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A prospective Randomized Double-Blind Study Comparing Adrenaline vs. combination of Adrenaline and Dexmedetomidine in Local Infiltration Block for Ear and Nose Surgeries

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Abstract

Background and Aims: For the achievement of clear bloodless surgical field, local infiltration of adrenaline is used routinely in Ear, Nose and Throat (ENT) surgeries. The present study was intended to study effectiveness of the addition of dexmedetomidine to local infiltration solution of lignocaine and adrenaline and any adverse effect associated with it. *Methods:* We recruited 80 patients in the age group of 18-65years by randomization posted for tympanoplasty or septoplasty under general anesthesia and divided into two groups of 40 each. Group A received local infiltration of 11.5ml of 2% lignocaine with adrenaline (1:200000) dilution with 0.5ml normal saline while Group D received local infiltration of 11.5 ml of 2% lignocaine with adrenaline (1:200000) dilution with 0.5ml (50µg) of dexmedetomidine. Monitoring involved-Heart rate, Blood pressure, Intraoperative surgical bleeding and Surgeon's satisfaction score. Intraoperative isoflurane and fentanyl requirement was calculated. Student's *t*-test was used for analysing statistical significance in time related variables. *Results:* Intraoperative tachycardia and hypertension which was seen after infiltration of solution of lignocaine and adrenaline was found to be abolished by addition of dexmedetomidine. Also dexmedetomidine containing solution significantly decreased intraoperative bleeding and thus increased surgeon's satisfaction. Isoflurane and fentanyl requirement was significantly reduced in study group. *Conclusion:* Addition of dexmedetomidine to local infiltration solution of lignocaine and adrenaline in ear and nose surgeries provides a good quality surgical field with stable haemodynamics with decreased requirement of other agents for the purpose of clear field, enhancing safety of the procedure and patient and cost effectiveness.

Keywords: Adrenaline; Clear Bloodless Surgical Field; Dexmedetomidine; Hypotensive Anesthesia.

Introduction

Requirement of clear bloodless surgical field in ENT surgeries is gaining popularity day by day. Even a minor bleeding in the field can lead to loss of precision in these surgeries. Anaesthetist in addition to providing anesthesia has to provide a clear bloodless surgical field in these surgeries, which can be achieved with hypotensive anesthesia using various physical and pharmacological methods [1,2]. In addition to that local infiltration of adrenaline is used routinely in ENT operation theatre. But these methods have their own demerits like danger of tissue hypoxia in case of controlled hypotension and toxic circulatory effects like hypertension and arrhythmias that ensue after systemic absorption of local adrenaline [3]. So, to provide safe and satisfactory anesthesia, it is necessary to avoid systemic side effects of local adrenaline, avoid administration of hypotensive anesthesia and still to have better surgical conditions of operatability.

To satisfy above requirements, we studied the effectiveness of addition of dexmedetomidine to local infiltration solution of lignocaine and adrenaline after obtaining approval from the Hospital Ethics Committee along with written informed consent from the patients. The study was

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intended to study the effect on baseline heart rate, blood pressure, quality of surgical field and hence surgeon's satisfaction, requirement of anaesthetic and other agents and any other adverse effect of the drug.

Dexmedetomidine is a potent and highly selective α-2 adrenoceptor agonist with sympatholytic, sedative, amnestic and analgesic properties [4,5] which has been described as a useful and safe adjunct in many clinical applications. Dexmedetomidine is the pharmacologically active dextro enantiomer of medetomidine, the methylated derivative of etomidine. It is considered primarily as α-2 adrenoceptor agonist, but also incorporates an imidazoline structure, thus having an agonist effect on imidazoline receptors.

Dexmedetomidine is chemically related to clonidine, but is approximately eight times more specific for α-2 adrenoceptors with α-2:α-1 selectivity ratio of 1600:1, compared with 220:1 for clonidine, especially for the 2a subtype, which makes dexmedetomidine more effective than clonidine for sedation and analgesia.

There are three types of α-2 isoreceptors - α-2a, α-2b, α-2c,which bind to α-2 agonists and antagonists with similar affinities and share an amino acid composition homology of approximately 70-75%. α-2a receptors appears to promote sedation, hypnosis, analgesia, sympatholysis, neuroprotection and inhibition of insulin secretion. Agonism at α-2b receptor suppresses shivering centrally, promotes analgesia at spinal cord sites and induces vasoconstriction in peripheral arteries. The α-2c receptor is associated with modulation of cognition, sensory processing, mood and stimulant induced locomotor activity and regulation of epinephrine outflow from the adrenal medulla. Inhibition of norepinephrine release appears to be equally affected by all 3α-2 subtypes [5].

