Dexmedetomidine supplementation for surgical field enhancement in endonasal surgery: a systematic review and meta-analysis*

Rodolfo B. Giffoni[1], J. Arguelles-Hernandez[2], M.E.P. Dalmaschio[3], P.O. Quintana[4], Adriano D. Lima[5]

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[1] Department of Health, State University of Feira de Santana, Feira de Santana, BA, Brazil
[2] Department of Head and Neck Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
[3] Centro Universitário do Espirito Santo, Colatina, ES, Brazil
[4] Instituto do Câncer Dr. Arnaldo Vieira de Carvalho, São Paulo, SP, Brazil
[5] Division of Postgraduate of Medical Sciences, University of Brasilia, Brazil

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Abstract

Background: Dexmedetomidine has been shown to effectively control intraoperative bleeding and improve surgical field visualization. However, its value in endonasal surgeries remains a matter of debate.

Methodology: We searched PubMed, Embase, and Cochrane Central Register of Controlled Trials for studies comparing dexmedetomidine with placebo in endonasal surgeries. Outcomes included bleeding, operative time (OT), surgeon's satisfaction, postoperative pain (POP), and nausea/vomiting (PONV). For statistical analysis, we used RevMan 5.4.1, and assessed heterogeneity with I^2 statistics.

Results: We included a total of 1386 patients from 22 studies. In the placebo group, there was higher bleeding volume, whereas the dexmedetomidine group showed lower scores on the Fromme-Boezaart scale. Additionally, the surgeon satisfaction risk ratio (RR) increased, and OT was reduced in the dexmedetomidine group. The dexmedetomidine group had lower incidences of POP and PONV.

Conclusions: In endonasal surgeries, dexmedetomidine was associated with improvements in surgical field visualization as evidenced by reduced intraoperative bleeding and postoperative morbidities.

Key words: dexmedetomidine, endonasal surgery, intraoperative bleeding, meta analysis, surgical field

Introduction

Endonasal surgery is a common procedure in otorhinolaryngology and neurosurgery involving manipulation of the nasal cavity and skull base structures [(1)]. Due to the intricate and unique anatomy of this region, and its proximity to critical structures like the base of the brain, eyes, nerves, and blood vessels, the surgeon must have a clear view [(2)]. Uncontrolled bleeding during endoscopic nasal surgery compromises visualization of anatomical landmarks, extends surgical duration, and increases the risk of complications [(3,4)].

Controlled hypotension is a technique used to achieve an oligemic surgical field and to regulate intraoperative bleeding [(5,6)]. It is achieved using different agents such as vasodilators, opioids, beta-adrenergic antagonists, high doses of inhaled anaesthetics, and magnesium sulfate. However, these substances have drawbacks such as delayed recovery, resistance to vasodilators, tachyphylaxis, and increased bleeding [(7-10)]. In this context, dexmedetomidine is an α2-adrenergic receptor agonist with sedative, anxiolytic, sympatholytic and analgesic-sparing effects. It offers stable haemodynamics, minimal respiratory function depression, and little impact on neuronal function [(11,12)]. Previous studies have demonstrated the significant potential of this drug in reducing bleeding and improving the surgical field's quality [(9,13)]. Moreover, it is also effective in controlling postoperative morbidity in nasal surgeries compared with other anaesthetic drugs [(14)].

Previous randomized controlled trials (RCTs) and a network meta-analysis [14-17] have shown the efficacy of dexmedetomidine in reducing blood loss compared with placebo and other drugs in intranasal surgeries. However, these results may have been underpowered due to the relatively small sample size and lack of other desired outcomes. Since then, numerous data from RCTs have been published [18-21], which may enhance the statistical power analysis and include other outcomes. To address the lack of consensus on the efficacy of dexmedetomidine in endonasal surgeries, we conducted a systematic review and meta-analysis to elucidate the efficacy of dexmedetomidine in improving surgical field quality and surgeon satisfaction, among other results, by reducing blood loss in endonasal procedures.

Table 1. Population, intervention, comparator, outcome, and study design (PICOS).

