ORIGINAL ARTICLE

Comparison of dexmedetomidine and clonidine as an adjuvant to lignocaine with adrenaline in infiltration anesthesia for tympanoplasty

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ABSTRACT

Background: Adjuvants to local anesthetics enhance the quality and duration of analgesia. Dexmedetomidine, a potent α2-adrenoceptor agonist, is approximately eight times more selective towards the α2-adrenoceptor than clonidine. Dexmedetomidine was compared with clonidine in infiltration anesthesia when added to local anesthetic in infiltration anesthesia in tympanoplasty.

Methodology: Sixty patients of age group 18-60 years, scheduled for tympanoplasty under local anesthesia were randomly divided into two equal groups. In Group C (n = 30), 12 ml of 2% lignocaine with adrenaline + clonidine 1 μg/kg; and in Group D (n =30), 12 ml of 2% lignocaine with adrenaline + dexmedetomidine 1 μg/kg were infiltrated. Onset and duration of analgesia, hemodynamic parameters, sedation score and grade of bleeding were recorded.

All the Quantitative data are presented as mean and standard deviation and compared using student's t-test. Qualitative data such as sedation score, grade of bleeding are presented as frequency and percentage and analyzed using chi-square test. P-value of < 0.05 was considered as significant and $p < 0.001$ was considered as highly significant.

Results: Both groups were comparable in terms of demographic and surgical parameters. Duration of postoperative analgesia was lasted longer in Group D as compare to Group C (690.00 ± 80.12 vs 417.67 ± 58.64 min, $P < 0.001$) and sedation scores were higher in Group D. No difference was observed in both of the groups regarding other parameters including onset of analgesia, mean pulse rate, mean blood pressure and grade of bleeding at different time intervals ($P > 0.05$).

Conclusion: Dexmedetomidine when used as an adjuvant to local anesthetic in infiltration anesthesia for tympanoplasty was found to be more effective than clonidine in terms of duration of postoperative analgesia and sedation score, with no difference in terms of onset of analgesia, grade of bleeding and hemodynamic parameters .

Key words: Dexmedetomidine; Clonidine; Lignocaine with adrenaline; Infiltration anesthesia; Tympanoplasty

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INTRODUCTION

Middle-ear surgeries can be done under local anesthesia and general anesthesia. Advantages and disadvantages of the both in this set of surgery have been debated a lot.[1] General anesthesia may be associated with intraoperative bleeding,

postoperative nausea / vomiting and graft rejection due to coughing and straining while extubation as well as due to intraoperative use of nitrous oxide. On the other hand, patients are not comfortable during surgery under local anesthesia due to inadequate duration of analgesia, constraints on movements for long durations, and the noise due to drilling and suction. The various local anesthetics used are quite effective but the duration of analgesia is a major limiting factor. To improve the quality and duration of analgesia several adjuvants have been tried in various types of surgeries. A selective α-2 adrenergic agonist clonidine has been tried as an adjuvant to local anesthetic solutions for peripheral nerve blocks. It has shown reduction in the onset time of the block, a significantly better quality of block with longer postoperative analgesia.[2,3,4] Clonidine possibly acts by membrane hyperpolarization during which cells remains unresponsive to excitatory stimuli, due to opening of the potassium channels and thereby enhancing and amplifying sodium channel blockade mechanism of local anesthetic agent.[5] Dexmedetomidine, the newer α-2 adrenoceptor agonist, is more potent and about eight times more selective for α-2 adrenoceptor. Previous clinical studies, have established intravenous use of dexmedetomidine for its opioid sparing effects and for reducing inhalational anesthetic requirements.[6] Dexmedetomidine has also been used in various peripheral blocks and in central neuraxial blocks in various strengths as an adjuvant to local anesthetics to prolong the duration of block and postoperative analgesia.[7,8] Very few studies have used α adrenergic agonists as adjuvants to local anesthetics in infiltration anesthesia.[9,10] We could not find comparison of these two α-2 adrenoceptor agonists as an adjuvant to local anesthetics in infiltration anesthesia, though studies comparing them in central neuraxial blocks[11] and in peripheral blocks are available.[12,13] In this prospective study, dexmedetomidine was compared to clonidine as an adjuvant to local anesthetic in infiltration anesthesia for tympanoplasty. Primary outcome measure was duration of postoperative analgesia and secondary outcome measures were sedation score, onset of analgesia, grade of bleeding and hemodynamic parameters.