Materials and Methods

After obtaining approval from the Hospital Ethics Committee along with written and informed consent from patients, 80 adults (18-65yrs) of either sex belonging to American society of Anaesthesiology (ASA) physical status class I and II and scheduled for Tympanoplasty and Septoplasty under general anesthesia, were enrolled in this prospective, randomized and double blind study. We excluded patients with organ dysfunction, allergy to any drug used, coagulation disorder, local infection at the site of block.

Patients were randomly divided into two groups of 40 patients each by computer generated random table number. Out of those 40 patients in each group, 20 underwent Tympanoplasty and remaining 20 underwent Septoplasty under general anesthesia. Patients of Group A received local infiltration of 11.5 ml of 2% lignocaine with adrenaline (1:200000) dilution with 0.5ml normal saline while Group D received local infiltration of 11.5 ml of 2% lignocaine with adrenaline (1:200000) dilution with 0.5ml (50μg) of dexmedetomidine. A standardized technique of infiltration administered by the same surgeon which provided reliable distribution of solution and eliminated operator bias was used. In case of tympanoplsty, infiltration was given in postauricular area to block greater auricular and lesser occipital nerves, in the incisura terminalis to block auriculotemporal nerve and the four quadrants of the external auditory canal and in case of septoplasty it was given under mucoperichondrium and mucoperiosteum.

All patients were admitted prior to the day of surgery and investigated for haemoglobin, bleeding and clotting time, urine examination, electrocardiogram (ECG). On arrival to the operation theatre, fasting of eight hours was confirmed. Written informed consent for surgery and anesthesia was taken. Intravenous (iv) line was secured by 18/20G cannula and ringer lactate solution was used as maintenance fluid. Baseline systemic blood pressure (BP), heart rate (HR), peripheral oxygen saturation (SpO2) and ECG were recorded using Philips MP 40 monitor. Patients were premedicated with Inj glycopyrrolate 5μg/kg intramuscular (im) 30 min before induction. Inj ondansetron 0.08mg/kg IV, inj midazolam 0.03mg/kg iv and inj fentanyl 1μg/kg iv were given just before induction of anesthesia. Inj hydrocortisone 2mg/kg and inj dexamethasone 0.2mg/kg iv was given in case of nasal surgeries.

After preoxygenation for 3 min, anesthesia was induced with inj thiopentone sodium 5mg/kg iv. Tracheal intubation with proper size endotracheal tube was facilitated with inj succinylcholine 2mg/kg iv under direct laryngoscopy.

Anesthesia was maintained with 50% nitrous oxide in oxygen and isoflurane dial concentration was titrated to achieve Fromme Boezaart scale of bleeding ≤2. Patients were ventilated manually with Bains circuit to maintain end tidal concentration of CO2 (EtCO2) between 30-35 mm Hg. Surgeon was asked to infiltrate locally at surgical site before tissue dissection. Operating surgeon or monitoring anaesthetist involved in data collection were not aware of the study solution.

Intraoperatively, heart rate, blood pressure, EtCO2, SpO2, temperature were monitored and recorded immediately after infiltration at 0min till 30min at 5min intervals and thereafter every 15min interval. Concentration of isoflurane was recorded in terms of percentage and total duration of set dial percent concentration was recorded. From these values total isoflurane volume required in ml was calculated by Dion's formula. Intraoperative surgical bleeding was assesed by Fromme Boezaart scale (0-6) and surgeon's satisfaction about field was graded as poor to excellent (1-5). Any adverse haemodynamic event was recorded and treated. Bradycardia (HR<50) was treated with atropine 0.6mg iv. Tachycardia (HR ≥ 20% of basal values) was treated with 50µgm increments of fentanyl. Hypotension or hypertension were defined as >30% changes in systolic blood pressure from basal values. Hypotension was treated with reducing isoflurane concentration to the minimum level of adequate plane of anesthesia (BIS 40-60) and if still not corrected iv fluids and mephentermine 6mg iv bolus were given. Hypertension was treated by increasing concentration of isoflurane.

Fromme Boezaart Scale for surgical bleeding [6,7] is; 0 – No bleeding, 1– Slight bleeding, no suctioning of blood required, 2– Slight bleeding, occasional suctioning required, surgical field not threatened, 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. Surgeon's Satisfaction was graded as; 1 – Poor, 2 – Good, 3 – Better, 4 – Best, 5 – Excellent. Dion's formula [8]- for calculation of total usage of volatile anaesthetics in ml = (Dialed conc. × Total fresh gas flow × Duration at that conc. × Mol. wt) / (2412 × Density).