Population	Adult patients aged 18 to 75 undergoing endoscopic endonasal procedures under general anaesthesia
Interventions	Intraoperative dexmedetomidine infusion
Comparisons	Intraoperative saline solute 0.9% infusion
Outcomes	intraoperative bleeding, operative time (OT), surgeon´s satisfaction/dissatisfaction, intraoperative mean arterial pressure (MAP), heart rate (HR), emergence agitation (EA), postoperative pain (POP), and postoperative nausea and vomiting (PONV)
Study design	Only randomized controlled trial

Materials and methods

Eligibility criteria

The systematic review and meta-analysis were conducted following the guidelines provided by the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [22]. Only studies that satisfied all the following criteria were included in this meta-analysis: 1) RCTs, 2) comparing dexmedetomidine with a placebo solution of saline 0.9%, 3) those conducted in patients undergoing general anaesthesia, and 4) those reporting any of the outcomes of interest. Exclusion criteria were studies with 1) no control group, 2) non-endonasal surgery modalities, 3) only local anaesthesia, 4) non-randomized studies, or 5) any type of hypotensive anaesthesia or specific haemostatic control restricted to the control group.

Search strategy and data extraction

We conducted a systematic search of PubMed, Embase, and the Cochrane Central Register of Controlled Trials in May 2023 using the following terms: 'dexmedetomidine', 'nasal', 'septoplasty', 'sinus surgery', 'FESS', and 'transsphenoidal'. Additionally, a manual search was conducted to identify any additional studies by reviewing the references from all included studies as well as previous systematic reviews and meta-analyses. Population, intervention, comparator, outcome, and study design (PICOS) summarizing study rationale was provided in a table (Table 1). Two authors (RG and JH) conducted the search independently. Three authors (RG, AL, and MD) independently extracted the data based on pre-defined search criteria and conducted a quality assessment. To extract data from images or graphs, the website WebPlotDigitizer v4.6 (https://apps.automeris.io/wpd/) was used. The prospective meta-analysis was registered on PROSPERO on 25 June 2023 under protocol CRD42023435501.

Endpoints and subgroup analyses

The primary outcomes of interest were intraoperative bleeding, operative time (OT), and surgeon's satisfaction/dissatisfaction. Other prespecified outcomes included intraoperative mean arterial pressure (MAP) and heart rate (HR), emergence agitation (EA), postoperative pain (POP), and postoperative nausea and vomiting (PONV).

Intraoperative bleeding was assessed by volume and the scale from Fromme et al. [23] and Boezaart et al. [2], which takes into account bleeding and the quality of surgical field visualization: 0 = no bleeding; 1 = slight bleeding where blood evacuation is not necessary; 2 = slight bleeding where blood evacuation is occasionally required; 3 = low bleeding with frequent blood evacuation and the operative field visible for a few seconds after evacuation; 4 = moderate bleeding with frequent blood evacuation, and the operative field visible only immediately after evacuation; and 5 = high bleeding requiring constant blood evacuation, with bleeding sometimes exceeding evacuation, making surgery challenging [24].

The efficacy of dexmedetomidine infusion relative to saline solution 0.9% in patient subgroups was also evaluated. We performed subgroup analyses of intraoperative bleeding volume in the following subgroups: 1) 1 µg/kg bolus with 0.5-0.7 µg/kg/hour−1 of dexmedetomidine and general anaesthesia without remifentanil; 2) isolated assessment of the surgical modalities endoscopic sinus surgery (ESS) and transsphenoidal surgery (TSS); and 3) endoscopic surgeries without septoplasty.

Quality assessment

Quality assessment of RCTs was performed with Cochrane's tool for assessing bias in randomized trials [25], studies are scored based on assessment measures as: high, low, or unclear risk of bias in five domains: selection, performance, detection, attrition, and reporting. Two independent authors (RG and PQ) conducted the risk of bias assessment. Disagreements between the authors were resolved through discussions, where they presented their reasons for the discrepancies and reached a consensus.

