BMC Anesthesiology

RESEARCH Open Access

Clonidine and dexmedetomidine for controlled hypotension during functional endoscopic sinus surgery: a comparative study

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Abstract

Background Functional endoscopic sinus surgery (FESS) is minimally invasive, ambulatory endoscopic surgical procedure usually performed in most paranasal sinus diseases. Controlled hypotension during anaesthesia (hypotensive anesthesia) improves surgical field visibility and reduces risk of injuring surrounding structures. Clonidine (C) and dexmedetomidine (D) are both used to reduce blood pressure and heart rate while maintaining tissue perfusion. This study was conducted to evaluate the efficacy of clonidine compared to dexmedetomidine for controlled hypotension during FESS.

Methods After ethical approval, 80 patients undergoing elective FESS were included in the study and randomly allocated to Group C or Group D. In Group C, 40 patients received intravenous clonidine with a loading dose of 3µg/Kg for 10 min and titrated maintenance dose of 0.4–0.8 µg/Kg/hour. In Group D patients received intravenous dexmedetomidine with a loading dose of 1µg/Kg for 10 min and titrated maintenance dose of 0.4–0.8µg/Kg/hour. The target was mean arterial blood pressure (MAP) between 55 and 65 mmHg and heart rate (HR) above 50 beats per minute. The primary outcome was blood loss. The secondary outcomes were surgical field quality assessed by Fromme Bezooart score, variations in MAP and HR intraoperatively, duration of surgery and anesthesia, and post-operative sedation assessed by Ramsay Sedation Score (RSS).

Results Demographic data of both groups were comparable. The difference between both groups in terms of blood loss and surgical field quality was not statistically significant ($p=0.579$, 1.000). MAP and HR were statistically significantly reduced to targeted level in both groups compared to baseline ($p<0.001$). Dexmedetomidine led to severe hypotension compared to clonidine, and the difference was statistically significant. Duration of return to baseline MAP and HR, duration of anesthesia and postoperative sedation were prolonged in group D compared to Group C.

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Conclusion Clonidine and dexmedetomidine provided good to excellent quality of surgical field visibility to surgeons during FESS. Dexmedetomidine produce more hypotension and bradycardia compared to clonidine which may be preferable for controlled hypotension in the setting of ambulatory surgery. However, considering the small sample of this study which could not detect small but clinically differences between both drugs, there is a need for a much larger and multicenter study to confirm these findings.

Trial registration This trial was retrospectively registered in the Pan African Clinical Registry (pactr.samrc, ac.za) on 15 August 2024 under trial number PACTR202408565688611.

Keywords Clonidine, Dexmedetomidine, Controlled hypotension, FESS, Egypt

Background

Nasal cavity and paranasal sinus diseases are mainly surgically treated by functional endoscopic sinus surgery (FESS) which is usually done as an ambulatory surgery [1]. FESS is a minimally invasive procedure, fast and safe which involves the use of fiberoptic technology to visualize on videoscope the nasal cavity and sinuses while doing surgical intervention through natural way to these cavities and without skin incision [1, 2].

Anatomically paranasal sinuses are in boundary with important anatomic structures (brain, eye, carotid artery, nerves) and there is high risk of injuring these structures during FESS if there is major bleeding obscuring the surgical field visibility [2, 3].

The outcome of FESS strongly depends on surgical blood loss and field quality. It is important to keep visible the surgical field during FESS. Controlled hypotension during anesthesia, a reduction of the mean arterial pression (MAP) to 50–65 mmHg or a 30% reduction of baseline MAP, is recommended to provide a better surgical field quality and minimize blood loss. Improved surgical field visibility decreases duration of surgery, and complications [4–6].

Controlled hypotension involves the use of non-pharmacological anesthetic techniques and adjuvant drugs to reduce MAP and HR to decrease surgical field perfusion without causing vital tissue ischemia [2, 7, 8]. Several drugs have been used as adjuvant in hypotensive anesthesia. The most effective are those which reduce MAP and heart rate (HR) while maintaining tissue perfusion [2, 8].

Alpha-2 adrenergic agonists, a class of drugs that selectively stimulates the alpha-adrenergic receptors α1 and α2, are preferred as adjuvant to total intravenous anesthesia for controlled hypotension in modern anesthesia. Their pharmacological action is mainly centrally mediated. They decrease MAP and HR and moreover they have anxiolytic, sedative and analgesic effects which decrease requirement in hypnotic, opioid and Minimal Alveolar Concentration (MAC) of inhalant anesthetic gases [8, 9]. Clonidine and recently dexmedetomidine are the two available alpha-2 adrenergic agonists used in modern hypotensive anesthesia [9, 10].

