ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 15, Issue 10, 2022

Online - 2455-3891
Print - 0974-2441

Research Article

A COMPARISON OF EFFECTS OF DEXMEDETOMIDINE VERSUS MIDAZOLAM-FENTANYL ON POST-OPERATIVE RECOVERY, SEDATION, ANALGESIA AND HEMODYNAMIC PARAMETERS IN PATIENTS UNDERGOING MIDDLE EAR SURGERY UNDER LOCAL ANESTHESIA

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Received: 09 June 2022, Revised and Accepted: 20 July 2022

ABSTRACT

Objective: The objective of the study was to compare the effects of dexmedetomidine versus midazolam-fentanyl on post-operative recovery, sedation, analgesia, and hemodynamic parameters in patients undergoing middle ear surgery under local anesthesia.

Methods: Seventy-two patients were randomly divided into two equal groups - Group D (dexmedetomidine) and Group MF (midazolam and fentanyl). Intra operative heart rate, mean blood pressure, respiratory rate (RR), and SPO_2 were recorded every 15 min for the 1st 30 min and then at every 30 min interval till the end of the surgery. In post-operative period, hemodynamic parameters, Aldrete score and pain were assessed at every 30 min till the patient was discharged from post anesthesia care unit (PACU). Post-operative sedation of the patient was checked at 1 h, 2 h, 4 h, and 8 h.

Observations: Midazolam and fentanyl combination caused more fall in Aldrete scores as compared to dexmedetomidine initially, but readiness to discharge from PACU was similar in both the groups. Patients of MF group had significantly higher sedation scores at post op 2 h, but overall duration of sedation was similar in both the groups. Post-op pain was significantly more in MF group patients, as compared to dexmedetomidine patients at 1.5 h. More number of patients of MF group demanded rescue analgesia in PACU. Both group of drugs caused similar changes in hemodynamic parameters during surgery but in post-operative period, dexmedetomidine produced less decline in RR and oxygen saturation as compared to midazolam and fentanyl combination.

Conclusion: The present study concluded that dexmedetomidine seems to be a better alternative to the combination of midazolam plus fentanyl sedation for patients undergoing middle ear surgeries done under local anesthesia due to better analgesia and lesser derangement of hemodynamic parameters in post-operative period.

Keywords: Analgesia, Dexmedetomidine, Fentanyl, Hemodynamic parameters, Midazolam, Middle ear surgery, Recovery, Sedation.

 DOI: http://dx.doi.org/10.22159/ajpcr.2022v15i10.45462. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Middle ear surgeries are usually done under local anesthesia with sedation under monitored anesthesia care (MAC). Sedation makes surgery very comfortable for the patient, anesthesiologist and the surgeon as well [1]. Commonly used sedative agents are midazolam, propofol, dexmedetomidine, methohexital, etc. These sedative agents have impact on hemodynamic parameters and produce other effects such as anxiolysis and analgesic effect [2]. An ideal sedative agent should be fast acting, has less impact on normal physiological and physical functions and produce faster recovery with lesser side effects. Recovery is complete when functions are restored and adverse symptoms have resolved [3]. In search of a better sedative agent we conducted this study comparing Dexmedetomidine versus midazolam and fentanyl combination which is commonly used nowadays. Dexmedetomidine is an α2-adrenoreceptor agonist. It has other beneficial properties such as analgesia and attenuation of the stress response without significant respiratory depression [4]. Midazolam is a benzodiazepine with rapid onset of action and short duration of sedative effect. Fentanyl is a phenylpiperidine derivative synthetic opioid agonist with a high affinity for μ receptors [5].

METHODS

This was a prospective, randomized controlled, and double-blind clinical study. Institutional ethics committee approval was taken prior to starting the study. The study was registered with Clinical Trials Registry of India prior to its initiation. Seventy-two patients of either sex or age between 18 and 60 years, undergoing middle ear surgery under local anesthesia were included in the study. Written informed consent was obtained from all the participants prior to the study. All the patients in the study belonged to grade I or II of American society of Anesthisiologists [6]. Patients with known sensitivity to local anesthetic drug lignocaine, allergy to study drugs, pregnant, and lactating females were excluded from the study. The patients were randomly divided into two equal groups - Group D (dexmedetomidine) and Group MF (midazolam fentanyl) on basis of a computer-generated randomization scheme. Group D patients received dexmedetomidine 1 μg/kg IV over 10 min followed by continuous infusion starting at 0.3 μg/kg/hr. This was incremented by 0.1μg/kg/hrup to 0.7 μg/kg/h till Ramsay sedation score of 3 was achieved. Group MF patients received midazolam 0.03 mg/kg IV and injection fentanyl 1 μg/kg IV bolus over 10 min followed by continuous infusion of midazolam (0.03–0.07 mg/kg/h and fentanyl 0.5–1.5 μg/kg/h) till adequate sedation score was achieved. Patients were then administered local anesthesia with 5–7 mg/kg of 2% lignocaine and adrenaline (1:200000). Surgery was started thereafter.