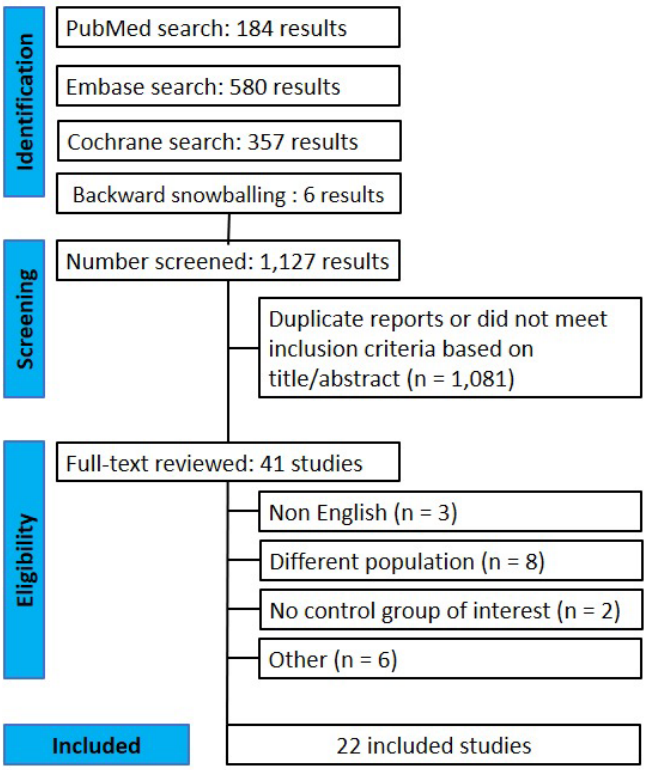


Figure 1. PRISMA flow diagram of study screening and selection.

Statistical analysis

Pooled treatment effects for continuous outcomes were assessed by mean differences (MD), while binary endpoints were evaluated using risk ratios (RR) along with their corresponding 95% confidence intervals (CI). Heterogeneity was assessed using the Cochrane Q test and I^2 statistics. For outcomes with low heterogeneity ($I^2 < 25\%$), a fixed-effect model was employed. In cases of significant heterogeneity, the DerSimonian and Laird random-effects model was used. Statistical analysis was performed using RevMan 5.4.1 (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). Sensitivity analyses were conducted to evaluate the impact of individual studies on the overall results of the meta-analysis.

Results

The initial search yielded 1127 results (Figure 1). After removing duplicate records and unrelated studies through a title and abstract review, 41 records remained, and each of them was fully reviewed. Of these, 22 were included in the qualitative and quantitative review after the exclusion of studies with populations different from the required (n=8) or no control group of interest (n = 2). Ultimately, a total of 1386 patients were included in this systematic review and meta-analysis [15-21,24,26-39]. Intraoperative supplementation with dexmedetomidine was used in 693 patients (50%). The main procedures included were endoscopic sinus surgery, transsphenoidal resection, and septoplasty. Baseline characteristics were comparable between groups (Table 2). Supplementary Table 1 provides a detailed bias evaluation of each RCT included in the meta-analysis performed by Cochrane Risk of Bias 2 (RoB-2)[25]. Seventeen studies were classified as having some concerns; most of these did not provide access to publication protocols. The remaining studies were classified as low risk . In most studies, bleeding was measured in volume or by the scale of Fromme et al. [23] and Boezaart et al. [2]. One study [17] provided a proprietary scale that was adjusted. Surgeon satisfaction was assessed by different scales [17,20,35,37,38]; therefore, responses indicating satisfaction were allocated in the following categories: extremely satisfied, satisfied, excellent, very good, and good. Surgeon dissatisfaction responses were allocated in the following categories: extremely dissatisfied, dissatisfied, very bad, bad, and poor. Intraoperative MAP and HR values were considered from 10 minutes after induction until the last measurement before the end of the surgery. EA was considered as a sedation agitation score ≥ 5 on the Riker scale, in which 1 is the least and 7 is the most agitated [40]. POP was considered ≥ 5 on the visual analog pain scale (from 0 [no pain] to 10 [worst pain possible]) or the patient's request for analgesia within 12 hours after surgery. PONV was considered as the presence of nausea, vomiting, or the need for antiemetics up to 12 hours after surgery.