Two meta-analysis evaluated randomized clinical trials that compared Alpha-2 adrenergic agonists (clonidine or dexmedetomidine) to placebo or other drugs (propofol, remifentanil, isoflurane, propranolol, esmolol, labetalol, nitroglycerine, magnesium sulfate, midazolam), and both consistently reported superiority of alpha 2 adrenergic agonists to reduce blood loss and improve surgical field quality during endoscopic sinus surgery [6, 10]. Pharmacodynamically, dexmedetomidine is 8 times more selective on alpha 2 adrenergic receptors comparing to clonidine [10].

There is no metanalysis comparing only clonidine to dexmedetomidine regarding their efficacy and safety for controlled hypotension in FESS. There is little evidence on superiority (efficacy and safety) of dexmedetomidine compared to clonidine in terms of decreasing blood loss, surgical field quality and recovery profile during controlled hypotension in the setting of ambulatory surgery [6, 8]. The aim of this study was to evaluate the efficacy and safety of clonidine compared to dexmedetomidine for controlled hypotension during FESS.

Methods

Study design and period

This study was a prospective, randomized and comparative study. It was approved by the Ethical Committee of Faculty of Medicine at Alexandria University (serial number: 0106833, approval dated July, 15, 2021). The study was conducted in the theater suite of the Oto-Rhino-Laryngology (ORL) department at the Main University Hospital of Alexandria University from 16 June 2021 to 16 November 2021.

The sample size was calculated using G-Power software and was based on a previous study, in which mean (SD) of blood loss in clonidine group was 168.82±11.23 mL and in dexmedetomidine 160.15±12.23 mL [7]. Using alpha error of 0.05 and power of 90%, the minimum sample size required was 80 patients, 40 for each group. Patients undergoing elective FESS were randomly included in the study.

Variables included demographic and general data: age in year, weight in kilograms (Kg), Body Mass Index (BMI) in Kg m^{-2} and the duration of surgery in minutes.

In addition to these variables, preoperative evaluation included detailed medical and surgical history, clinical examination, routine laboratory investigations (complete blood count, coagulation profile, blood urea and serum creatinine, liver enzymes), electrocardiogram in patient more than 40 years old or if indicated was done.

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Patients aged between 20 and 50 years, American Society of Anesthesiologists Physical Status (ASA-PS) I-II, undergoing elective FESS were included in the study after obtaining an informed consent. Patients with a known allergy to clonidine or dexmedetomidine, systemic hypertension, anemia with hemoglobin concentration less than 10 gram per deciliter, patients with cardiac disease and arrhythmias, Diabetes Mellitus, medical history of stroke, chronic kidney disease, liver diseases and coagulopathies or receiving drugs influencing blood coagulation and obesity were excluded from the study.

The CONSORT flow diagram of the study is presented in Fig. 1. Patients were allocated randomly into two groups of 40 patients each using a closed envelop method:

- Group C: 40 patients received clonidine.
- Group D: 40 patients received dexmedetomidine.

After anesthetic equipment check, preparation of anesthetic drugs and alpha-2 adrenergic agonist (dexmedetomidine 4 µg per mL or clonidine 3 µg per mL) intravenous infusion in an electric pump syringe driver, the patient entered in the operating room.

Patients were connected to multiparameter monitor (Drager vista 120 Dragerwerk AG and Co. KGaA,

