e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(11); 896-904

Original Research Article

Comparative Study of Perioperative Infusion of Dexmedetomidine Versus Labetalol for Controlled Hypotension in Functional Endoscopic Sinus Surgeries

Deepa Kattishettar[1], Lakshmi Priya[2], Shambhavi A Prakash[3], Vinayaka C S[4], Vijayalakshmi B C[5], Manjunath H G[6]

[1] Associate Professor, Dept. of Anaesthesiology, Mysore Medical College & Research Institute, Mysuru
[2] Assistant Professor, Dept. of Anaesthesiology, Mysore Medical College & Research Institute, Mysuru
[3] PG – Resident, Department of Anaesthesiology, Mysore Medical College & Research Institute, Mysuru
[4] Assistant Professor, Sri Jayadeva Institute of Cardio thoracic Sciences & Research, Mysuru
[5] Professor, Dept. of Anaesthesiology, Mysore Medical College & Research Institute, Mysuru
[6] Professor, Department of Anaesthesiology, Mysore Medical College & Research Institute, Mysuru

Received: 26-09-2023 / Revised: 25-10-2023 / Accepted: 10-11-2023
Corresponding Author: Deepa Kattishettar
Conflict of interest: Nil

Abstract

Background and objectives: A prospective, randomized study was undertaken to compare perioperative infusion of dexmedetomidine versus labetalol for controlled hypotension in functional endoscopic sinus surgeries under general anaesthesia.

Methods: Sixty adult patients undergoing FESS were randomly allotted to two groups. Group Dexmedetomidine (n=30) received a bolus dose of 1mcg/kg over 10 minutes followed by infusion at 0.4-0.8mcg/kg/hr and group Labetalol (n=30) received a bolus dose of 0.25 mg/kg/hr infused over 10 mins followed by 1-2 mg/min/IV infusion dose titrated during maintenance to achieve target MAP of 70-75mmHg. Haemodynamic parameters were recorded at regular intervals. Surgical site assessment was done by surgeons using Fromme's scale. Awakening time before extubation, recovery time (by Aldrete score), sedation score (using RSS scale) and surgeon satisfaction score were recorded. Statistical analysis was done with Chi-square test for qualitative data and Independent t test to identifythe mean difference between two quantitative variables.

Results: Both drug regimens were able to produce and maintain controlled hypotension and thus optimal surgical conditions. Early recovery times were seen in Labetalol group whereas higher surgeonsatisfaction and higher sedation scores noted in the Dexmedetomidine group.

Conclusion: Both dexmedetomidine and labetalol provide controlled hypotension and oligemic surgical fielddur-ing FESS under general anaesthesia. However, surgeon satisfaction and postoperative sedation were better with dexmedetomidine although early recovery was seen with labetalol.

Key words: Dexmedetomidine, Labetalol, Hypotension controlled.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Functional endoscopic sinus surgery (FESS) indicated for acute and chronic sinus pathologiesrestores the drainage and aeration of paranasal sinuses.[1] Because of decreased surgical invasiveness, this procedure is less painful and a safe and effective treatment method for paranasal sinus disorders. Bleeding during surgery reduces the visibility in the operative field and increases the risk of injury to major vessels and the surrounding structures, hence control of bleeding is beneficial.[2]

Controlled hypotension is defined as a reduction of the systolic blood pressure to 80-90 mm Hg, a reduction of mean arterial pressure (MAP) to 50-65 mm Hg or a 30% reduction of baseline MAP.[3]

Labetalol is a combined selective alpha-1 and non-selective beta- adrenergic receptor blocker with an alpha to beta blocking ratio of 7:1. The hypotensive action begins within 2 to 5 minutes after its IV administration, peak effect at 5 to 15 minutes andlasts for about 2 to 4 hours. Labetalol reduces the systemic vascular resistance without reducing total peripheral blood flow. Due to its β-blocking effects, the heart rate is eithermaintained or slightly reduced. Labetalol maintains cardiac outputunlike other pure β- adrenergic blocking agents. Labetalol should be used with caution in patients with heart failure and avoided in patients with severe sinus bradycardia, heart block greater than first degree and asthma.[4]

Dexmedetomidine is a highly selective α2-agonist with an affinity ratio α2:α1 of 1620:1. It causes a dose dependent decrease in arterial blood pressure and HR possibly due to a decrease in serum norepinephrine concentrations. It has a very short half-life of approximately 6 min, and elimination time of 2 hours.[5,6] It has analgesic, sedative, antihypertensive, and anaesthetic sparing effects when used by the systemic route. Prior administration of Dexmedetomidineis also shown to induce a hypotensive anesthesia and to provide a better surgical field and an abbreviated operative duration in spinal and middle ear surgeries.[7,8]

Hence the present study is designed to evaluate and compare the effectiveness of combined selective α1 adrenergic receptor blocker and nonselective β blocker Labetalol versus selective α2-agonist Dexmedetomidine in producing intraoperative controlled hypotension during FESS.