Intraoperative outcomes

Bleeding volume (MD -81.4 mL; 95% CI -34.5 to -128.3; $p = 0.0007$; $I^2 = 99\%$; Figure 2A) was significantly higher in the control group while the score on the scale of Fromme et al. [23] and Boezaart et al. [2] (MD -0.98; 95% CI -1.21 to -0.74; $p < 0.00001$; $I^2 = 60\%$; Figure 2B) was lower in the intervention group. Surgeon satisfaction (RR 3.63; 95% CI 1.61 to 8.20; $p = 0.002$; $I^2 = 81\%$; Figure 3A) was superior in dexmedetomidine group, and dissatisfaction risk was significantly diminished in the same group (RR 0.17; 95% CI 0.08 to 0.37; $p = 0.00005$; $I^2 = 0\%$). In addition, OT was lower in the dexmedetomidine group (MD -5.46 min; 95% CI -9.35 to -1.56; $p = 0.006$; $I^2 = 57\%$;; Figure 4). Intraoperative MAP (MD -9.3 mmHg; 95% CI -14.05 to -2.83; $p = 0.007$; $I^2 = 99\%$; Figure 5A) and HR (MD -11.5 bpm; 95% CI -15.8 to -7.4; $p < 0.00001$; $I^2 = 97\%$; Figure 5B) were lower in the intervention group.

Postoperative outcomes

There were significant differences between groups in emergence agitation (RR 0.50; 95% CI 0.36 to 0.69; $p = 0.0001$; $I^2 = 0\%$), postoperative pain (RR 0.43; 95% CI 0.30–0.62; $p < 0.00001$; $I^2 = 0\%$; Figure 6), and postopertive nausea and vomiting (RR 0.47; 95% CI 0.32–0.67; $p = 0.0001$; $I^2 = 0\%$; Figure 7).

Subgroup analysis

Studies that used a similar dose of dexmedetomidine (1 µg/ kg

Table 2. Baseline characteristics of included studies.

Study	Surgical procedure	DD, µg/kg	Anaesthesia drugs	BV, mL† DX/PL	OT, min† DX/PL	Age, y† DX/PL	Weight, kg† DX/PL	FS, n DX/PL	MS, n DX/PL	SS
Ayoglu, 2008[15]	Septo-plasty	1 bolus/ 0.7 hour^{-1}	Thiopental, sevoflurane, lidocaine	52,7/ 130	101.9/ 140.0	34.7/ 32,3	69.8/ 73.3	10/8	10/12	40
Bala, 2019[18]	Transsp-henoidal resection	1 bolus/ 0.5 hour^{-1}	Propofol, fentanyl, sevoflurane	153,3/ 218	114.6/ 130.5	37.2 / 41	67.7/ 71.2	14/13	16/17	60
Che, 2020[26]	ESS	1 bolus/ 0.5 hour^{-1}	Propofol, remifentanil	121,32/ 148,32	N/A	33.01/ 33,01	N/A	N/A	N/A	62
Ding, 2017[27]	ESS	0.5 bolus/ 0.5 hour^{-1}	Propofol, remifentanil	195/ 260.7	70.3/ 83.8	35.7/ 36,2	65.3/ 61.9	10/14	21/17	62
Gopalakrishna, 2015[28]	Transsp-henoidal resection	1 bolus/ 0.7 hour^{-1}	Propofol, fentanyl, isoflurane	135/ 225	187/ 199	41.9/ 48,1	63.5/ 64.9	12/7	10/15	44
Gousheh, 2017[19]	ESS	1 bolus/ 0.5 hour^{-1}	Propofol, remifentanil	116.33/ 250.69	N/A	31.33/ 33,20	N/A	12/12	18/18	59
Guven, 2011[29]	ESS	1 bolus/ 0.2 hour^{-1}	Propofol, fentanyl, sevoflurane	N/A	92.25/ 90.75	38.9 /31,0	75.15 / 71.25	8/10	12/10	40
Kim, 2021[30]	Septoplas-ty, ESS	0.5 hour^{-1}	Propofol, remifentanil	N/A	35/ 30	40/40	74 /73	9/5	14/19	47
Jena, 2023[31]	ESS	0.4 hour^{-1}	Propofol, fentanyl, sevoflurane	N/A	N/A	N/A	N/A	N/A	N/A	100
K. Gupta, 2016[16]	ESS	1 bolus/ 0.4 -0.7 hour^{-1}	Propofol, fentanyl, isoflurane	N/A	96.8/ 105	29.7/ 31,2	54.7 / 52.91	9/11	16/14	50
Kang, 2020[33]	Transsp-henoidal resection	1 bolus/0.2 -0.7 hour^{-1}	Propofol Re-mifentanil	N/A	2.3/ 2.8 (hours)	55/48	N/A	15/12	8/11	46
Kaur, 2016[34]	ESS	0.5 bolus/ 0.2 hour^{-1}	Propofol, fentanyl, sevoflurane	N/A	125.19/ 128.07	36.96/ 34,03	72.42/ 67.36	N/A	N/A	52
Mahajan, 2020[20]	ESS	1 bolus/ 0.2 -0.5 hour^{-1}	sevoflurane	117.77/ 183.9	129/ 129.67	38.9/ 38,1	66.5/ 66.4	14/11	16/19	60
Neethirajan, 2020[21]	ESS	1 bolus/ 0.5 hour^{-1}	Propofol, fentanyl, sevoflurane	145.22/ 223.26	76.63/ 79.35	35/ 33,76	N/A	18/20	28/26	92
P. Gupta, 2016[17]	ESS	1 bolus/ 0.6 hour^{-1}	Propofol, fentanyl, isoflurane	N/A	N/A	31.03/ 34.13	50.53/ 55.43	9/10	11/10	40
Parvizi, 2019[35]	ESS	1 bolus/ 0.4-0.8 hour^{-1}	Propofol fentanyl remifentanil	N/A	86.67/ 85.14	38.39/ 42,94	N/A	13/15	23/21	72
Rahman, 2014[24]	ESS	0.4 hour^{-1}	Dexmede-tomidine*, propofol, fentanyl, isoflurane	N/A	112/ 118	42/39	42/39	10/6	5/9	30
S. Y. Kim, 2014[36]	Septoplas-ty, ESS	0.4 hour^{-1}	Propofol, fentanyl, desflurane	N/A	51/ 57	32/33	66 /66	13/15	37/35	100
Salimi, 2017[37]	Transsphe noidal resection	0.6 hour^{-1}	Propofol, fentanyl	160/ 305	203.83/ 209.54	42.76/ 43,85	72.33/ 76,89	16/15	14/15	60
Somayaji, 2016[38]	ESS	1 bolus/ 0.25 hour^{-1}	Propofol, fentanyl, isoflurane	106.1/ 152.7	N/A	35.58/ 36,88	62.36/ 63.7	20/22	30/28	100

