rate were monitored every 5 min. for first 15 minutes and then every 10 minutes throughout the procedure. Any decrease in HR <45/min. or a fall of MAP<60mm Hg was managed by inj. iv Atropine sulphate 0.01mg/kg or incremental doses of iv mephentermine 6 mg respectively with fast bolus iv fluids. Fall in SpO₂<90% was managed by increasing O₂ flow upto 6 lit/min and if needed by bag and mask ventilation giving 100% Oxygen. Respiratory rate <8 breaths/min was managed by waking up the patient and asked to take deep breaths.

Patients in either group having RSS<3 intraoperatively was administered inj midazolam iv bolus 0.01mg/kg which was repeated if necessary or iv Propofol 0.5mg/kg was added. Similarly, inadequate analgesia was treated by asking surgeon to infiltrate additional doses of 2% lignocaine with adrenaline at the surgical site. If the pain still persisted (VAS>5) then rescue analgesia in the form of inj. Fentanyl 1mcg/kg bw was administered and the total number of doses of both sedative and analgesics were noted in both the groups. Efficacy of the sedation technique was defined as the ability to complete the surgery without any rescue sedatives and analgesics. Cases were excluded from the study if the patients were not cooperative inspite of supplementing adjuvants, thus converting the technique into general anaesthesia.

The maintenance infusion of iv dexmedetomidine was discontinued at the time of closure of skin. Duration of surgery as well as anaesthesia was recorded in both the groups. After the completion of the surgery, all patients were shifted to PACU for a minimum of one hour after discontinuation of the study drugs. The patients were monitored for any change in haemodynamic parameters, fall in SpO₂, respiratory rate, RSS, VAS. The need of postoperative analgesia were also noted in both the groups till one hour. Patients were shifted to concerned ward if the Aldrete Score was ≥9.

Assessment of Surgeon satisfaction score was evaluated in both the groups on 5 point scale (5=Excellent, 4=Very good, 3=Good, 2=Fair, 1=Poor). Patients were also asked about Satisfaction score on

similar 5 point scale before shifting them to concerned ward.

Statistical Analysis

The number of patients required in each group was determined by using Power analysis based on the previous study³. The sample size required detecting a 20% difference in sedoanalgesia at 5% level of significance and 80% power was 30 patients in each group. Data was entered and analysed by SPSS version 19.0. Mean and Standard deviations were estimated for haemodynamic and respiratory data using unpaired t-test for intergroup and paired t-test for intra group comparison. Chi square test was used to analyse categorical data and. *P* value less than 0.05 was considered as significant.

Results

No significant differences were found between patient characteristics and surgical data. There was no difference in baseline measurements of HR and MAP between both the groups. Mean HR and MAP showed a significant fall from baseline in group BD as compared to patients in group D. ($P < 0.05$). After 20 min. of infusion of Dexmedetomidine, there was greater fall of HR (Fig.1) than MAP (Fig.2) in group BD as compared to group D ($P < 0.001$). Bradycardia was seen in 3 patients in group BD only during maintenance infusion of iv Dexmedetomidine. The results were comparable in both the groups with regard to desaturation and none

of the patients had fall of SpO₂. There was significant difference in respiratory rate in group BD (13.80 ± 1.00) as compared to group D (14.80 ± 1.1) ($P < 0.001$).

At the end of the loading dose of Dexmedetomidine, all patients reached RSS at 3 and none of the patients required additional supplementation of sedation at that time. Mean RSS was also significantly more in group BD as compared to group D throughout the surgery. ($p < 0.001$). Only 3 patients in group BD required rescue sedation in the form of iv midazolam single dose as compared to 9 patients in group D, where iv midazolam and iv propofol were supplemented. ($p < 0.01$). (Tab.1)

Intraoperatively, 6 patients required rescue analgesia inj fentanyl in group BD. Time to first rescue analgesia being at the mean of 80 ± 10.95 min. as compared to 27 patients in group D where it was given at the mean time of 33.33 ± 13.59 min. ($p < 0.001$). There was highly significant difference in the VAS at 20th and 30th minutes between the two groups ($p < 0.001$). (Tab.2) Rescue analgesics or sedatives did not affect the haemodynamic parameters in both the groups. Patients satisfaction with regard to sedation and analgesia was higher in group BD than in group D ($P < 0.0001$). 4 patients in group D had VAS > 5 and they required post operative analgesia before shifting the patient to ward while none of the patient in group BD demanded analgesia postoperatively.