Recovery from anesthesia was assessed by Aldrete score. Here, five features of the patient namely activity, respiration, circulation (blood pressure), color (oxygen saturation), and consciousness were assessed. A score of 0–2 was given for each of the five categories assessed. In this study, Aldrete score was assessed every 30 min starting from the time of shifting of patient to post anesthesia care unit (PACU) till the time patient was discharged from PACU. Patient was discharged from PACU when Aldrete score reached 9 or 10.

Post-operative sedation of the patient was checked at 1 h, 2 h, 4 h, and 8 h after completion of surgery by applying Ramsay Sedation Scale (RAS). Awake, anxious, agitated, or restless patient was given a score of (1) Awake, cooperative, orientated, and tranquil patient was given a score of (2) Drowsy patient who did not respond to commands was given a score of (3) If the patient was asleep and there was only a brisk response to glabella tap or loud auditory stimulus he was allotted a score of (4) Score of 5 was given to the patient who was asleep and had only sluggish response to stimulus. Score of 6 was given to patient has no response to firm nail-bed pressure or other noxious stimuli.

Post-operative pain was evaluated by a 10-point visual analog scale (VAS). Patient was asked to rate their pain on a scale of 0–10 assuming that 0 means no pain and 10 means worst imaginable pain. It was assessed at every 30 min starting from the time of shifting of patient to post-anesthesia care unit till the time patient was discharged from PACU.

Intra operative heart rate (HR), mean blood pressure (MAP), respiratory rate (RR), and SPO_2 were recorded every 15 min for the 1st 30 min and then every 30 min interval till the end of the surgery. In post-operative period, parameters were checked every 30 min till the patient was discharged from PACU.

Observations

Post-operative recovery

In our study, post-operative recovery was assessed by Aldrete score. In both the groups mean Aldrete scores of the patient were highly significantly lower as compared with Aldrete score of 9 (discharge criteria) till 2.5 h postoperatively. Dexmedetomidine group patients had significantly higher Aldrete score as compared to MF group patients till 1 h post-operative period. The time to reach Aldrete score of 9 was 2.43±0.667 h in Group D and 2.40±0.558 h in Group MF. The difference was statistically insignificant. The results of Aldrete scores are shown in Table 1.

Post-operative sedation

In our study, post-operative sedation was assessed by RAS. As shown in Table 2, RSS scores in both the groups were highly significantly greater than pre-op values (RSS=1) till 2 h post-operative period. Group MF had significantly higher sedation scores than group D at 2 h post-operative period. The mean time to reach back to RSS score of 1 was 3.89±1.90 h in Group D and 4.00±1.65 h in Group MF and these values were not significantly different from each other.

Table 1: Aldrete score of patients

Time of assessment	Group D	Group MF	p-value
30 min (mean±SD)	7.50±0.507##	7.31±0.467##	0.015*
1 h (mean±SD)	7.72±0.454##	7.53±0.506##	0.006*
1.5 h (mean±SD)	7.78±0.540##	7.75±0.604##	0.374
2 h (mean±SD)	8.56±0.504##	8.47±0.506##	0.659
2.5 h (mean±SD)	8.67±0.478##	8.69±0.467##	0.620
3 h (mean±SD)	8.89±0.319	8.97±0.377	0.614
3.5 h (mean±SD)	9.08±0.439	9.14±0.351	0.833
4 h (mean±SD)	9.64±0.487	9.61±0.494	0.634

*Indicates significant difference between the groups (p≤0.05), ##Indicates highly significant difference (p≤0.001) as compared to the Aldrete score of 9 (discharge criteria)

Table 2: Ramsay Sedation Scale score of patients

Time of assessment	Group D	Group MF	p-value
1 h (mean±SD)	2.06±0.232##	2.03±0.167##	0.243
2 h (mean±SD)	1.67±0.478##	1.78±0.422##	0.040*
4 h (mean±SD)	1.14±0.351	1.11±0.319	0.483
8 h (mean±SD)	1.00±00	1.00±00	

*Indicates significant difference between the groups (p≤0.05), ##Indicates highly significant difference (p≤0.001) as compared to the baseline value (RSS=1)

Post-operative pain

As depicted in Table 3, post-operative pain, as assessed by mean VAS score was significantly more in Group MF as compared to Group D at 1.5 h post-op. No. of patients requiring analgesics during their stay in PACU were 24 in Group MF and 18 in Group D.