Study	Surgical procedure	DD, µg/kg	Anaesthesia drugs	BV, mL† DX/PL	OT, min† DX/PL	Age, y† DX/PL	Weight, kg† DX/PL	FS, n DX/PL	MS, n DX/PL	SS
Wu, 2022[39]	ESS	0.5 bolus/ 0.2 hour^{-1}	Propofol, sufentanil, remifentanil	180/ 180	93.54/ 94.52	44.83/ 41,52	N/A	24/19	24/29	110
Xu, 2016[32]	ESS	0.5 bolus	Propofol, fentanyl, sevoflurane, remifentanil	N/A	79.6/ 86.2	37.5/ 40.2	64.6/ 61.8	9/11	21/19	60

† mean; * However, intrasurgical supplementation was performed with dexmedetomidine vs. placebo, with random allocation between groups and blinding of both anaesthesiologists and surgeons. BV: bleeding volume; DD: dexmedetomidine dose; DX: dexmedetomidine; ESS: endoscopic sinus surgery; FS: female sex; MS: male sex; OT: operation time; PL: placebo; SS: sample size.

in bolus/0.5-0.7 µg/kg/hour^{-1}) and general anaesthesia without remifentanil were assessed [15,18,21,28] for intraoperative bleeding volume. Bleeding volume remained higher in the control group, with a significant reduction in heterogeneity (MD -78.1 mL; 95% CI -59.2 to -97.1; $p < 0.00001$; $I^2 = 0\%$; Figure 3B). In both ESS (MD -70 mL; 95% CI -111.9 to -28.2; $p < 0.001$; $I^2 = 96\%$) and TSS (MD -112.5 mL; 95% CI -165.1 to -60; $p < 0.0001$; $I^2 = 66\%$), there was a significant reduction in volume of blood loss in the dexmedetomidine group. Importantly, the test for subgroup differences showed no significant interaction in the effect of dexmedetomidine among the ESS/TSS subgroups (p-value for interaction=0.22). Similarly, when excluding studies with septoplasty, there was also a significant reduction in blood loss volume favoring the dexmedetomidine group (MD -81.9 mL; 95% CI -132.2 to -31.6; $p < 0.0001$; $I^2 = 99\%$), similar in magnitude to the overall analysis.