(Conc = Concentration; Mol.wt= Molecular weight). In case of isoflurane, Molecular weight is 184.5 gm/mol and Density is 1.496 gm/ml. After surgery the residual neuromuscular blockade was antagonised with neostigmine 0.05mg/kg and glycopyrrolate 0.01mg/kg iv. Patients were extubated after observing adequate motor recovery and spontaneous breathing efforts. Patients were transferred to post anesthesia care unit for observation of any respiratory depression, haemodynamic changes, nausea and vomiting.

Statistical Analysis

The recorded data were tabulated and expressed in mean±standard deviation (SD). Statistical analysis was performed using SPSS for Windows software package (version 21.0, IBM Corp., Armonk, NY, USA). The demographic data for categorical variables were compared using Chi-square test. Student's *t*-test was used for analysing statistical significance in time related variables. $P < 0.05$ was considered as statistically significant.

Primary outcome of the study was quality of surgical field measured by Fromme Boezaart Scale. To detect 15% difference between two groups with 80% power and 5% significance level, sample size required was 32 patients in each group but considering dropout and to enable detection of potential variations, we included 40 patients in each group. This sample size was calculated based on a pilot study in the beginning of our study.

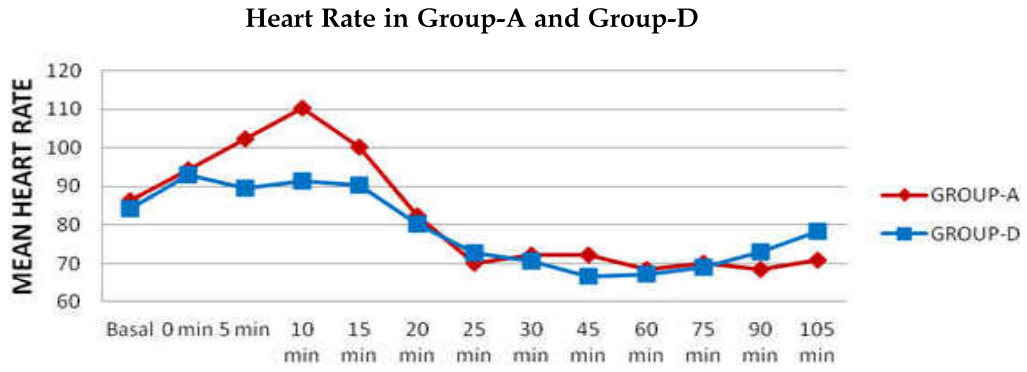
Results

The study was completed successfully in 80 patients. The demographic data of Patients i.e. age, Sex, weight, ASA physical status and surgical duration were comparable between the groups (Table 1). The baseline Heart Rate and Mean Arterial Pressures (MAP) were comparable between two groups. Heart Rate values were statistically significant at 5, 10, 15, 45 and after 90 minutes of surgeries in group-D (Figure 1). MAP were statistically significant at 5, 10, 15, 20, 30 and again after 90 minutes of surgeries in group-D (Figure 2).

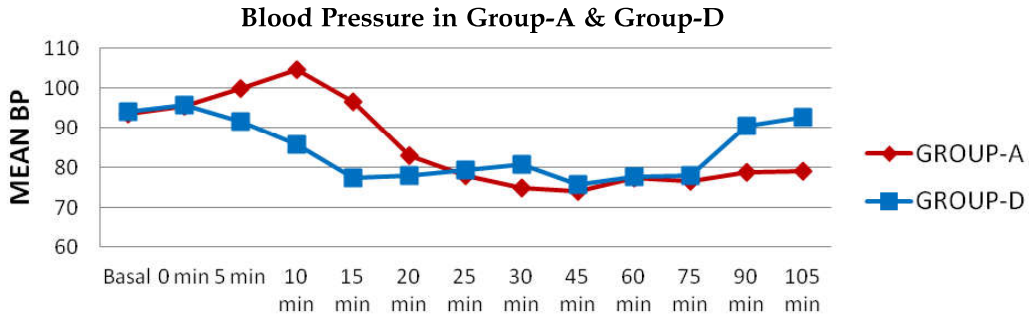
Table 1: Patients Demographic characteristics in Group-A and Group-D