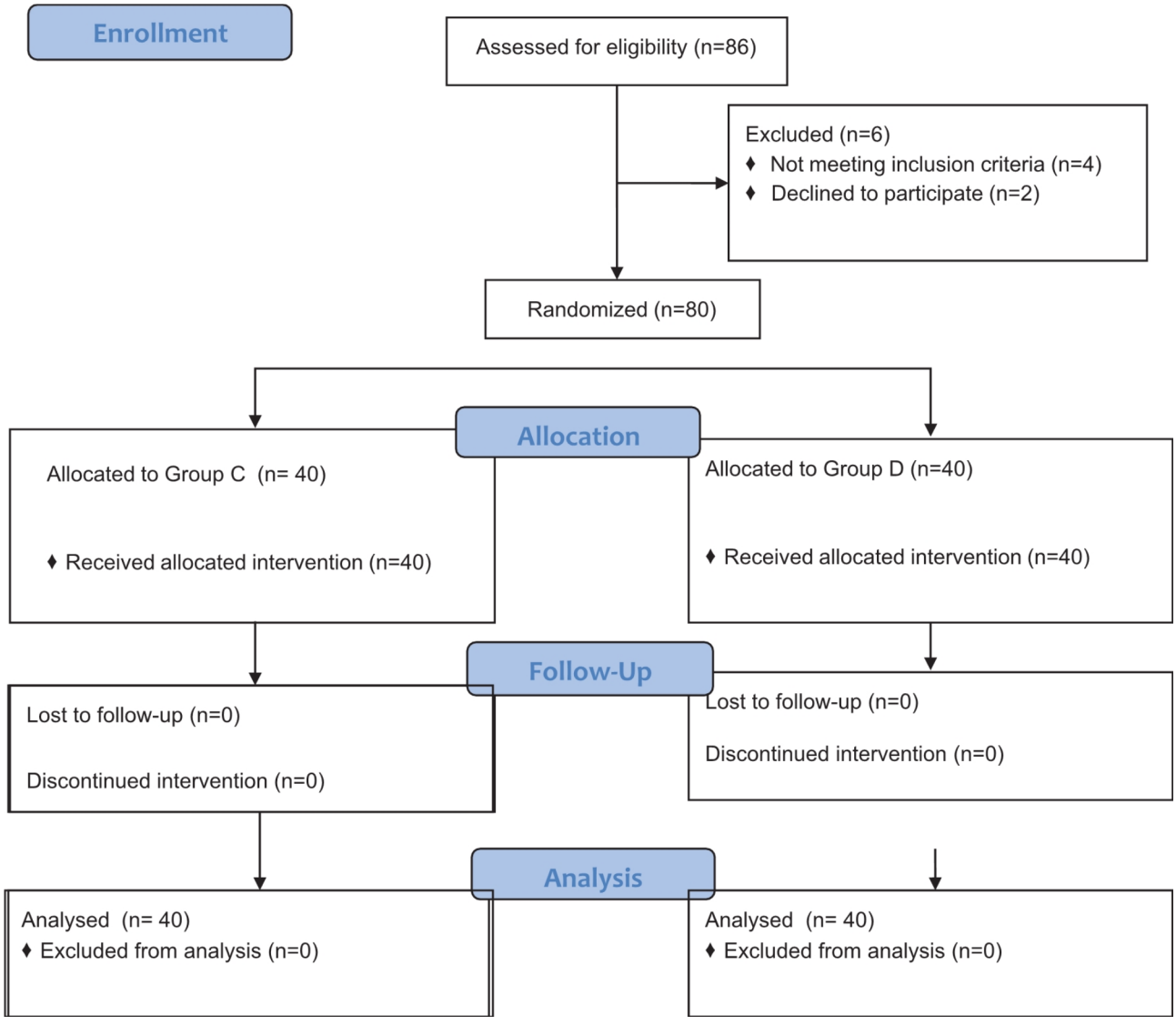

Fig. 1 CONSORT 2010 flow diagram of the study

Germany) displaying Heart Rate (beat per minute), non-invasive mean arterial blood pressure (mmHg), continuous electrocardiography monitoring (lead II and V), Oxygen Saturation (%), and End Tidal Carbon Dioxide (mmHg).

In the operating room, two large bore cannula (18 Gauge) were inserted, one for infusion of dexmedetomidine or clonidine and the other for administration of intravenous fluids and other drugs.

Patients were preloaded with Ringer's Lactate 10ml/kg, antibiotic prophylaxis (ceftriaxone 1g intravenous) and anti-emetic prophylaxis (dexamethasone 0.1mg/kg after induction of anesthesia and ondansetron 0.1mg/kg 30 min before end of surgery) were given.

Interventions

In Group C, patients received 3μg/Kg of clonidine hydrochloride (catapressan) diluted in 10ml 0.9% Normal Saline infused intravenously over 10 min before induction of anesthesia followed by continuous infusion, starting at 0.4μg/Kg/hr and could be titrated up to 0.8μg/Kg/hr in order to maintain the targeted mean arterial blood pressure and heart rate (Concentration of 3mcg per ml in a volume of 50ml of 0.9% Normal Saline) [7].

In Group D, patients received loading dose of 1μg/Kg of dexmedetomidine (precedex) diluted in 10ml 0.9% Normal Saline infused over 10 min before induction of anesthesia, followed by continuous infusion, starting at 0.4μg/Kg/hr and could be titrated up to 0.8μg/Kg/hr to maintain the targeted mean arterial blood pressure and heart rate (Concentration of 4mcg per ml in a volume of 50ml of 0.9% Normal Saline) [7]. In both groups the infusion was stopped at the end of surgery.

Anesthetic management in both groups

In both groups, no premedication was given, after preoxygenation with 100% oxygen for 3 min, anesthesia was induced with fentanyl (2μg/Kg), propofol (2mg/Kg) in titrated doses up to the loss of verbal response, followed by atracurium 0.5mg/Kg to facilitate endotracheal intubation and mechanical ventilation.

Anesthesia was maintained with oxygen (O_2) (2L per minute), air (2L per minute), isoflurane (targeting expired Minimum Alveolar Concentration of 1.2), atracurium (0,1mg per Kg) each 30 min and fentanyl (25μg) as required. Multimodal analgesia using IV paracetamol 1000mg and ketorolac 30mg IV was given in both groups.

The oropharynx was packed with a saline soaked throat pack. Application of topical vasoconstrictor (adrenaline 1: 200 000) with local anesthetic (lidocaine 1%) was done prior to starting the procedure. All patients were positioned in a 15° reverse Trendelenburg position to improve the venous drainage.