METHODOLOGY

The present study was conducted at L.N. Medical College and J.K. Hospital, Bhopal, during the period from May 2015 to April 2016. After institutional ethics committee approval, 60 ASA physical status I and II patients of age group between 18 to 60 years, both genders, scheduled for tympanoplasty by post auricular approach, were included in the study after informed written consent. Patients having chronic systemic diseases including hypertension, ischemic heart disease, diabetes mellitus, any bleeding disorder, infection at incision site and the patients on antiplatelet or anticoagulant drugs were excluded from the study.

Patients were randomly distributed in two equal groups.

Group C: lignocaine with adrenaline 2% 12 ml + clonidine 1 μg/kg

Group D: lignocaine with adrenaline 2% 12 ml + dexmedetomidine 1 μg/kg

Sample size was based on previous studies.[12,16] Estimated sample size for two sample comparison of means test with assumption: alpha=0.05 (two-sided), power=0.90; to get the difference of 167 minutes (289 ± 62 min, 456 ± 97 min) for duration of analgesia in both groups turned out to be 5 in each group.

Post-hoc power analysis was carried out after complete study of 60 patients, for duration of analgesia. This study had 100% power to detect effect size of 272.33 minutes between Group C and Group D.

Method of randomization of patients was block randomization. [total blocks 15, size of block 4, allocation 1:1]. The drug solutions were prepared by an anesthesiologist not involved in the study. The surgeon performing the block, the attending anesthesiologist, and the patients were blinded to the treatment group. Postoperative data collection was done by care givers who were unaware of the group allocation. Intravenous (IV) access was secured in the operating room. All noninvasive monitoring devices (noninvasive blood pressure, electrocardiograph leads and pulse oximeter) were attached (Schillers Truscope II Monitor), and the baseline cardiorespiratory parameters were recorded at predefined intervals during surgery.

Group C patients received local infiltration by hypodermic needle (23 G) of clonidine (Cloneon®, Neon Laboratories) with lignocaine 2% with 1 in 200,000 adrenaline (LOX® 2% with adrenaline 1:200,000, Neon Laboratories), while Group D patients received infiltration of dexmedetomidine (DEXTOMID®, Neon Laboratories) plus lignocaine with 1:200,000 adrenaline. Post auricular region

and four quadrants of external auditory canal were infiltrated by the same surgeon to avoid operator bias. It also minimized the differences in tissue handling and assessment of grade of bleeding. Absence of response to painful stimulus at the surgical site was marked as effectiveness of block following which surgery was started. Supplemental oxygen was given through oxygen mask. Any sedative or analgesic drugs were avoided until patient became uncooperative due to pain hampering the surgery when injection diclofenac sodium 75 mg was given intravenously. Onset, duration of anesthesia, sedation score and degree of bleeding were assessed.

Onset of analgesia was defined as the period between the time of infiltration to the time of loss of sensation to pinprick in the retroauricular area.

Duration of surgery was defined as the period between the time of incision to the time of completion of suturing.

Sedation score was assessed by Ramsay Sedation Score[14] [1 = awake, conscious, no sedation; 2 = calm and compose; 3 = awake on verbal command; 4 = brisk response to gentle tactile stimulation; 5 = awake on vigorous shaking; 6 = unarousable]. Sedation scores were recorded just before the initiation and at predefined time periods during surgery.

Total duration of analgesia was taken to be from the administration of the block to time of first request of analgesic or VAS score ≥ 2.

Grade of bleeding in the surgical field was assessed by operating surgeon using Boezaart's grading system for bleeding[15] [grade 1 = cadaveric conditions with minimal suction required, 2 = minimal bleeding with infrequent suction required, 3 = brisk bleeding with frequent suction required, 4 = bleeding covers surgical field after removal of suction before surgical instrument can perform maneuver, 5 = uncontrolled bleeding].

All patients were observed in postoperative recovery ward after completion of surgery. Analgesia was assessed using a standard 10 point visual analogue scale (VAS), at an interval of every 30 min. Time for first analgesic demand or VAS score ≥ 2 was recorded. On reaching that point of time, study was terminated and for breakthrough pain relief patient was given systemic analgesic as per individual requirement. Side effects e.g. bradycardia, hypotension, respiratory depression and incidence of postoperative nausea and vomiting were noted.