Discussion

In this systematic review and meta-analysis of 22 studies and 1386 patients, we compared the efficacy of intraoperative dexmedetomidine supplementation versus placebo in patients undergoing various endonasal surgical modalities. The main findings from the pooled analyses with the use of dexmedetomidine were: 1) a reduction of 81.4 mL in intraoperative bleeding and a decrease of 0.98 points on the Fromme et al. [23] and Boezaart et al. [2] scale; increase in the RR of satisfaction with surgery by 260%; 2) surgery time reduction in 5.4 minutes; 3) MAP and HR reductions of 9.3 mmHg and 11.5 bpm, respectively; and 4) reduction in the risk of POP by 57% and in the risk of PON by 53%.

In nasal endoscopic surgeries, bleeding is probably the most relevant variable that compromises the visualization of surgical planes [41]. In sinus surgery, the main cause of bleeding comes from small blood vessels and arterioles. Bleeding can be exacerbated in certain situations, particularly in revision surgeries, tumour removal procedures, and chronic inflammatory processes with polyps [42]. In this analysis, the supplementation of dexmedetomidine significantly reduced blood loss, improving the quality of the surgical field. This outcome was subjectively assessed by surgeons using scales developed by Fromme et al. [23] and Boezaart et al. [2], which showed a noticeable reduction. As an implication of improved visual quality and reduced need for recurrent aspirations, a higher satisfaction with the surgery would be expected as the as the ultimate result. In congruence with this, our pooled data showed an increase in the RR for surgeon satisfaction.

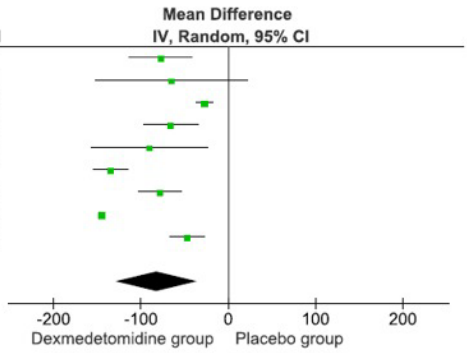
However, the reduction in blood loss depends on multiple variables such as the dose of dexmedetomidine, types of drugs used for general anaesthesia, surgery duration, and underlying morbidity [6,24,26]. The selected studies exhibited significant variability, particularly in terms of dexmedetomidine dosage, pre-surgical hemostatic techniques, and anaesthetic drugs, which likely contributed to a high level of heterogeneity in the analysis of intraoperative bleeding volume ($I^2 = 99\%$). In a subgroup analysis, studies with similar doses of dexmedetomidine were grouped to identify and exclude other factors that could interfere with blood loss, resulting in a heterogeneity of $I^2 = 0\%$. Remifentanil was the main confounding drug, and previous studies indicate that this opioid, when administered as a supplement, can maintain hemodynamic stability and improve the surgical field like dexmedetomidine doses [30,43].

TSS leads to intense activation of the sympathetic nervous system due to nociceptive stimuli originating from the insertion of nasal speculum, sphenoid drilling, and tumor dissection, inducing a profound cardiovascular response with hypertension and tachycardia [28]. This may cause haemodynamic instability, elevated intracranial pressure, and more intense bleeding at the surgical site [18,28]. ESS, in contrast, is typically performed in the setting of primary involvement of the paranasal sinuses due to chronic mucosal inflammation, which results in a greater propensity for bleeding when compared to a disease-free nasal sinus [38,41]. Despite these mechanistic differences, dexmedetomidine had a similar benefit in patients who underwent TSS and ESS.