Table 1 Fromme-Boezaart scale

Grade	Definition
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 threatened surgical field a few
4	Seconds after suction was removed.
5	Moderate bleeding: frequent suctioning required; bleeding threatened surgical field Directly after suction was removed.
6	Severe bleeding: constant suctioning required, bleeding appeared faster than could be removed by suction, surgical field severely threatened and surgery not possible.

Table 2 The surgeon satisfaction grading

Grade	Fromme-Boezaart scale	Definition of the field quality
A	0–1	Excellent surgical field quality
B	2–3	Good surgical field quality
C	4–5	Poor surgical field quality

Heart rate was reported at different time interval targeting a HR >50 beats/min. If there was sinus bradycardia of <50 beats/min, atropine 0,5mg was given intravenously.

Mean arterial blood pressure was also reported at different time intervals targeting a MAP between 55 and 65 mmHg in both groups. If MAP was <55 mmHg, the inspired isoflurane concentration was reduced by 0.5% and an intravenous bolus of Ringer's Lactate (250mls) was given. If hypotension persisted, ephedrine 3 mg in incremental dosage was administered.

At the end of the procedure, the anesthetic agent (isoflurane) was discontinued, neuromuscular blockade (atracurium) was reversed with intravenous injection of Neostigmine 0.04mg/kg with Atropine 0.01mg/kg and throat pack was removed. Patients were extubated when awake and monitored in recovery room.

Measurements of outcomes

The primary outcome was blood loss, the secondary outcomes were surgical field quality assessed by Fromme Bezooart score, hemodynamic variations (HR and MAP), recovery profile (from anesthesia, hypotension and post operative sedation assessed by Ramsay Sedation Score).

Regarding primary outcomes, blood loss was estimated by measuring the volume in the suction bottle and subtracting the amount of saline flush used during the procedure.

Regarding secondary outcomes, the main surgeon on each procedure, graded the surgical field at the end of the procedure using Fromme–Boezaart scale (Table 1). The surgeon's satisfaction was derived and graded from the Fromme-Boezaart ranking (Table 2) [11, 12]. Clear

surgery field with no suctioning required was defined as "bloodless" field.

Mean arterial blood pressure was measured non-invasively by oscillometric occlusive cuff technique and was reported preoperatively, before and after the α-2-adrenergic agonist loading dose, before and after laryngoscopy and intubation, at time of incision, 5 min after incision and at 15, 30, 45, 60, 75, 90,105,120 min and at the end of surgery.

Heart Rate was measured from a continuous electrocardiography and pulse rate. It was reported preoperatively, before and after the α-2-adrenergic agonists loading dose, before and after laryngoscopy and intubation, at time of incision, 5 min after incision, and 15, 30, 45, 60, 75, 90,105,120 min and at the end of surgery.

Time taken from the end of the α-2-adrenergic agonist's infusion to the moment the patient reaches ± 20% of the preoperative MAP. Postoperative sedation was assessed in Recovery Room with Ramsay Sedation Score (Table 3) at 10,20,30,45 and 60 min after awake extubation [7].

Table 3 Ramsay Sedation score (RSS)

Score	Response
1	Anxious or restless or both
2	Cooperative, orientated and tranquil
3	Responding to command
4	Brisk response to stimulus
5	Sluggish response to stimulus
6	No response

Statistical analysis

Data were encoded into Excel sheet to the computer and analyzed with IBM SPSS software package. (Armonk, NY: IBM Corp). Qualitative data were described using absolute frequencies and percentage. The Shapiro-Wilk test was used to verify the normality of distribution. Normally distributed quantitative data were compared using the analysis of variance (ANOVA) with repeated measures to compare between more than two periods or stages with a post hoc test using Bonferroni correction for multiple pairwise comparisons to avoid type I errors [13], and /or with a general linear regression model with repeated measures as needed. Means were given with their standard deviation and 95% confidence interval (CI). The two-sided *p*-value (p) was calculated at the level of significance of 5%.

Chi-square test was used for categorical variables, to compare between the two groups. Fisher's Exact correction was used for correction of chi-square when more than 20% of the cells have expected count less than 5. The student t-test was used for normally distributed quantitative variables, to compare between two studied groups.

Results

The demographic data of the two groups (C and D) were comparable, with no significant difference (Table 4).