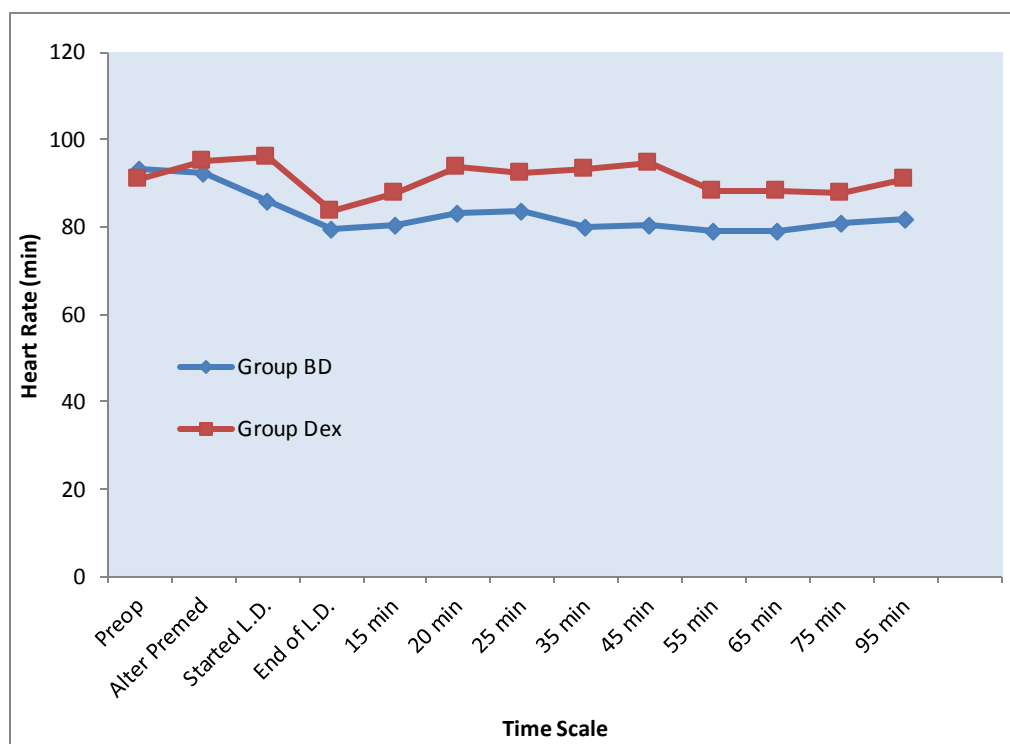


Fig. 1: comparison of Mean HR in both the groups

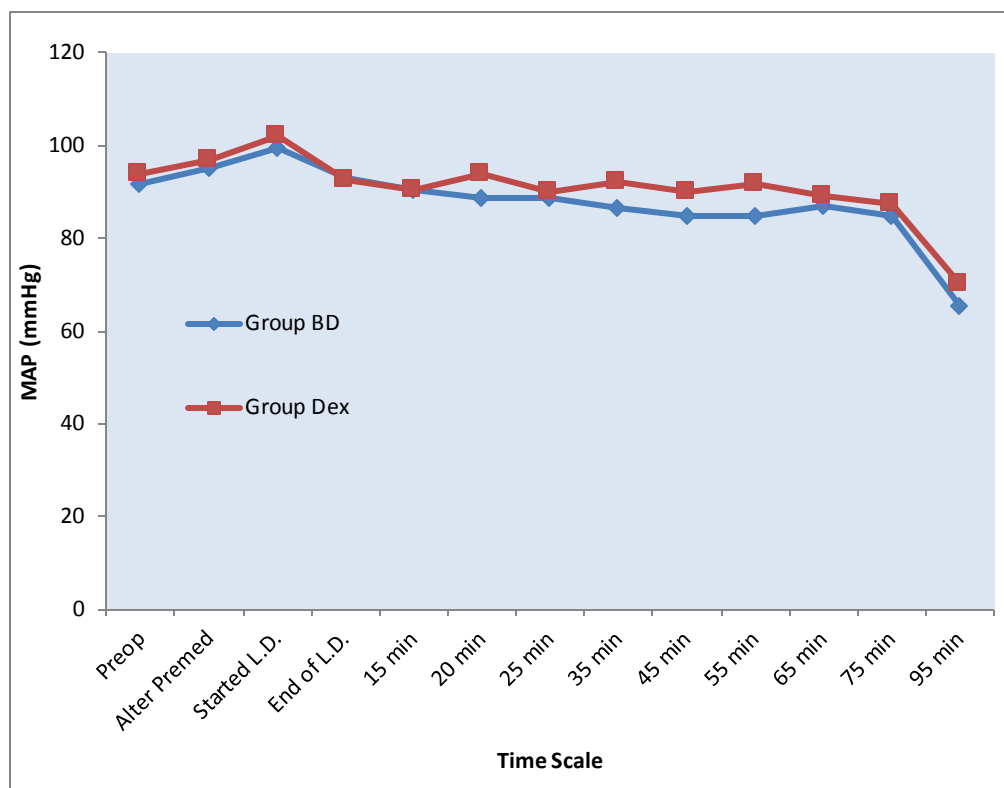


Fig. 2: comparison of Mean MAP in both the groups

Table 1: Showing Ramsay Sedation Score (RSS) & Intraoperative Rescue Sedation

1. RSS	Group BD	Group D	P Value	
	Mean + SD	Mean + SD		
10 Min.	2.90 + 0.31	3.00 + 0.00	0.08	
20 Min.	2.90 + 0.31	2.50 + 0.68	<0.001	
30 Min.	3.00 + 0.00	2.50 + 0.51	<0.001	
40 Min.	3.00 + 0.00	2.30 + 0.65	<0.001	
60 Min.	3.00 + 0.00	2.80 + 0.41	0.01	
90 Min.	3.00 + 0.00	2.70 + 0.47	<0.001	
2. Intra op. Rescue sedation (total dose)	Midazolam (mg.)	1.00 + 0.00 (n=3)	1.50 + 0.43 (n=9)	<0.001
	Propofol (mg.)	0.00 + 0.00	46.67 + 10.00 (n=9)	<0.001

Table 2: showing Visual Analogue Score (VAS) & intraoperative Rescue analgesia

1. VAS Score	Group BD	Group D	P Value
	Mean + SD	Mean + SD	
10 Min.	0.60+0.81	0.00+0.00	-
20 Min.	0.70+1.51	2.90+1.47	<0.001
30 Min.	0.30+0.92	2.10+1.06	<0.001
40 Min.	0.00+0.00	3.00+1.64	-
60 Min.	0.00+0.00	2.10+1.24	-
90 Min.	0.00+0.00	1.90+0.96	-
2. Intraop. Fentanyl	1.00+0.00	1.44+0.51	<0.001
A. No. of Doses	(n=6)	(n=27)	
B. Total Doses (mcg.)	100.00+0.00	116.67+28.42	<0.001
C. Time to 1 st Rescue Analgesia	80.00+10.95	33.33+13.59	<0.001

Discussion