Aims and Objectives

Aim:

A comparative study of the effects of Dexmedetomidine and Labetalol infusion on Hemodynamic parameters and surgical condition during Functional Endoscopic Sinus Surgery.

Objectives:

The primary objectives are to study and compare the Hemodynamic parameters after Dexmedetomidine and Labetalol infusion during Functional Endoscopic Sinus Surgery based on the Mean Arterial Pressure (MAP)(mmHg), Heart Rate (HR)(bpm) and the Intra-operative surgical field visibility based on Fromme's scale. Secondary objectives compared were duration of recovery (time to extubation, time to Aldrete score>9), Postoperative sedation score, Satisfactionof surgeons and adverse effects if any

Materials and Methods:

This randomized, comparative study was conducted on 60 ASA I-II patients of either sex, aged between 20-60 years scheduled for FESS in Krishna Rajendra hospital attached to Mysore Medical College and Research Institute, Mysore over a period of 15 months from January 2020 to March 2021. Approval of the Scientific Review Committee and Ethical Committee of our Institute was obtained and a detailed written informed consent taken from the patients during the preoperative interview.

Patients with BMI>30kg/m^2, cerebrovascular diseases, cardiovascular diseases, hypertension, diabetes mellitus, asthma, COPD, coagulation disorders, hepatic or renal failure, psychiatric diseases, known drug allergy, or substance abuse were excluded from the study. Study patients were randomly allocated by shuffled sealed envelope method to the following two groups of 30 each by a senior anaesthesiologist who also prepared the infusion solutions of the study drugs and administered the loading dose and maintenance infusions of the study drugs to all the patients, while the operating surgeon and observing anaesthesiologist were blinded to the administered studydrugs.

Group-L: Patients received Labetolol 0.25 mg/kg/IV as bolus given over 10 mins followed by infusion at the rate of 1-2mg/min/IV for maintenance.

Group D: Patients received Dexmedetomidine at 1μg/Kg over 10 min followed by 0.4-0.8 mcg/Kg infusion for maintenance.

Study drug preparation: Both Labetolol and Dexmedetomidine were diluted in 50 ml normal saline in syringe pumps for blinding purpose. In group D, 2 mL of 200μg of Dexmedetomidine (Dextomid 100 mcg/ ml, Neon LaboratoriesLtd.,India)was diluted with 48ml 0.9%saline.

After arrival in the pre-anaesthetic room, 2 intravenous cannula were inserted at different sites – one for infusion of the study drugs, and one for administration of fluids, other drugs, blood etc. All the patients were premedicated with Inj.Midazolam 0.02mg/kg and Inj.Fentanyl lμg/kg IV.Patients were monitored with 5 leads ECG, non- invasive blood pressure [NIBP], pulseoximetry [SpO2] and Capnography [ET CO2]. Invasive arterial blood pressure monitoring was not done since the facility for the same was not routinely available at our hospital and due to the cost limitations. Before induction of anaesthesia, baseline measurements of heart rate (HR), mean arterial pressure (MAP), and oxygen saturation by pulse oximetry (SpO2) were obtained. After 3 min of preoxygenation, anaesthesia was induced with Thiopentone 5 mg/kg. Succinylcholine 1.5mg/kg iv was given to facilitate endotracheal intubation with appropriate size cuffed oral endotracheal tubes and Lidocaine iv 1.5 mg/kg was given to suppress hemodynamic response to laryngoscopy and tracheal intubation. All patients were operated on by the same ENT surgical team. Anaesthesia was maintained with 50% O2-N2O & Isoflurane 0.5-1% (Tec 7 vaporizer). Muscle relaxation was achieved by Vecuronium 0.05mg/kg iv bolus & subsequent calculated doses at required intervals. Patients were ventilated with tidal volume of 8-10ml/kg, inspiratory/expiratory ratio of 1:2 and a respiratory rate to maintain an end-tidal CO2 level of 30- 45mm of Hg and SpO2 level above 98%.

Group D Patients received a 1μg/Kg loading dose of Dexmedetomidine within 10 min followed by 0.4-0.8mcg/kg/hr infusion during maintenance. Patients in Group L received 0.25 mg/kg/IV as bolus given over 10 mins followed by infusion at the rate of 1-2mg/min/IV. The infusion rates were then titrated to maintain MAP between 70-75 mmHg. If MAP decreased below 60 mmHg, the administered infusion dose was to be reduced by half, and if no response was obtained within 5 minutes, infusion of the

hypotensive agent was to be discontinued and iv Mephenteramine 6mg was to be given to correct hypotension. The dose of Mephenteramine required in each patient was recorded. In case of bradycardia (HR <40 bpm) a 0.012µg /kg atropine IV was to be administered & its use recorded. Heart rate, Systolic blood pressure, diastolic blood pressure & mean arterial pressure, were measured every 2 mins during bolus and every 5 min during maintenance till end of the surgery. Oxygen saturation(SpO2) and EndtidalCO2 were continuously monitored. Intra operative assessment of surgical field and blood loss was done by the surgeon when the desired MAP of 70-75 mmHg was achieved and maintained for atleast 10 minutes, using a predefined category scale adopted from that of Fromme et al[10] [Table 1]. Fromme's scale less than or equal to