Hemodynamic changes in mean arteria blood pressure

Comparing both groups (Fig. 2), mean (± SD) of baseline MAP were comparable with 87.03±3.63 mmHg (95% CI 85.86–88.19) in group C and 87.08±4.98 (95% CI 85.48–88.67) in group D, t(*p*) = 0.051(0.959). The variations of MAP throughout the intraoperative period were not statistically different in both groups ($p = 0.119$). The mean intraoperative MAP was 66.44 mmHg with Standard Error (SE) of 0.65 (95% CI 65.13–67.83) mmHg in Group

Table 4 Comparison between the two groups according to demographic data (age, sex, weight, BMI, ASA)

General characteristics	Group C (*n* = 40) [*n* (%)]	Group D (*n* = 40) [*n* (%)]	Test	*p*-value
Age (in years)				
Min	19	22	t = 0.830	0.409
Max	48	46		
Mean ± SD	33.90 ± 6.85	35.15 ± 6.62		
BMI (kg/m^2)				
Min	22.31	22.84	t = 0.117	0.907
Max	28.41	28.73		
Mean ± SD	25.75 ± 1.53	25.71 ± 1.28		
Sex				
Male	22 (55.0%)	20 (50.0%)	$\chi^2 = 0.201$	0.654
Female	18 (45.0%)	20 (50.0%)		
ASA Classification				
ASA I	27 (67.5%)	28 (70.0%)	$\chi^2 = 0.058$	0.809
ASA II	13 (32.5%)	12 (30.0%)		
Duration of surgery (minutes)				
Min	60	55	t = 1.593	
Max	150	135		0.115
Mean ± SD	103.50(22.45)	95.83(20.59)		

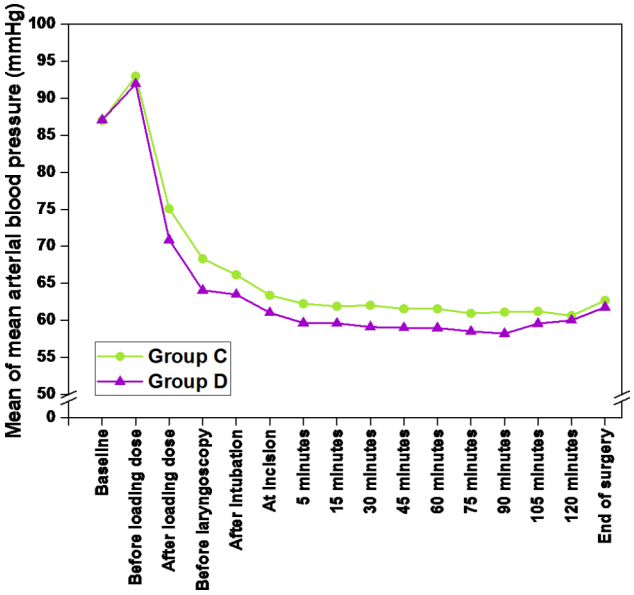

Fig. 2 Comparison of mean arterial pressure variation between group C and group D

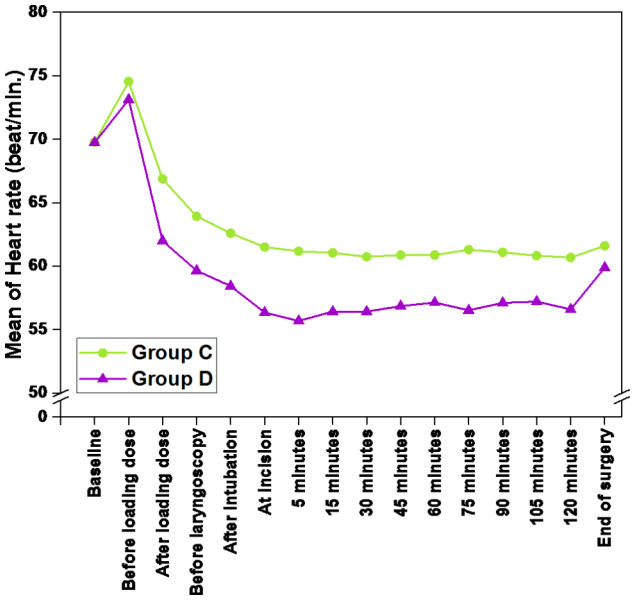

Fig. 3 Comparison of heart rate variations between group C and group D

C and 64.75 with SE 0.84 (95% CI 63.01–66.50) mmHg in Group D. MAP stayed significantly reduced with stimulations such as laryngoscopy($p<0.001$), intubation ($p<0.001$) or first incision ($p<0.001$) and remained reduced throughout the procedure.

Changes in heart rate (HR)

Comparing both groups (Fig. 3) the mean of HR throughout the intraoperative period was 62.69 beats per minute with SE 0.61 (95% CI 61.43–63.95) in Group C while it was 59.88 beats per minute with SE 0.79 (95% CI 58.25–61.50) in Group D. Much lower means of HR were recorded in Group D compared to Group C. The difference was statistically significant, with successively $p$value≤ 0.001 throughout intraoperative time measurement at surgical incision, 5, 15, 30, 45, 60, 75, 90, 105 and 120 min. Simulations such as laryngoscopy ($p<0.001$), intubation ($p<0.001$) or first incision ($p<0.001$) did not increase the HR which remained reduced throughout the procedure ($p<0.001$).