Monitored anaesthesia care has become the common practice in middle ear surgeries like Tympanoplasty and Myringoplasty. Fine microscopic nature of the surgery may even lead to graft failure if the patients are anxious and uncooperative. Proper patient selection, preoperative counseling about the procedure and use of appropriate sedation and analgesics are important factors for the success of the ear surgery^{7,18}.

Parikh.DA et al³ compared dexmedetomidine as a sole agent against the traditional midazolam-fentanyl combination in patients for Tympanoplasty under MAC and found qualitatively better sedation profile with dexmedetomidine. Verma.R et al⁹ compared dexmedetomidine with propofol for Tympanoplasty under LA and results suggested dexmedetomidine provided adequate sedoanalgesia without any adverse effects. Harde. A et al¹¹ compared midazolam-remifentanyl versus remifentanyl-Dexmedetomidine and concluded the latter combination to be superior for day care anaesthesia in cystoscopies.

This study was aimed to assess the efficacy of adding adjuvant to dexmedetomidine, like Butorphanol which is agonist antagonist opioid. There are limited studies on perioperative analgesic use in humans, so this study was evaluated to compare dexmedetomidine as a sole sedoanalgesic versus butorphanol with dexmedetomidine to evaluate its efficacy as an appropriate addition to our analgesic drug armamentarium.