3 was considered as adequate condition for surgery.The time to complete recovery after anaesthesia in the present study was assessed using Aldrete score [Table 2]. The sedation score was measured using the Ramsay Sedation Score scale at 15, 30and 60 minutes after tracheal extubation [Table 3]. The awakening time was taken as the time from administration of reversal agents to spontaneous eye opening for more than 5 seconds, Surgeon's satisfactionof the surgical site was scored by the same surgeon on a 4-point surgeon satisfaction scale(1-bad, 2-moderate, 3- good, 4-excellent). In the recovery room, adverse effects such as nausea, vomiting, agitation, bradycardia, coughing, shivering, reflex tachycardia and rebound hypertension if any were recorded.

Statistical Analysis:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data.Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs. P value<0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data

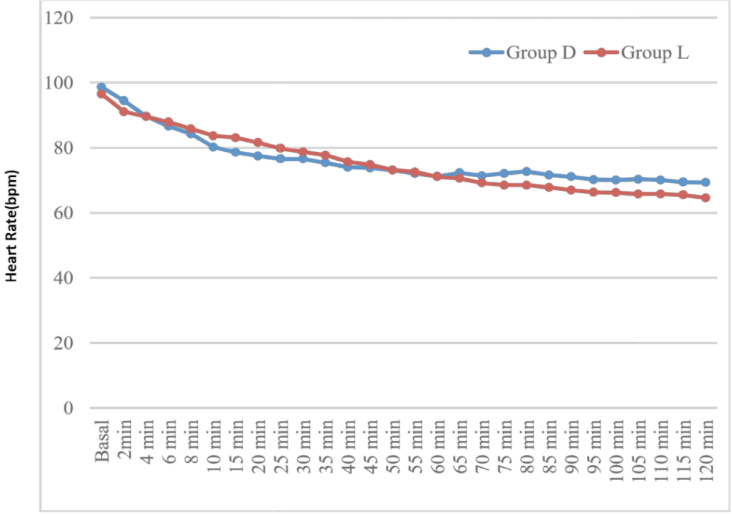
Results:

We found that the two groups were comparable with respect to demographic data and baseline haemodynamic variables.

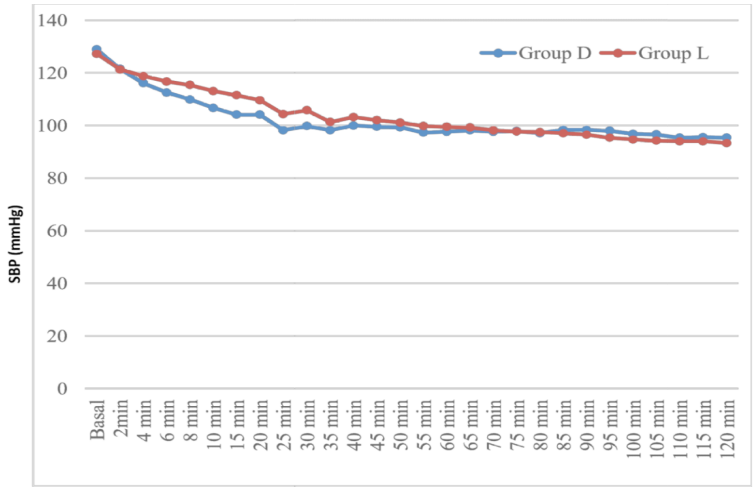
Table 1:

Parameters	Group D	Group L
Mean Age(years)	39.47+9.944	35.47+6.862
Sex Ratio M:F	17:13	16:14
Mean weight(kg)	66.17+5.395	65.40+3.607
Mean height(cms)	166.20±5.480	164.20±2.578
Mean baseline HR(bpm)	98.73+13	96.57+11
Mean baseline MAP(mmHg)	97.2+8	93.9+5.1