Intra-operative hemodynamic parameters

Intra-operative values of mean HR and RR were highly significantly lower from pre-operative value in both the groups throughout surgery. No statistically significant difference was present in mean intra-operative oxygen saturation as compared to the pre-op value in both the groups. Intra-operative mean systolic and diastolic BP also dropped down significantly in both the groups throughout the surgery. On intergroup analysis, none of the intra-operative hemodynamic parameters value was found to be statistically significantly different in between the two groups.

Post-operative hemodynamic parameters

The post-operative hemodynamic parameters of the patients are shown in Table 4 and 5. On intra group analysis it was observed that as compared to pre-operative values, post-operative value of HR were significantly lower till 2 h in group D. However, in group MF HR values were significantly lower only till 1 h post-operative. Post-operative mean RR values were significantly lower from pre-operative value only in group MF and that too till 1 h post-operative. No clinically significant fall in post-operative mean oxygen saturation values were noted in both the groups. As compared to the baseline, post-operative mean systolic BP values were highly significantly lower in both the groups till 1 h post-operative period. Post-operative diastolic blood pressure values were significantly lower till 2 h in both groups.

On intergroup comparison post-operative mean RR was highly significantly lower in group MF till 1 h post-operative period. Post-operative mean oxygen saturation levels were significantly greater in Group D as compared to group MF till 1.5 h post-operative period. Post-operative HR, systolic, and diastolic blood pressure values were not significantly different among the groups at any point in post-operative period.

DISCUSSION

Our study indicated that midazolam and fentanyl combination cause more fall in Aldrete score as compared to drug dexmedetomidine initially, but the readiness to discharge from PACU was similar in both the groups. However, another similar study done by Alhashemi in 2006 which compared dexmedetomidine versus midazolam for MAC during cataract surgery revealed that patients receiving dexmedetomidine had delayed readiness for discharge as compared to patients who received midazolam [7]. Similar results were noted by the study done by Ali and Shrinivas in 2019 which compared the recovery profile in Fentanyl, Dexmedetomidine and Placebo Groups. Patients receiving fentanyl and dexmedetomidine showed statistically higher recovery scores than patients who received placebo [8]. Iniya *et al*. in 2015 compared the effect of midazolam with dexmedetomidine and with control group in patients undergoing cataract surgery. This study concluded that mean time to reach Aldrete score of 10 was prolonged in Group D as compared to Group M [9]. Thus this study shows different findings from

Table 3: Visual analog scale score of patients

Time of assessment	Group D	Group MF	p-value
30 min (mean±SD)	3.50±0.737	4.14±0.723	0.485
1 h (mean±SD)	3.64±0.723	4.64±0.543	0.065
1.5 h (mean±SD)	4.53±0.810	5.33±0.535	0.007*
2 h (mean±SD)	4.81±0.749	5.22±0.722	0.900
2.5 h (mean±SD)	4.67±0.676	4.58±0.554	0.390
3 h (mean±SD)	4.50±0.655	4.44±0.607	0.583
3.5 h (Mean±SD)	4.42±0.649	4.36±0.639	0.651
4 h (mean±SD)	3.61±0.639	3.61±0.549	0.474

*Indicates significant difference between the groups (p≤0.05)

Table 4: Post-operative heart rate and respiratory rate

Time of assessment	Heart rate			Respiratory rate		
	Group D	Group MF	p-value	Group D	Group MF	p-value
Pre-operative (mean±SD)	83.77±7.37	85.11±6.88	0.391	20.61±1.57	20.55±1.62	0.558
30 min (mean±SD)	75.67±8.546##	80.11±10.949#	0.088	19.78±0.929	17.89±1.753##	<.001**
1 h (mean±SD)	75.22±13.215#	80.33±8.688#	0.972	19.89±0.820	18.81±1.117##	<.001**
1.5 h (mean±SD)	79.14±5.866##	82.17±7.941	0.121	20.00±0.956	20.17±0.561	0.390
2 h (mean±SD)	80.31±5.626#	83.67±7.616	0.340	20.28±0.701	20.33±0.756	0.519

*Indicates significant difference in between the groups (p≤0.05), #Indicates significant difference (p≤0.05) as compared to the baseline value. **/##Indicates highly significant difference (p≤0.001)