A

Study or Subgroup	Dexmedetomidine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ayoglu, 2008	52.7	39	20	130	73.1	20	11.2%	-77.30 [-113.61, -40.99]
Bala, 2019	153.3	147.9	30	218	193.1	30	8.5%	-64.70 [-151.74, 22.34]
Che, 2020	121.32	17.68	31	148.42	20.15	31	12.0%	-27.10 [-36.54, -17.66]
Ding, 2017	195	52.5	31	260.7	71.6	31	11.4%	-65.70 [-96.95, -34.45]
Gopalakrishna, 2015	135	94	22	225	129	22	9.7%	-90.00 [-156.70, -23.30]
Gousheh, 2017	116.33	29.43	30	250.69	45.74	29	11.8%	-134.36 [-154.06, -114.66]
Neethirajan, 2020	145.22	42.73	46	223.26	73.34	46	11.6%	-78.04 [-102.57, -53.51]
SALIMI, 2017	160	4.5	30	305	6.6	30	12.0%	-145.00 [-147.86, -142.14]
Somayaji, 2018	106.1	36.99	50	152.7	61.83	50	11.8%	-46.60 [-66.57, -26.63]
Total (95% CI)			**290**			**289**	**100.0%**	**-81.46 [-128.34, -34.57]**

Heterogeneity: Tau² = 4756.94; Chi² = 672.87, df = 8 (P < 0.00001); I² = 99%
Test for overall effect: Z = 3.41 (P = 0.0007)



B

Study or Subgroup	Dexmedetomidine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ayoglu, 2008	1.7	1.2	20	3.3	1	20	8.2%	-1.60 [-2.28, -0.92]
Guven, 2011	1.4	1.27	20	3.15	0.74	20	8.9%	-1.75 [-2.39, -1.11]
K. Gupta, 2016	1.76	0.59	25	2.36	0.56	25	17.9%	-0.60 [-0.92, -0.28]
P.Gupta, 2016	2.4	1.09	20	3.35	1.18	20	7.9%	-0.95 [-1.65, -0.25]
Parvizi, 2019	2.13	0.93	36	2.94	0.71	36	15.7%	-0.81 [-1.19, -0.43]
Rahman, 2014	1.4	0.3	15	2.4	0.4	15	20.4%	-1.00 [-1.25, -0.75]
Somayaji, 2018	1.96	0.44	50	2.8	0.75	50	20.9%	-0.84 [-1.08, -0.60]
Total (95% CI)			**186**			**186**	**100.0%**	**-0.98 [-1.21, -0.74]**

Heterogeneity: Tau² = 0.05; Chi² = 15.15, df = 6 (P = 0.02); I² = 60%
Test for overall effect: Z = 8.11 (P < 0.00001)

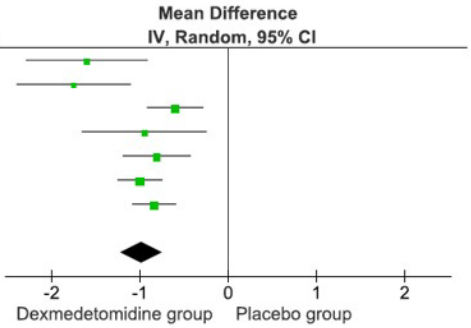
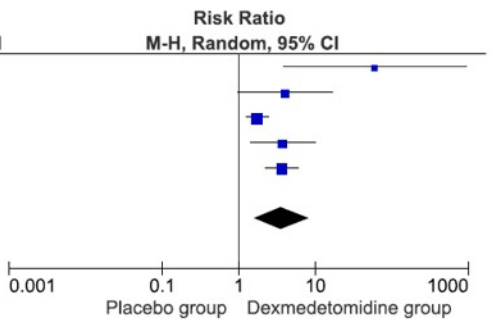


Figure 2. (A) Bleeding volume was significantly lower in patients with dexmedetomidine (p = 0.0007). (B) The Fromme-Boezaart scale was significantly different between groups (p < 0.00001).