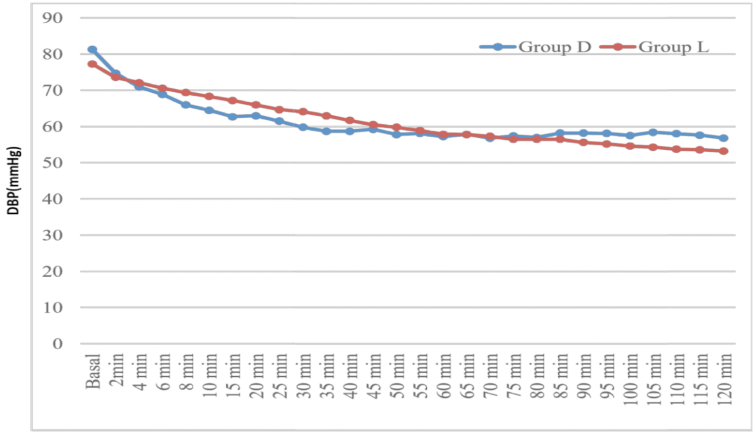
Mean baseline HR was comparable in both the groups [Group D- 98.73±13 and Group L-96.57 ± 11]. Though the HR started to fall in group D compared to group L from 6th min after starting the loading dose till 60th min it was not statistically significant. There was statistically significant difference between two groups with respect to HR from 80th min till 120mins with lower values in Group L than Group D



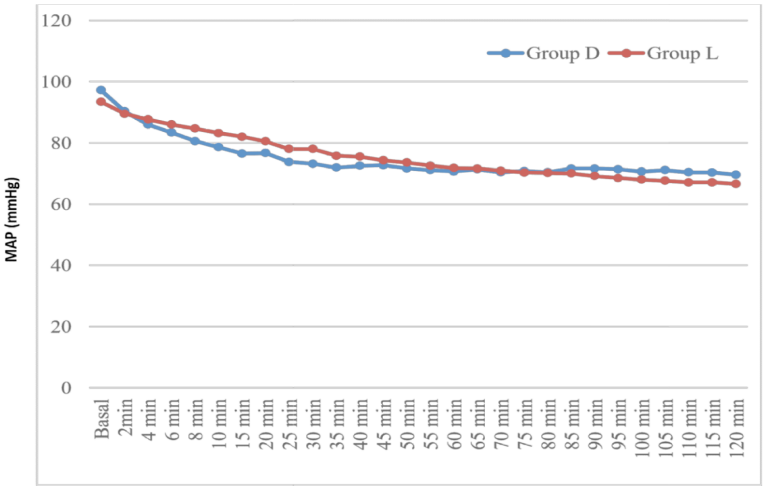
Both the groups were comparable with respect to baseline SBP and after administration of loading dose of the study drugs. Statistically significant difference was found between two groups after 6 min of loading dose till 30mins. Thereafter both groups were comparable in terms of SBP till 120 min



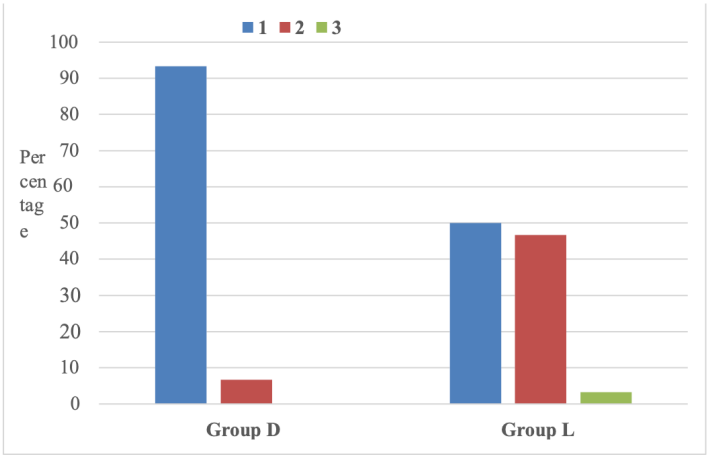
DBP was comparable in both the groups at baseline and after intubation till 90mins which was statistically not significant. Statistically significant difference in DBP was found from 95mins till 120mins with lower values in group L than group D



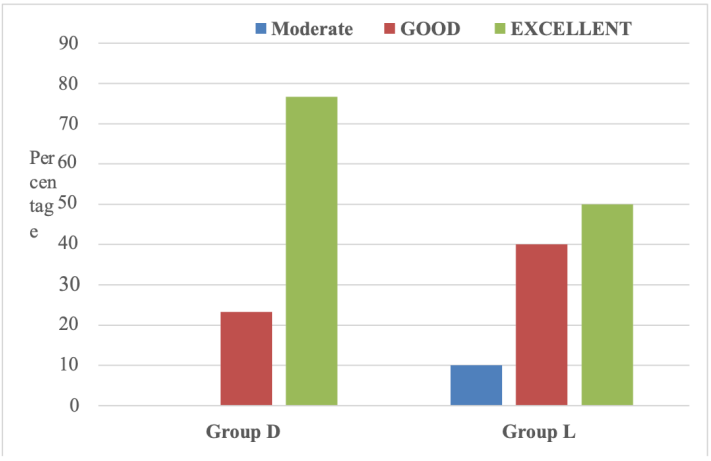
In our study, the target MAP was 70 to 75 mmHg. Both the groups were comparable with respect to MAP at baseline (97.2±8.0) in group D and (93.9±5.1) in group L and after administration of loading dose till 6mins. Statistically significant difference in MAP was found Post intubation from 8thmin till 35mins with lower values in Group D as compared to Group L ($p < 0.005$). Target MAP was achieved early in Group D compared to Group L [25th min vs 45th min] post intubation.Thereafterboth groups were comparable in terms of MAP till 85thmin