Blood loss and surgical field quality

Blood loos in Group C ranged from 50 to 180ml with a mean (SD) of 133.50(36.48) ml (95% CI 121.83-145.17) while in Group D it ranged from 50 to 170 mL with a mean (SD) of 129.50(27.08) mL (95% CI 120.44-138.16). The mean of blood loss was lower in Group D compared to Group C but difference was not statistically significant, p-value was 0.579.

Surgical field quality as assessed by Fromme-Boezaart scale was comparable in both groups with predominance of class 2 with 67.5% in both groups. No surgery was classified into classes 0, 4 or 5 (Table 5). Computing the satisfaction score, surgeon satisfaction was rated good (classes 2–3) in 82.5% and excellent (Class 1) in 17.5% in both groups.

Recovery

Time taken for MAP to reach±20% range of the baseline values after stopping the alpha-2 adrenergic agonist and isoflurane, was different between the group C and D. In the group C, hemodynamic recovery time ranged from 9 to 28 min with a mean (SD) of 16.35(4.36) minutes while in group D it ranged from 10 to 35 min with

Table 5 Comparison between the two studied groups according to surgical field quality assessed by Fromme- Boezaart Scale

Fromme- Boezaart Scale for Surgical field quality	Group C $n=40$ (%)	Group D $n=40$ (%)	$\chi^2(p)$
0- No bleeding	0 (0%)	0 (0%)	0.0 (1.000)
1- Slight bleeding, No suctioning required	7 (17.5%)	7 (17.5%)	
2- Slight bleeding, occasional suctioning	27 (67.5%)	27 (67.5%)	
3- Slight bleeding, frequent suctioning	6 (15.0%)	6 (15.0%)	
4- Moderate bleeding	0 (0%)	0 (0%)	
5- Severe bleeding	0 (0%)	0 (0%)	

a mean of 22.40(6.62) minutes. Lower hemodynamic recovery time was observed in group C comparing to group D and difference was statistically significant with t(p)=4.829 (p<0.001).

Time taken for the patient to regain consciousness after stopping the alpha-2 adrenergic agonist and isoflurane was different between the group C and D. In group C, it ranged from (14–30) minutes with a mean (SD) of 20.40(3.84) minutes and in group D it ranged from (15–35) minutes with a mean (SD) of 25.53(5.51) minutes. Lower recovery time was observed in group C comparing to group D and the difference was statistically significant with t(p)=4.823 (p<0.001).

Post-operative sedation was assessed at 10, 20, 30, 45 and 60 min after awake extubation using Ramsay Sedation Score. Regarding post-operative sedation, Group C had rapid recovery from anaesthesia as assessed by RSS compared to group D.

The difference was statistically significant at 10 min with χ^2 (p)=39.200 (p<0.001), 20 min χ^2 (p)=5(p<0.025), and at 30 min χ^2 (p)=7.813(p<0.005) (Table 6).

No major complications (sinus arrest, Heart block, anaphylaxis) were observed in both groups in the intraoperative or postoperative period.

In the intraoperative period, in group D, 2 (5%) patients developed severe bradycardia treated with atropine 0.5 mg and severe hypotension was recorded in 2 (5%) patients treated with ephedrine 3mg in incremented dose. No complication (severe bradycardia, severe hypotension or rebound hypertension) was recorded in group C. In the post-operative period we didn't record shivering, postoperative nausea and vomiting (PONV) or respiratory depression in both groups. Postoperative sedation was significantly prolonged in group D comparing to group C.

Discussion

This study was a randomized controlled trial comparing clonidine to dexmedetomidine for controlled hypotension during FESS. The study identified both drugs as potential agent for controlled hypotension during anaesthesia with some dissimilarities. Age, gender and duration of surgery were similar in both groups. Our results are similar to those observed by Escamilia et al. in Spain [3].

MAP in both groups were comparable from baseline to the end of the surgery. The targeted MAP (55–65 mmHg) was reached and maintained in both groups during surgery, without need of additional drug to decrease blood pressure. However, HR was lower in D compared to group C but not reaching severe bradycardia from baseline to the end of the surgery. Our results are similar to the results of Suggala et al. and Bafna et al. [7, 14].

In fact, Alpha-2 adrenergic agonist (clonidine or dexmedetomidine) induce decrease in HR and MAP secondary to inhibition of central sympathetic outflow by stimulation of alpha-2 adrenergic receptors which cause decrease in norepinephrine release. Dexmedetomidine has higher selectivity to alpha-2 receptors (α2:α1 ratio of 1620:1) comparing to clonidine (α2:α1 ratio of 200:1), consequently dexmedetomidine is eight time more potent than clonidine regarding their pharmacological action on alpha-2 adrenergic receptor [9, 14].