In our study there was no significant changes in HR and MAP from baseline values during the infusion of loading dose of dexmedetomidine. It has a biphasic cardiovascular response when given as a faster iv bolus or in larger doses. A 1mcg/kg bolus dose, results in transient increase in blood pressure and reflex decrease in HR. This was attributed to direct effect of α_2 adrenoreceptor stimulation of vascular smooth muscle. After the transient increase, it is followed by decrease in blood pressure which occurs presumably due to inhibition of sympathetic outflow that overrides the direct effect of Dexmedetomidine on vasculature⁸. We did not observe the biphasic effect of dexmedetomidine as we administered the loading dose of 1 mcg/kg in 10 minutes. However there was a significant decrease in HR and MAP from 20 min. of the initial bolus which was subsequently maintained at significantly lower levels as compared to baseline values in group BD. This might be attributed to the sympatholytic, vagotonic and baroreflex sensitivity reducing effect of dexmedetomidine along with butorphanol which also causes small reduction in SBP and HR but changes are not significant¹². Hall JE et al⁸ compared the safety and efficacy of two doses (0.2 Vs 0.6 mcg/kg/hr infusion) of Dexmedetomidine and found a 20% & 16% decrease respectively of HR from baseline during the 10 min. of initial dose. Padmaja A et al¹³ compared the efficacy of

Dexmedetomidine Vs Midazolam under MAC in minor ENT surgeries and the results showed significant fall in HR (15-20%) and reduction in MAP from the baseline values in Dexmedetomidine group as compared to the Midazolam group.

Our results correlate with the prospective randomized study conducted by Mohamed. H et al¹⁵ for ear surgery who found that Dexmedetomidine/ Nalbuphine group had lower HR and MAP values than Midazolam/ Nalbuphine group after 10 min. from the start of infusion till the end of surgery. Respiratory rate and SpO₂ were insignificant throughout the procedure.

In the present study, in addition to significantly comparable respiratory rates, there was no evidence of Bradyapnea in any group. Dexmedetomidine does not cause respiratory depression because its effect are not mediated by the GABA system and there is evidence that butorphanol lacks appreciable respiratory depressant properties¹². There are limited studies that shows absolute respiratory depression associated with coadministration of opioids with Dexmedetomidine. Similar to our study Candiotti et al² found that fentanyl with Dexmedetomidine was not associated with absolute respiratory depression (<8 breaths/min.) Parikh DA et al³ also showed better patient and surgeons satisfaction scores with lesser no. of top up rescue fentanyl and midazolam needed to maintain RSS= 3 in Dexmedetomidine group as compared to midazolam – fentanyl group. On the contrary, study carried out by Padmaja A et al¹³ concluded that dexmedetomidine and midazolam were equally comparable in effectiveness of sedation during MAC in minor ENT surgical procedures. It was found that mean sedation score was higher in dexmedetomidine group as compared to midazolam group (p>0.05) but number of rescue analgesic doses requirement being less in dexmedetomidine group.

Our study demonstrated significantly higher patient and surgeon satisfaction score with Butorphanol Dexmedetomidine combination. This suggests a difference in the quality of sedation and analgesia in both the groups. Similar findings have also been reported by a study carried by Mohamed H et al¹⁵ where group Dexmedetomidine/ nalbuphine showed less VAS and RSS intraoperatively as well as postoperatively that led to less number of rescue sedoanalgesia as compared to group midazolam/ nalbuphine leading to significantly higher patient and doctor's satisfaction.

The sedation and analgesic property of Dexmedetomidine is attributed to stimulation of α_2 adrenoreceptor in locus coeruleus in the brain and modulation of transmission of nociceptive signals in CNS and at spinal level. Butorphanol besides analgesia also leads to mild sedation so combination of Butorphanol Dexmedetomidine had increased sedation in the patients.

Dexmedetomidine also provides intense analgesia during postoperative period. Combining Butorphanol to

dexmedetomidine have synergistic effect and none of the patient in this group complained of pain during the stay in PACU as compared to 4 patients in dexmedetomidine group who received iv diclofenac before shifting from PACU. However all the patient in either groups had RSS ≤ 2 at the time of shifting to ward. Limitation of our study includes the following. In our study, we have only observed sedation by RSS because of unavailability of the Bispectral Index. Secondly the limited sample size in our study was mostly due to surgeons preference to general anaesthesia for middle ear surgery procedures. In future a larger study can be executed as surgeons and patients become more comfortable with the technique of MAC.

Conclusion

To conclude, the addition of Butorphanol to Dexmedetomidine in Monitored Anaesthesia Care with local anaesthetics for middle ear surgery proves to be a better technique of MAC as compared to Dexmedetomidine alone in terms of haemodynamic stability, intraoperative analgesia, sedation scores and satisfaction scores (surgeons and patients).

Conflict of Interest: None

Source of Support: Nil

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