Table 5: Post-operative systolic blood pressure and diastolic blood pressure

Time of assessment	Systolic blood pressure			Diastolic blood pressure		
	Group D	Group MF	p-value	Group D	Group MF	p-value
Pre-op (mean±SD)	121.33±71	121.00±8.19	0.348	80.72±7.02	81.66±7.16	0.828
30 min (mean±SD)	113.44±6.788##	114.72±6.747##	0.798	72.39±6.570##	72.28±5.558##	0.346
1 h (mean±SD)	115.28±7.362##	114.78±5.519##	0.120	73.22±5.372##	72.83±4.494##	0.649
1.5 h (mean±SD)	118.28±7.090	117.78±5.693	0.063	75.67±4.498##	75.28±4.438##	0.860
2 h (mean±SD)	119.94±5.962	120.00±5.514	0.965	77.44±4.843#	77.89±4.874#	0.963

#Indicates significant difference (p≤0.05) as compared to the baseline value. **/##Indicates highly significant difference (p≤0.001)

our study. The possible reason for this could be that they compared dexmedetomidine with midazolam alone where as in our study we compared dexmedetomidine with midazolam-fentanyl combination.

In our study, we found that MF patient had significantly higher sedation scores at post-operative 2 h. Time to reach the RSS score of 1 is almost equal in both the groups. Findings of our study were supported by the study done by Parikh *et al*. in 2013 which compared dexmedetomidine versus combination of midazolam-fentanyl for tympanoplasty surgery under MAC. In this study, it was observed that at the end of 30 min, patients in both the groups had reached RSS of 2 [10].

In our study, the pain was significantly more in group MF as compared to group D at 1.5 h post-operative. More patients required analgesic drug in Group MF as compared to Group D postoperatively. A similar study was conducted by Badheka *et al*. in 2019 which compared dexmedetomidine versus midazolam and fentanyl for tympanoplasty done under local anesthesia. This study concluded that post-operative analgesia was better in Group D as compared to group MF because of less no. of patients requiring rescue analgesic drug in Group D as compared to group MF [11]. The study done by Parikh *et al*. in 2013 observed that lesser number of patients (11.1%) receiving dexmedetomidine demanded rescue analgesics as compared to the midazolam-fentanyl group (40%) [10]. Thus these studies showed similar results like ours.

In our study, it was observed that during intra-operative period, both groups of drugs causes similar changes in hemodynamic parameters but in post-operative period, dexmedetomidine produces less decline in RR and oxygen saturation as compared to midazolam and fentanyl combination. However, the changes in the hemodynamic parameters HR, BP, and SPO_2 were within normal range.

Another study done by Dere in 2010, compared dexmedetomidine versus midazolam for sedation, pain, and hemodynamic control during colonoscopy under conscious sedation. In this study it was observed that midazolam cause statistically significant decrease in SpO_2, MAP, and HR at post-operative 5 min as compared to pre-operative value. Changes in MAP were similar between the groups throughout the study. This study revealed that Dexmedetomidine provides more efficient hemodynamic stability as compared to midazolam [12]. The study comparing dexmedetomidine versus combination of midazolam-fentanyl for tympanoplasty surgery observed that intraoperative HR and mean arterial pressure in Group D were lower than the values in Group MF ($p<0.05$) [10]. Another study done by Liao in 2012 compared dexmedetomidine versus midazolam for conscious sedation in postoperative patients undergoing flexible bronchoscopy. In this study, it was observed that the mean peripheral oxygen saturation at 5 min after the beginning of bronchoscopy and at the end of bronchoscopy were significantly lower in the midazolam group than in the dexmedetomidine group. HR and systolic arterial pressure was both significantly higher during bronchoscopy in the midazolam group than in the dexmedetomidine group. Final conclusion was that as compared to midazolam, dexmedetomidine provided better oxygen saturation. However, midazolam cause lesser fall in blood pressure and HR as compared to dexmedetomidine [13]. Another study done by Jo *et al*. in 2016 compared intravenous dexmedetomidine and midazolam during spinal anesthesia. This study showed that during surgery, hypotension was more common in the midazolam group and bradycardia was more common in the dexmedetomidine group. During sedation, no patient experienced arterial desaturation, defined as a SaO_2 of <90%. In the PACU, hemodynamic changes were similar in the 2 groups [14]. Thus, the effect of dexmedetomidine and MF on hemodynamic parameters is seen to be different in different studies.