Laryngoscopy and tracheal intubation cause reflex sympathetic stimulation (hypertension and tachycardia) known as pressor response [15, 16]. In our study, both drugs provided acceptable conditions for laryngoscopy and intubation by blunting the pressor response. Contrary to our results, Hussain et al. comparing three groups receiving either clonidine 2μg/kg in 100mL normal saline over 10 min, or dexmedetomidine 1μg/kg in 100mL of normal saline over 10 min or normal saline 100mL of over 10 min (control group) for attenuation of the hemodynamic response to laryngoscopy and intubation, found that there was significant reduction in hemodynamic response in clonidine and dexmedetomidine group as compared to controls but attenuation of pressor response to laryngoscopy and intubation was acceptable with dexmedetomidine than with clonidine [15]. This difference may be explained by the use of different doses and absence of alpha-2 agonist infusion after loading dose in their studies.

Table 6 Comparison between the two studied groups according to post-operative sedation assessed by RSS

Score	Post-operative Ramsay Sedation Score									
	At 10 min		At 20 min		At 30 min		At 45 min		At 60 min	
	Gr. C	Gr. D	Gr. C	Gr. D	Gr. C	Gr. D	Gr. C	Gr. D	Gr. C	Gr. D
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
1	19 (47.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
2	12 (30)	4(10.0)	25(62.5)	15(37.5)	35(87.5)	24(60.0)	40(100.0)	37(92.5)	40(100.0)	39(97.5)
3	9 (22.5)	36(90.0)	15(37.5)	25(62.5)	5(12.5)	16(40.0)	0 (0)	3(7.5)	0 (0)	1 (2.5)
4	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
5	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
χ^2 (p)	39.200* (<0.001*)		5.0* (0.025*)		7.813* (0.005*)		3.117(0.241)		1.013(1.000)	

*: Statistically significant at $p \leq 0.05$

Throughout the operative time, the mean of MAP was maintained in the targeted range of 55–65 mmHg in both groups. Lower means of HR were observed in Group D, and the difference was statistically significant throughout the intraoperative period. In a randomized controlled trial to compare clonidine and dexmedetomidine using the same loading and infusion dose as in this study, Suggala et al. found that the targeted MAP (55–65 mmHg) was achieved in group C and D but there was not significant difference from incision up to 15 min. From 15 min up to 120 min, it was significantly lowered in group D comparing to group C with a p value < 0.005 [7].

Bafna et al. also compared clonidine (IV loading dose 2 μg/kg followed by 1μg/kg/h infusion) and dexmedetomidine (IV loading dose 1μg/kg followed by 1μg/kg/h infusion) in 70 adults patients undergoing elective FESS. In both groups targeted MAP (65–70 mmHg) was achieved, MAP and HR were statistically significantly reduced in dexmedetomidine group similar to our results [14].

Contrary to this present finding, Escamilia et al. conducted a randomized controlled trial to compare both drugs when used for hypotensive anesthesia during FESS, 47 patients received clonidine (1.5μg/Kg in 100mL normal saline infusion for 20 min before surgery) and 47 patients received dexmedetomidine (bolus of 1μg/Kg followed by maintenance dose of 0.2–1μg/Kg), they didn't find statistically significant difference regarding variations of MAP and HR when comparing both groups [3].

Gupta et al. conducted a randomized controlled study comparing oral clonidine (300μg) and oral dexmedetomidine (50μg) administered 2 h before surgery for hypotensive anesthesia in 50 patients undergoing elective FESS [16]. They found that the targeted MAP (55–65 mmHg) was achieved in both groups, and it was significantly reduced in dexmedetomidine group only at 15- and 30-minutes interval, then it was comparable in both groups up to 120 min. The HR was significantly reduced in dexmedetomidine group but was higher than in this present study. The difference might be due to pharmacokinetic differences of oral and iv alpha-2 adrenergic administration and absence of maintenance dose [9]. The prolonged time of normalization of MAP in group D compared to Group C can be explained by the fact that dexmedetomidine is more selective and 8 times more potent than clonidine regarding the affinity on α-2 adrenergic receptors [9, 14].

Both groups were comparable in terms of blood loss, surgical field quality and surgeon satisfaction. These results are similar to the results of four previous randomized controlled trial studies: Escamilia et al. in 2019, Suggala et al. in 2020, Bafna et al. in 2021 and Gupta et al. 2018 [3, 7, 14, 17]. Clonidine or dexmedetomidine may be used for controlled hypotension surgery subject to their availability.

FESS is usually an ambulatory surgery. The anesthetic plan for FESS should be safe, fast, efficient and cost-effective. Alpha-2 adrenergic agonists (clonidine and dexmedetomidine) administration during anesthesia can affect the recovery from anesthesia due to their pharmacological effects which can prolonged the recovery period (bradycardia, hypotension, sedation) and consequently delay patient discharge [2, 9]. In this study, lower recovery time was observed in clonidine group, mean(SD) of 20.40(3.84) minutes comparing to dexmedetomidine group, 25.53(5.51) minutes. The difference was statistically significant t(p)=4.823(<0.001). In agreement with this present study, Bafna et al. found that mean(SD) of emergence time was statistically significantly longer in dexmedetomidine group (p=0.001) compared to clonidine group [14]. Contrary to this result Escamilla et al. found that there was no statistically significant difference between clonidine and dexmedetomidine group regarding duration of anesthesia [3].