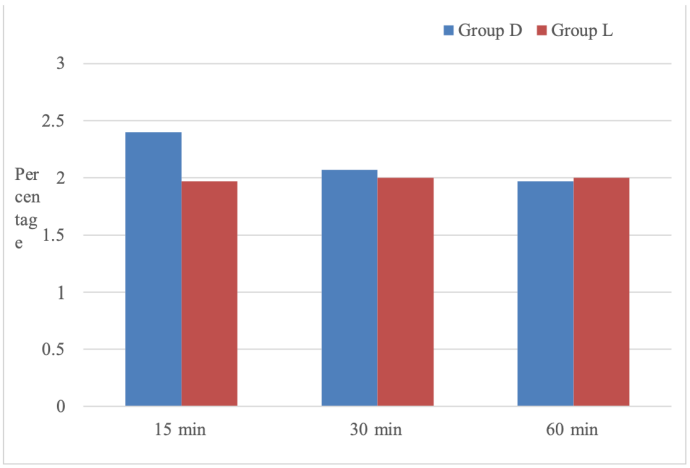
The surgical field assessment during FESS was done by the operating surgeon using Fromme's scale 10 minutes after stable targeted MAP range was reached. Both the study drugs, labetalol and dexmedetomidine were able to provide adequate surgical field Graph showing Distribution of subjects according to FROMME'S SCALE between two groups



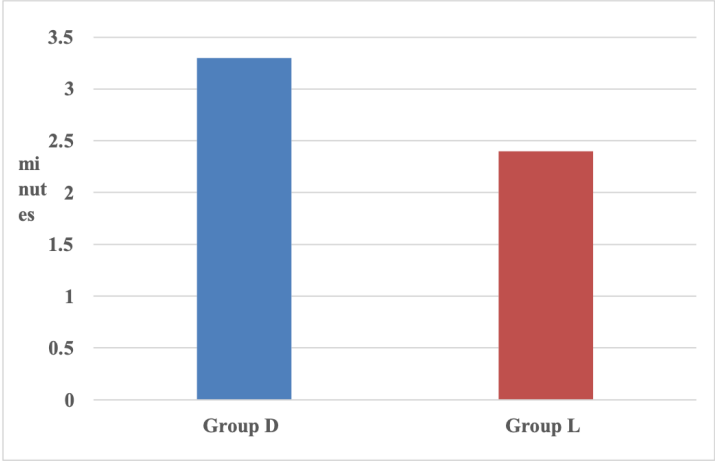
The operating surgeon scored the conditions for surgery on a four point surgeon satisfaction score and both groups had high scores. Surgeon satisfaction score was better with Group D compared to Group L
Graph showing Distribution of subjects according to surgeon satisfaction Score between two groups



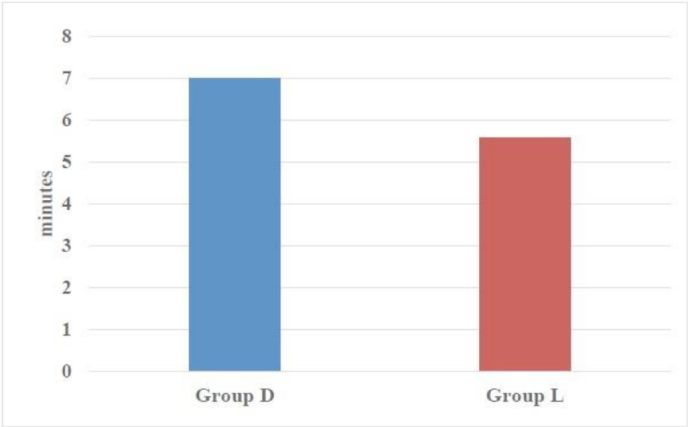
The postoperative sedation was assessed using RSS scores at 15, 30, 60 minutes post extubation. At 15 minutes more patients in Group D had higher sedation scores than in Group L, which was statistically significant with p value <0.001. At 30min and 60 min there was no statistically significant difference found between two groups.
Graph showing Comparison of mean sedation score at various time interval between two groups.