Sr. No.	Parameters	Group-A (40 patients)	Group-D (40 patients)
1	Age (Mean± SD) yrs	39.27 ± 9.40	41.02 ± 9.42
2	Sex (M,F)	M=23,F=17	M=25,F=15
3	Weight (Mean± SD) kg	58.65 ± 8.47	57.37 ± 8.62
4	ASA Status (I,II)	I=33,II=7	I=32,II=8
5	Surgical Duration (Mean ± SD) min	109.55 ± 5.45	110.25 ± 4.45

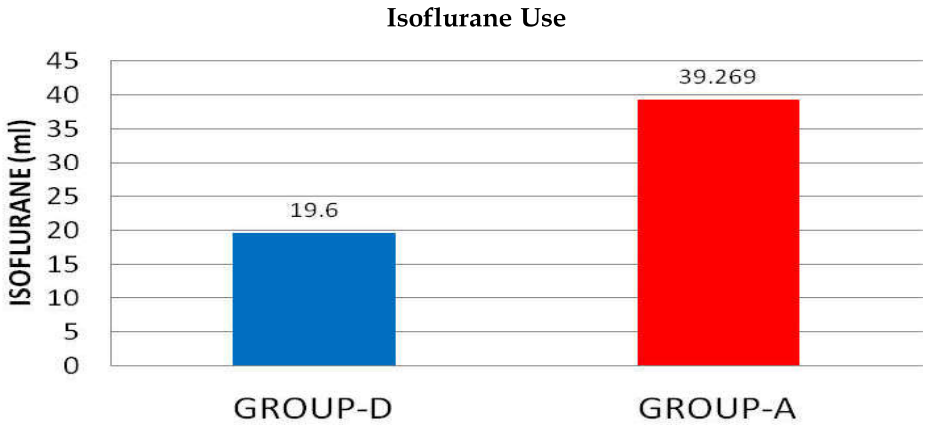
(SD –Standard Deviation, M-Male, F-Female)
Patient Demographic data were comparable between two groups



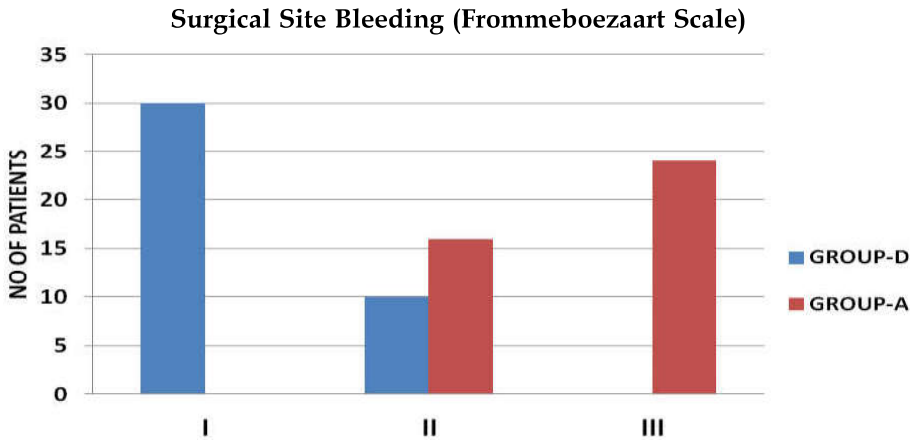
Graph 1: Mean Heart Rate in Group-A and Group-D



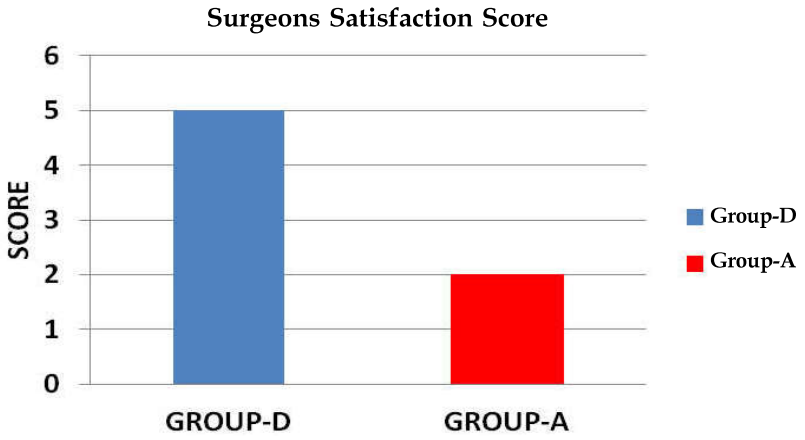
Graph 2: Mean arterial BP (MAP) mm/Hg in Group-A and Group-D