Post-operative sedation was prolonged in Group D in comparison to Group C with statistically significant difference. The sedative effect of both drugs is mediated through their action on α-2 A adrenergic receptor in the locus coeruleus [9]. Alpha-2 agonist and especially dexmedetomidine is known to provide conscious sedation without causing respiratory depression [9, 17]. Comparable to our findings, four recent randomized controlled trial studies : Escamilia et al., Suggala et al., Bafna et al., and Gupta et al. found that post-operative sedation was statistically significantly longer in dexmedetomidine group compared to clonidine group [3, 7, 14, 17]. The prolonged sedation and hemodynamic recovery in patients receiving dexmedetomidine for hypotensive anaesthesia might delay patient discharge which is not needed for ambulatory surgery and anaesthesia. For successful ambulatory surgery and anesthesia, postoperative pain, nausea, vomiting, dizziness, and intestinal and bladder obstruction, which may delay a patient's discharge and increase the likelihood of readmission, must be minimized [3, 18]. Regarding our findings, we suggest the use of clonidine because of safety profile and short duration of sedation and hemodynamic recovery from hypotension and bradycardia.

Limitations

This study has demonstrated that both clonidine and dexmedetomidine offered excellent pharmacological profile for controlled hypotension. It has the privilege of showing that the cheap and easily affordable clonidine has a comparable profile to dexmedetomidine. However, this study has some limitations, first blood pressure was measured non-invasively. Second, thought this study was

blinded for the patient, it was not blinded for the anesthetist for patient safety concerns. To better understand the effects of both drugs and discover small significant differences, future studies should consider double blinding in specialized eye, nose and throat departments where patient safety can be guarantee with the blinding.

Conclusion

Clonidine and dexmedetomidine provided good to excellent quality of the surgical field visibility to the surgeon. Blood loss and duration of surgery were comparable. Both drugs provided reduced mean arterial blood pressure and heart rate. Bradycardia were observed with dexmedetomidine group. Post-operative sedation was longer with dexmedetomidine compared to clonidine, which favors the choice of clonidine use over dexmedetomidine in the setting of day case surgery. However, considering the small sample of this study which could not detect small but clinically differences between both drugs, there is a need for a much larger and multicenter study to confirm these findings.

Abbreviations

ASA	American Society of Anesthesiologists
ASA-PS	American society of anesthesiologists-physical status
BMI	Mass index
CONSORT	Consolidated standards of reporting trials
FESS	Functional endoscopic sinus surgery
HR	Heart rate
MAC	Minimal alveolar concentration
MAP	Mean arterial blood pressure
ORL	Oto-rhino-laryngology
RSS	Ramsay sedation score

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-024-02809-x.

Supplementary Material 1

Acknowledgements

Erick Namegabe Mugabo is thankful to the Else-Kröner-Fresenius-Stiftung, the Holger-Poehlmann-Stiftung and the NGO Förderverein Uni Kinshasa e.V., fUNIKIN through the Excellence Scholarship Program "Bourse d'Excellence Bringmann aux Universités Congolaises, "BEBUC", Nile Basin Scholarship and Provincial General Referral Hospital of Bukavu (Eastern DR Congo, South Kivu province) for funding master's training in Anesthesia and Surgical Intensive Care at Alexandria University in Egypt. Furaha Nzanzu Blaise Pascal is also thankful to the Else-Kröner-Fresenius-Stiftung, the Holger-Poehlmann-Stiftung, the NGO Förderverein Uni Kinshasa e.V., fUNIKIN through the Excellence Scholarship Program "Bourse d'Excellence Bringmann aux Universités Congolaises, "BEBUC", the Safe Anaesthesia Worldwide and the Gertrud & Wolfgang Pollach Award for supporting his master of medicine studies in Anaesthesia and Intensive Care in Malawi.

Author contributions

E.N.M., this author helped in the conception, design, and conduction of the study, analyzed the data, and wrote the draft of the manuscript. Y.M.K., R.A.S., R.S.B., F.N.B.P.: these authors helped in data analysis and interpretation, reviewed, and edited the manuscript. All authors read and approved the final manuscript.

Funding

This study received no funding.

Data availability

All data and material used in this article are available at any reasonable request from the corresponding author.

Declarations

Ethics approval and consent to participate

The protocol was approved by the Ethical Committee of Faculty of Medicine at Alexandria University under serial number: 0106833, approval dated July 15, 2021. All the participants gave their informed consent. The data were anonymous on the data collecting form and in the electronic database. All research was performed in accordance with relevant guidelines/ regulations for research at Alexandria University. This study adhered to CONSORT guidelines.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 23 August 2024 / Accepted: 12 November 2024
Published online: 25 November 2024

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