Statistical analysis: All the quantitative data are presented as mean and standard deviation and compared using student's t-test. Qualitative data such as sedation score, grade of bleeding are presented as frequency and percentage and analyzed using chi-square test. P-value of < 0.05 was considered as significant and $p < 0.001$ was considered as highly significant.

RESULTS

All the sixty selected patients completed the study without any dropout. No patients required intraoperative analgesia and sedation. Demographic parameters showed no difference in both the groups (Table 1). Duration of surgery and onset of analgesia did not show any significant differences between two groups. The duration of analgesia was significantly prolonged in Group D as compared to Group C ($p < 0.001$) (Table 2).

Table 1: Demographic parameters

Characteristics		Group C (n=30)	Group D (n=30)
Age (years) (Mean ± SD)		30.33 ± 8.96	30.27 ± 9.24*
Weight (kg) (Mean ± SD)		52.37 ± 8.8	52.3 ± 8.87*
Gender [N (%)]	Male	16 (53.33)	15 (50)*
	Female	14 (46.66)	15 (50)*
ASA Grade [N (%)]	I	26 (86.66)	25 (83.33)*
	II	4 (13.33)	5 (16.66)*

p-value > 0.05;p-value significant at 0.05; ***p-value significant at 0.001*

Table 2: Intraoperative parameters

Parameters	GROUP C (N = 30)	GROUP D (N = 30)
	Mean ± SD	Mean ± SD
Duration of surgery (min)	69.3 ± 7.64	69.8 ± 7.84*
Onset of analgesia (sec)	92.33 ± 6.26	90.33 ± 8.08*
Duration of analgesia (min)	417.67 ± 58.64	690.00 ± 80.12***

p-value > 0.05;p-value significant at 0.05; ***p-value significant at 0.001*

Table 3: Hemodynamic parameters at different stages of surgery

Hemodynamic parameters	Time interval	Group C (N = 30)	Group D (N = 30)
		Mean ± SD	Mean ± SD
HR (per min)	Baseline	87.43 ± 7.86	88.26 ± 7.06*
	At incision	69.63 ± 2.68	68.86 ± 2.14*
	Annulus lifting	70.67 ± 4.20	70.46 ± 3.50*
	End of surgery	70.30 ± 2.98	69.64 ± 2.74*
MAP (mm Hg)	Baseline	83.00 ± 6.75	82.46 ± 7.11*
	At incision	70.6 ± 2.60	70.60 ± 3.11*
	Annulus lifting	74.86 ± 5.57	74.70 ± 5.20*
	End of surgery	69.83 ± 3.30	69.40 ± 3.20*

p-value > 0.05;p-value significant at 0.05; ***p-value significant at 0.001*

Table 4: Sedation score at different stages of surgery Data shown as N (%)

Time interval	Sedation Score	Group C (N = 30)	GroupD (N = 30)	
Baseline	1	30 (100)	30 (100)	
	2	0 (0)	0 (0)	
	3	0 (0)	0 (0)	
At incision	1	16 (53.33)	8 (26.66)	
	2	14 (46.66)	18 (60)	**
	3	0 (0)	4 (13.33)	
Annulus lifting	1	10 (33.33)	9 (30)	
	2	20 (66.66)	18 (60)	**
	3	0 (0)	3 (10)	
End of surgery	1	16 (53.33)	8 (26.66)	
	2	14 (46.66)	18 (60)	**
	3	0 (0)	4 (13.33)	

**p-value > 0.05 **p-value significant at 0.05; ***p-value significant at 0.001*

Hemodynamically, mean blood pressure (MAP) and pulse rate between the two groups were comparable at different intervals during surgery (p > 0.05) (Table 3).

Sedation score was significantly higher in dexmedetomidine group as compared to clonidine group (Table 4). Bleeding was equal in both groups and no significant difference was observed between two groups (Table 5).