The awakening time and extubation time were comparable in both groups Graph showing Comparison of mean awakening time in minutes between two groups



Though there was a statistical significant difference in the mean awakening time with Group L patients awakening earlier than group D (12.40±0.724 vs 3.30±0.65s) with p-value 0.001, it was not clinically significant. The time to complete recovery after anaesthesia in the present study was significantly faster in patients in Group L than GroupD. Comparison of mean time to recovery between two groups



No side effects attributable to the study drugs were observed during the present study.

Discussion

Functional endoscopic sinus surgery (FESS) is a common surgical procedure for patients with medically refractory chronic rhinosinusitis. Good surgical field visibility can be achieved with controlled hypotension during surgery.

Dexmedetomidine, is a selective, short-acting, central α2-adrenergic agonist causes dose- dependent decrease in arterial blood pressure, heart rate (HR), cardiac output, and norepinephrine release[5]

Labetalol is a unique parenteral anti-hypertensive drug that has selective α1 and non-selective β1 and β2 adrenergic antagonist effects. It can reduce blood pressure by declining systemic vascular resistance (α1 blockade), whereas reflex tachycardia triggered by vasodilation is attenuated by simultaneous β blocking[4] effects.

Hence the present study was undertaken to compare the efficacy of Dexmedetomidine and labetalol having different mechanisms of action at different receptors levels in producing controlled hypotension during FESS and also to compare them in terms of recovery profile.

There was no significant difference in demographic parameters between the groups in our study which was similar to most of the studies mentioned in the literature. In the present study both alpha 2 agonist Dexmedetomidine and beta antagonist labetalol were given as a loading dose after induction followed by a titrated infusion. We were able to achieve targeted induced reduction of blood pressure during general anaesthesia. The SBP,DBP and MAP values at various time intervals during the administration of drugs and at regular intervals during the next 120 minutes showed that it was possible to achieve the target blood pressure levels (MAP=70- 75mmHg) with their use and this could be maintained at the same levels during the procedure by titration of the infusion. There was no incidence of resistant hypertension requiring other antihypertensive agents.

Also, no patient in both the study drug groups developed hypotension requiring slowing or stopping of infusion or administration of vasopressors.

In the present study mean baseline HR were comparable in both the groups (98.73±13 and 96.57 ± 11). Draping of the surgical site, nasal packing with vasoconstrictor and the surgical incision occurred within 15 min post intubation. Rise in HR which should be the response with lower concentration of inhalational agents (0.4% Isoflurane) or lighter plane of anaesthesia was not found in both the groups. This shows that with maintenance infusion of study drugs, adequate depth was maintained which abolished the tachycardia response. Heart rate started to fall in both group D and group L after starting the loading dose till 60th min but it was statistically not significant.

However, from 80th min we observed statistically significant reduction in heartrate with group L compared to group D till end of surgery. However, no patients required any pharmacological intervention (atropine). These findings were similar to findings by Sujay et al[8] who also reported no intergroup difference in HR between the 2 groups (Group D 70.8± 4.2 vs Group L-73.4 ±4.4 min).C N Navya et al[9] reported statistically significant decrease in heart rate in group D than group L, immediately after administration of study drugs till 10 mins of intubation and also heart rate were comparable between both groups from 15 min postintubation till end of surgery.

Both the groups in the present study were comparable with respect to MAP at baseline (97.2±8.0vs 93.9±5.1)in group D and group L respectively and after administration of loading dose till 6mins. Statistically significant difference was found post intubation from 8thmin till 35mins with lower value in Group D as compared to Group L ($p < 0.005$). This may be attributed to sympatholytic effect of $\alpha 2$ agonist Dexmedetomidine. Target MAP (70-75 mmHg) was achieved earlier in Group D than in Group L (25 min vs 45 min). Thereafter both groups were comparable in terms of MAP till 85 mins. Similar results were obtained by Sujay J N et al [8] where the target MAP (65-75mmHg) was achieved early in the Dexmedetomidine group at the 20th min post intubation. In C N Navya et al[9] study there was statistically significant early decrease in MAP in group D than group L immediately after administration of study drugs till 10 min of intubation ($p<0.000$). MAP were comparable between both groups from 15min post intubation till end of surgery. In both these studies MAP was achieved earlier compared to our study, this could be because the loading dose of the study drugs was started 10 mins before induction. and the maintenance dose of study drugs as increments of 1/4th of loading dose over 2 mins. However the findings of Aliakbar Eghbal et al[10] study showed trend of MAP in group L was significantly lower compared to group D and also in Ali Alizadeh et al[11] study, MAP was significantly higher in group D than group L which is at variance from our findings.