CONCLUSION

The present study concluded that readiness for discharge is similar in both the groups and sedative effect of both the drug also persists for equivalent duration. Drug dexmedetomidine provides better analgesia as compared to drug midazolam and fentanyl combination. During intra-operative period, both group of drugs causes similar changes in hemodynamic parameters but in post-operative period, dexmedetomidine produces less decline in RR and oxygen saturation as compared to midazolam and fentanyl combination.

Therefore, dexmedetomidine seems to be a better alternative to the combination of midazolam plus fentanyl sedation for patients undergoing middle ear surgeries done under local anesthesia.

AUTHORS' CONTRIBUTIONS

Dr. Abhinav Goyal – The writer, collected the data, conceived, and designed the analysis. Dr. Garima Bhutani, Dr. Meena Singh and Dr. Naveen Sharma – Contributed in structure and designing the analysis, editing the article and data collection.Dr. Seema Rani, Dr. Rahul Saini, assisted in interpretation of data. Dr. Mohd Fazal Ahmed Makki helped in revising it critically for important intellectual content.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

AUTHORS' FUNDING

Nil.

REFERENCES

1. Thota RS, Ambardekar M, Likhate P. Conscious sedation for middle ear surgeries: A comparison between fentanyl-propofol and fentanyl-midazolam infusion. Saudi J Anaesth 2015;9:117-21. doi: 10.4103/1658-354X.152818, PMID 25829896
2. Höhener D, Blumenthal S, Borgeat A. Sedation and regional anesthesia in the adult patient. Br J Anaesth 2008;100:8-16. doi: 10.1093/bja/aem342, PMID 18070783
3. Misal US, Joshi SA, Shaikh MM. Delayed recovery from anesthesia: A postgraduate educational review. Anesth Essays Res 2016;10:164-72. doi: 10.4103/0259-1162.165506, PMID 27212741
4. Tang C, Xia Z. Dexmedetomidine in perioperative acute pain management: A non-opioid adjuvant analgesic. J Pain Res 2017;10:1899-904. doi: 10.2147/JPR.S139387, PMID 28860845
5. Vahedi HS, Hajebi H, Vahidi E, Nejati A, Saeedi M. Comparison between intravenous morphine versus fentanyl in acute pain relief in drug abusers with acute limb traumatic injury. World J Emerg Med 2019;10:27-32. doi: 10.5847/wjem.j.1920-8642.2019.01.004, PMID 30598715
6. Doyle DJ, Goyal A, Garmon EH. American Society of Anesthesiologists Classification. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441940 [Last accessed on 2021 Oct 09].
7. Alhashemi JA. Dexmedetomidine vs midazolam for monitored anaesthesia care during cataract surgery. Br J Anaesth 2006;96:722-6. doi: 10.1093/bja/ael080, PMID 16595611
8. Ali L, Shrinivas TR. The sedation score (Ramsay sedation score) and recovery profile (modified Aldrete's score) in fentanyl, dexmedetomidine and placebo groups. Acad Anesthesiol Int 2019;4:357-61.
9. Iniya R, Narayanan SV, Venkatesan K, Rajalekshmi M. Conscious sedation for cataract surgery done under retrobulbar block-a comparative study evaluating the effects of midazolam and dexmedetomidine. Indian J Clin Anaesth 2016;3:478-87. doi: 10.5958/2394-4994.2016.00081.0
10. 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. doi: 10.4103/0970-9185.111671, PMID 23878436
11. Badheka J, Doshi P, Shrividhya P, Gol J, Parmar V. A comparative study of dexmedetomidine versus midazolam with fentanyl for monitored anaesthesia care in tympanoplasty under local anaesthesia. Med Int J Med 2019;10:152-6.
12. Dere K, Sucullu I, Budak ET, Yeyen S, Filiz AI, Ozkan S, *et al*. A comparison of dexmedetomidine versus midazolam for sedation, pain and hemodynamic control, during colonoscopy under conscious sedation. Eur J Anaesthesiol 2010;27:648-52. doi: 10.1097/EJA.0b013e3283347bfe, PMID 20531094
13. Liao W, Ma G, Su QG, Fang Y, Gu BC, Zou XM. Dexmedetomidine versus midazolam for conscious sedation in postoperative patients undergoing flexible bronchoscopy: A randomized study. J Int Med Res 2012;40:1371-80. doi: 10.1177/147323001204000415, PMID 22971488
14. Jo YY, Lee D, Jung WS, Cho NR, Kwak HJ. Comparison of intravenous dexmedetomidine and midazolam for bispectral index-guided sedation during spinal anesthesia. Med Sci Monit 2016;22:3544-51. doi: 10.12659/msm.896461, PMID 27701366