DISCUSSION

Local infiltration analgesia which is defined as the administration of large volumes of local anesthetics with or without adjuvants in the different tissue planes perioperatively[17] is a commonly used anesthetic procedure in middle ear surgeries. During local anesthesia surgeon can test hearing and detect complications intraoperatively It is also devoid of the complications associated with general anesthesia, reduces hospital stay and expenditure but at the same time sympathetic stimulation due to anxiety of conscious and aware patient may increase bleeding leading to increased chances of graft failure. In addition the slightest movement can disturb the surgeon due to the microscopic nature of the surgery. The success of surgery under local anesthesia demands patient cooperation that can be achieved by preoperative counseling, and appropriate sedation. Both α-2 adrenoceptor agonists, clonidine and dexmedetomidine, have been studied in various strengths as an adjuvant to local anesthetics to prolong the duration of block and postoperative analgesia in various peripheral blocks[12,13] as well as central neuraxial blocks.[8] But there are very few studies directly comparing these two drugs as adjuvant to local anesthesia infiltration. For uniformity in type, nature, and duration of pain, we included only tympanoplasty in our study. Singelyn et al[18] used clonidine in minimum dose (0.5 μg/kg) as an adjuvant to mepivacaine in brachial plexus block and observed a prolonged duration of anesthesia and analgesia. No added benefits were found with doses exceeding 1.5 μg/kg. We decided to use clonidine at a dose of 1 μg/kg in our study based on previous studies that confirmed the analgesic efficacy of dexmedetomidine 1 μg/kg rather than 0.5 μg/kg and 0.75 μg/kg.[19] In our study duration of analgesia was found to be significantly longer in Group D than in Group C. These results are

Table 5: grade of bleeding

Grade of bleeding	Group C N (%)	Group D N (%)
I	6 (20)	6 (20)*
II	21 (70)	20 (66.66)*
III	3 (10)	4 (13.33)*

** p-value > 0.05 * * p-value significant at 0.05; * * * p-value significant at 0.001*

similar to other studies.[12,13] Aggarwal S, et al[20] compared the effects of adding dexmedetomidine to bupivacaine in supraclavicular brachial plexus block in fifty patients. They observed shorter onset of analgesia, prolonged duration of sensory and motor blocks and duration of analgesia due to addition of dexmedetomidine. Swami et al[12] also reported significantly longer duration of analgesia and better quality of block with dexmedetomidine as compared to clonidine. Harshavardhan HS[13] also reported similar findings. Prolongation of duration of analgesia by α-2 agonists when used as an adjuvant with local anesthetics in peripheral blocks has been proven in several studies, their peripheral action has been considered to be responsible for it. Possibly analgesic effect of α-2 agonists at the peripheral level is by reduction of norepinephrine release as well as inhibition of nerve action potential, and thus is receptor independent. Inhibition of release of substance P in the nociceptive pathway and activation of α-2 receptors in the locus cerulus are the contributing factors for the central analgesia and sedation caused by α-2 agonists. Dexmedetomidine and clonidine both are α-2 adrenergic agonists, they work in a similar manner. However dexmedetomidine has eight times higher selectivity for α-2 adrenoceptors. Stimulation of the α-2 adrenoceptors in the locus ceruleus is mainly responsible for sedative and antinociceptive effects of dexmedetomidine. Dexmedetomidine has more specificity for α-2 A adrenoceptor subtype which is accountable for relaying the sedative and analgesic properties,[21] causing it to be a much more effective sedative and analgesic agent than clonidine. In our study we found high sedation score in dexmedetomidine group at the time of incision, painful procedure of annulus lifting and at the end of surgery, and patients were more comfortable and arousable as compared to clonidine group. The results of our study are similar to other studies.[12] Addition of 1 μg/kg dexmedetomidine to ropivacaine for cervical plexus block has been found to decrease sensory block onset time and extend the duration of analgesia, and increase the quality of analgesia so that patients were sedated and arousable.[22] However, Swami et al observed no such difference in onset when they compared both drugs as adjuvant to local anesthetics in brachial plexus blocks.[12] We also observed no difference in onset of analgesia between the groups. Regarding intraoperative bleeding, though lower bleeding grades were observed in both groups, we did not find significant difference between the groups, an observation similar to other studies.[23,24] A possible factor for the reduced bleeding at surgical site could be the contributory effect of clonidine and dexmedetomidine in reducing the blood pressure by sympatholysis. In our study patients were hemodynamically stable throughout the surgery and in postoperative period equally in both groups. No side effects like hypotension, bradycardia, respiratory depression, or nausea / vomiting were noted in our study.

CONCLUSION

We conclude that dexmedetomidine is more effective than clonidine in terms of prolongation of duration of postoperative analgesia and sedation score, when added as an adjuvant to local anesthetic in infiltration anesthesia for tympanoplasty, with no difference in terms of onset of analgesia, grade of bleeding and the effect on hemodynamic parameters.

Conflict of interest: None declared by the authors

Authors' contribution: All authors took part in the concept and conduct of the study, as well as manuscript preparation

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