Barak et al[3] in a review of literature about hypotensive anaesthesia during major maxillofacial surgery in 2015 concluded that intra operative MAP of 50-65mmHg may have the risk of tissue hypo perfusion. Boezaart et al[12]demonstrated that the optimal surgical conditions for FESS were obtained with minimal induced hypotension (MAP≥65mmHg). Taking this into consideration and since we are using noninvasive blood pressure monitoring, in the present study, the target MAP for controlled hypotension for FESS was set at 70-75mmHg to avoid lowering of MAP below lower limit of auto regulation of blood flow to vital organs and to prevent deleterious effects of controlled hypotension on them. The monitored ETCO2 levels in subjects in both the groups in thepresent study during the intraoperative period were comparable and there was no statistical significant difference between the two groups. This normocarbia suggests intact tissue perfusion during periods of mild controlled hypotension is consistent with the findings of Guney A et al[13].

During the study period in both the groups, all patients participating in the study were able to maintain oxygen saturation at 98-100%. No desaturation was observed in these patients during the recovery time and in the postoperative period. These findings are consistent with the results obtained by studies of Shams T et al[14], Nazir O et al[15], Bajwa SJ et al[16].

The surgical field assessment was done by the operating surgeon using the Fromme's scale, both the study drugs were able to provide adequate surgical field in the present study similar to findings by C N Navya et al[9]and Sujay J N et al[8] where Dexmedetomidine provided better hemodynamic stability and operative field visibility as compared to labetalol during FESS. In the present study, both the groups had high scores on the four point surgeon satisfaction score by the surgeons, though better with Group D. This may be because of the superior surgical site visibility as suggested by Fromme's scale assessment and less bleeding. Similar findings were reported by C N Navyaet al[9] and Rokhtabnak F et al[17] where surgeon satisfaction score was better with DEX group than with magnesium sulfate group.

Post operative sedation was more at 15 minutes in Group D than in Group L(p value <0.001) but after 30min there was no statistically significant difference found between two groups similar to reports by Shams T etal[14], and Valecha DS et al]18] Kol IO et al[19]. This confirms the sedative effects of Dexmedetomidine. Bajwa SJ et al[16]observed that 72%

of patients given Dexmedetomidine had sedation scores 3 and above while only 20% of patients given Esmolol had such higher sedation score which is similar to the present study.

The mean awakening time was earlier in Group L compared to group D (2.40±0.724 vs 3.30±0.651) and was statistically significant with p-value 0.001 but clinically not significant. The time to complete recovery after anaesthesia in the present study was faster in patients in Group L than group D. Similarly rapid recovery with labetalol compared to Dexmedetomidine is reportedby Aliakbar Eghbal et al[10] study. The extubation time was comparable in both the groups. No side effects attributable to the study drugs were observed during the present study. There was no postoperative tachycardia or rebound hypertension in any patients in both the groups.

Limitations of the Study

1. This was not a placebo controlled study as no control group was used.
2. Only noninvasive monitoring was done in the intraoperative period. Use of IABP monitoring might have allowed for a finer titration of the study drugs but was not used due to cost limitation in the government hospital setup.
3. The effect of study drug on intraoperative anaesthetic and analgesic requirements and on postoperative analgesia were not included in our study design. BIS monitoring could not be done in the present study.
4. The possible effects of hypotension on organ functions were not investigated in the postoperative period in the present study.
5. Dexmedetomidine and Labetalol were compared based on their known optimal as well as safe premedicating doses. Their equipotent doses have not been established.
6. The desired MAP could not be achieved early. Probably the target MAP could have beenattained earlier if the loading dose of the study drugs had been given before induction of anesthesia.

A larger study with different dosages, invasive monitoring and postoperative investigations may be needed to obtain equipotent doses of the drugs and to extrapolate our results to different set of patient population.

Conclusion:

The present study evaluated the efficacy of Dexmedetomidine and Labetalol in providing controlled hypotension in FESS surgeries. Both Dexmedetomidine and Labetalol can be safely used in doses mentioned in the study protocol to achieve target MAP of 70 to 75 mmHg. Target MAP was achieved earlier, the quality of surgical field and the surgeon satisfaction score was better in Dexmedetomidine group. Labetalol patients demonstrated early recovery time.