Graph 3: Isoflurane Use in Group-A and Group-D



Graph 4: Surgical site bleeding according to Frommeboezaart scale



Graph 5: Surgeons Satisfaction Score in Group-A and Group-D

Total intraoperative isoflurane requirement in order to achieve Surgical Field Grading ≤ 2 was significantly reduced in group-D patients (Figure 3). Group-A patients required additional fentanyl supplement intraoperatively. In case of Group-D, none of the patients required it additionally which was statistically significant. Majority of patients in Group-D had Grade-I surgical site bleeding which was Grade-III in case of Group-A (Figure 4). Due to better surgical field, Surgeon's satisfaction score was higher in Group-D which was statistically significant (Figure 5). None of the patients in study group had any adverse haemodynamic event, nausea or vomiting due to dexmedetomidine.

Discussion

We could not find the study assessing the effect of addition of dexmedetomidine to local infiltration solution in ENT surgeries to minimise surgical bleeding though studies showing role of iv dexmedetomidine to produce oligaemic field and decrease intraoperative anaesthetic and analgesic requirement are available. Gupta et al in a prospective randomized study proven that dexmedetomidine infusion during middle ear surgery under general anesthesia provide oligaemic surgical field [9].

There are various techniques to produce clear bloodless field. Various intravenous or inhalational agents have been used to produce controlled hypotension. We used dexmedetomidine in infiltration instead of by intravenous route to avoid systemic adverse effects of intravenous dexmedetomidine like initial hypertension, hypotension, nausea, dry mouth, and bradycardia. Overdose may cause first degree or second-degree atrioventricular block. Most of the adverse events associated with dexmedetomidine use occur during or shortly after loading dose [10,11]. At clinically effective doses, dexmedetomidine has been shown to cause much less respiratory depression than other sedatives [12]. However, coadministration of dexmedetomidine with anaesthetic agents, sedatives, hypnotics, or opioids is likely to cause additive effect [13]. Inspite of giving drug by infiltration, there was some systemic absorption of drug as there was moderate decrease in heart rate and blood pressure after some time (Figure 1 and 2), but this change was beneficial for surgery.

Tachycardia and hypertension caused by systemic absorption of adrenaline immediately after infiltration was suppressed after 5 min of infiltration in Group D, while in Group A that was sustained and surgeon started complaining of bleeding in the field. To overcome these systemic effects and bleeding, increased concentration of isoflurane and iv fentanyl were given in titrated dosages in an attempt to achieve clear field in Group A. In Group D patients we didn't need to change dial concentration of isoflurane.

Total isoflurane requirement was very less in Group D than Group A as calculated from Dion's formula. This formula is only a crude method for estimating the amount of isoflurane used. Nevertheless it is an easy and quick method to derive the amount of inhalational agent used at places where more sophisticated equipment like those used to calculate the end tidal concentration of inhalational agent are not available. Also it saves on the time for meticulous and lengthy calculations. Though not highly accurate, it definitely gives an objective value to indicate the anaesthetic sparing effect of dexmedetomidine.

In some patients of Group D there were higher values of heart rates and blood pressures than Group A after 80-90 min of surgery as Group A patients were managed on isoflurane and fentanyl for the purpose of clear bloodless surgical field. In spite of higher values of blood pressures and heart rates there was good surgical field in Group D patients and not required any additional measure. So there were less interruptions during surgery and hence excellent surgeon's satisfaction was achieved in Group D patients.

As there is no literature proposing the mechanism of action of local infiltration of dexmedetomidine to reduce surgical bleeding, it can be proposed as it is due to direct action of dexmedetomidine on peripheral α2b receptors which are present on vascular smooth muscles at the infiltration site causing local vasoconstriction in addition to adrenaline.

Simultaneously as local dexmedetomidine was absorbed systemically it was opposing the systemic effects of adrenaline by α2a receptors. These both effects were favourable for reducing surgical site bleeding. As this was the first study where dexmeditomidine was used by local infiltration to reduce surgical site bleeding, there was no study to compare the outcomes of the study. Secondly we didn't know exact optimal dose of dexmedetomidine for local infiltration which was derived from a pilot study done before. These are limitations of the study.

Conclusion

Addition of dexmedetomidine to local infiltration solution of lignocaine and adrenaline in tympanoplasty or septoplasty surgeries under general anesthesia provide good surgical field with excellent surgeon's satisfaction with haemodynamic variations within physiological range with decreased requirement of isoflurane and other agents reducing the cost of anesthesia.

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