Bibliography

1. Re M, Massegur H, Magliulo G, Ferrante L,Sciarretta V, Farneti G, et al.Traditional endonasal and microscopic sinus surgery complications versus endoscopic sinus surgery complications: a meta-analysis.Eur Arch Otorhinolaryngol 2012; 269: 721-9.
2. Papalia R, Simone G, Ferriero M, Costantini M, Guaglianone S, Forastiere E, Gallucci M. Laparoscopic and robotic partial nephrectomy with controlled hypotensive anesthesia to avoid hilar clamping: feasibility, safety and perioperative functional outcomes. J Urol. 2012 Apr;187 (4):1190-4. doi: 10.1016/j.juro.2011.11.100. Epub 2012 Feb 14. PMID:22335869.
3. Barak M, Yoav L, Abu el-Naaj I. Hypotensive anesthesia versus normotensive anesthesia during major maxillofacial surgery: a review of the literature. Scientific World Journal. 2015; 480728. Doi:10.1155/2015/480728.
4. DegouteCS. Controlled hypotension: A guide to drug choice. Drugs 2007;67:1053- 76.
5. R.H. Jamaliya, R. Chinnachamy, J. Maliwad, V.P. Deshmukh, B.J. Shah, I.A. Chadha. The efficacy and hemodynamic response to Dexmedetomidine as a hypotensive agent in posterior fixation surgery following traumatic spine injury J Anaesthesiol Clin Pharmacol, 30 (2) (2014), pp.203-207.
6. K.S. Vora, U. Baranda, V.R. Shah, M. Modi, G.P. Parikh, B.P. Butala The effects of dexmedetomidine on attenuation of hemodynamic changes and there effects as adjuvant in anesthesia during laparoscopic surgeries Saudi J Anaesth, 9 (4) (2015), pp.386-392
7. M.D. Karol, M. Maze Pharmacokinetics and interaction pharmacodynamics of dexmedetomidine in humans Best Pract Res Clin Anaes, 14 (2000), pp. 261- 269.
8. Sujay J N, Kumar S, Vijay T. To Compare the Efficacy of Dexmedetomidine Versus Labetalol in Providing Controlled Hypotension in Functional Endoscopic Sinus Surgery. Anesth Pain Med. 2021;11(1):e108915. doi: 10.5812/ aapm. 108915.
9. C.N. Navya, Ranganathan, Sambandan, Dexmedetomidine over Labetalol for oligemic surgical field in middle ear microsurgeries- A prospective randomized clinical trial. Medica Innovetica J Jan - Jun 2018, Volume 7 - Issue 1,Pages 26-31.
10. Eghbal A, Modir H, Moshiri E, Khalili M, Barsari FZ, MohammadbeigiA. Hypotensive effect of labetalol and dexmedetomidine blood loss and surgical conditions in functional endoscopic sinus surgery: A double-blind randomized clinical trial. Formos J Surg2018;51:98-104.
11. Özcan AA, Özyur Y, Saraçoğlu A, Erka Hl, Süslü H, Arslan G, Temizel F

Dexomeditomidine versus Remifentanil for Controlled Hypotensive Anaesthesia in Functional Endoscopic Sinus Surgery, Turk J AnesthReanim 2012; 40(5): 257-61.
12. Boezaart AP, van der Merwe J, Coetzee A. Comparison of sodium nitroprusside-and esmolol-induced controlled hypotension for functional endoscopic sinus surgery. Canadian journal of anaesthesia. 1995 May 1;42(5):373-6
13. Guney A, Kaya FN, Yavascaoglu B, Gurbet A, Selmi NH, Kaya S, Kutlay O, Comparison of Esmolol to Nitroglycerine in Controlling Hypotension During Nasal Surgery EAJM 2012; 44: 99-105
14. Shams T, El Bahnasawe NS, Abu-Samra M, El-Masry R. Induced hypotension forfunctional endoscopic sinus surgery. A comparative study of Dexmedetomidine versus Esmolol. Saudi J Anaesth2013;7:175-80.
15. Nazir O, Wani MA, Ali N, Sharma T, Khatuja A, Misra R, and Maqsood M Use of Dexomeditomedine and Esmolol for Hypotension in Lumbar Spine Surgery, Trauma Mon. 2016; July;21(3):e22078.
16. Bajwa SJ, Kaur J, Kulshrestha A, Haldar R, Sethi R, Singh A. Nitroglycerine, esmolol and dexmedetomidine for induced hypotension during functional endoscopicsinus surgery: A comparative evaluation. J Anaesthesiol Clin Pharmacol. 2016 Apr- Jun;32(2):192-7. doi: 10.4103/0970-9185.173325. PMID: 27275048; PMCID: PMC4874073.
17. RokhtabnakF,Djalal-iMotlaghS,GhodratyM,etal.ControlledHypotensionDuring Rhinoplasty: A Comparison of Dexmedetomidine with Magnesium Sulfate. Anesth Pain Med. 2017;7(6):e64032. Published 2017 Dec 26. doi:10.5812/aapm.64032.
18. Valecha DS, Gandhi M, Arora KK. Comparison of dexmedetomidine and esmolol for induction of controlled hypotension in spine surgeries. J Evolution Med. Dent. Sci. 2016;5(35):2030-2035, DOI: 10.14260/jemds/2016/477.
19. Kol IO, Kaygusuz K, Yildirim A, Dogan M, Gursoy S, Yucel E, MimarogluC. Controlled hypotension with desflurane combined with esmolol or dexmedetomidine during tympanoplasty in adults: A double-blind, randomized, controlled trial. CurrTher Res Clin Exp. 2009 Jun;70(3):197-208. doi: 10.1016/j.curtheres.2009.06.001. PMID: 24683230; PMCID: PMC3967361.