A

Study or Subgroup	Dexmedetomidine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Mahajan, 2020	29	30	0	30	6.8%	59.00 [3.77, 923.39]
P.Gupta, 2016	8	20	2	20	15.8%	4.00 [0.97, 16.55]
Parvizi, 2019	33	36	19	36	29.0%	1.74 [1.26, 2.40]
SALIMI, 2017	15	30	4	30	21.1%	3.75 [1.41, 9.99]
Somayaji, 2018	44	50	12	50	27.3%	3.67 [2.22, 6.07]
Total (95% CI)		**166**		**166**	**100.0%**	**3.63 [1.61, 8.20]**
Total events	129		37			

Heterogeneity: Tau² = 0.57; Chi² = 21.46, df = 4 (P = 0.0003); I² = 81%
Test for overall effect: Z = 3.11 (P = 0.002)



B

Study or Subgroup	Dexmedetomidine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ayoglu, 2008	52.7	39	20	130	73.1	20	27.3%	-77.30 [-113.61, -40.99]
Bala, 2019	153.3	147.9	30	218	193.1	30	4.8%	-64.70 [-151.74, 22.34]
Gopalakrishna, 2015	135	94	22	225	129	22	8.1%	-90.00 [-156.70, -23.30]
Neethirajan, 2020	145.22	42.73	46	223.26	73.34	46	59.8%	-78.04 [-102.57, -53.51]
Total (95% CI)			**118**			**118**	**100.0%**	**-78.17 [-97.15, -59.20]**

Heterogeneity: Chi² = 0.22, df = 3 (P = 0.98); I² = 0%
Test for overall effect: Z = 8.07 (P < 0.00001)

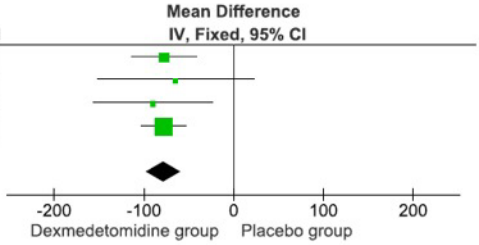


Figure 3 (A) The surgeon satisfaction was significantly higher in the intervention group (p = 0.002). (B) In the subgroup analysis intervention group demonstrated a decrease in intraoperative bleeding (p < 0.00001).

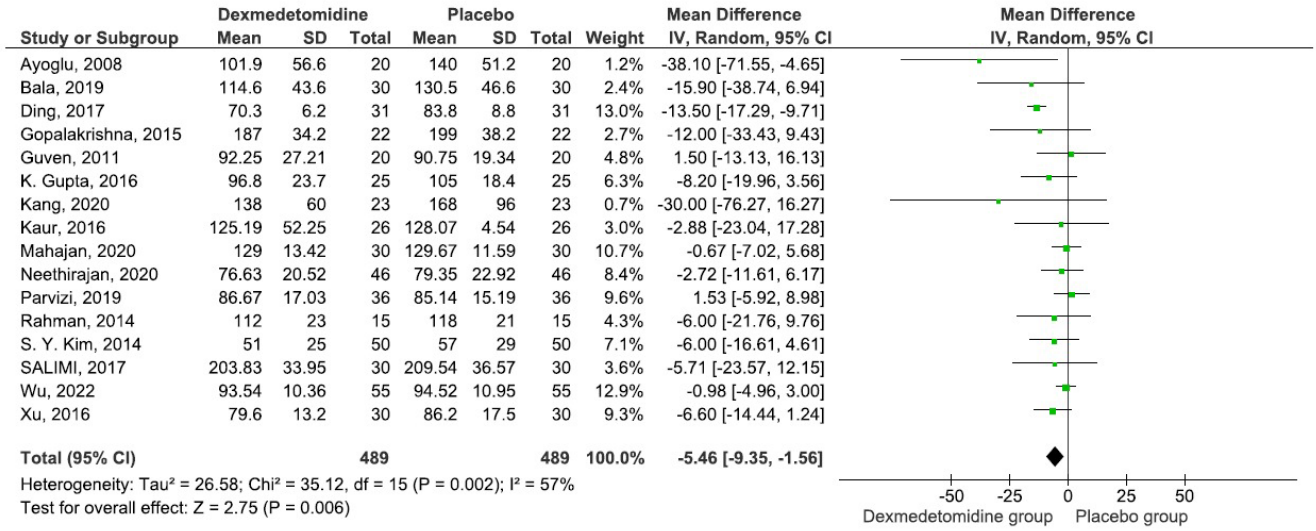


Figure 4. Operative time was shortened among the dexmedetomidine group (p = 0.006).

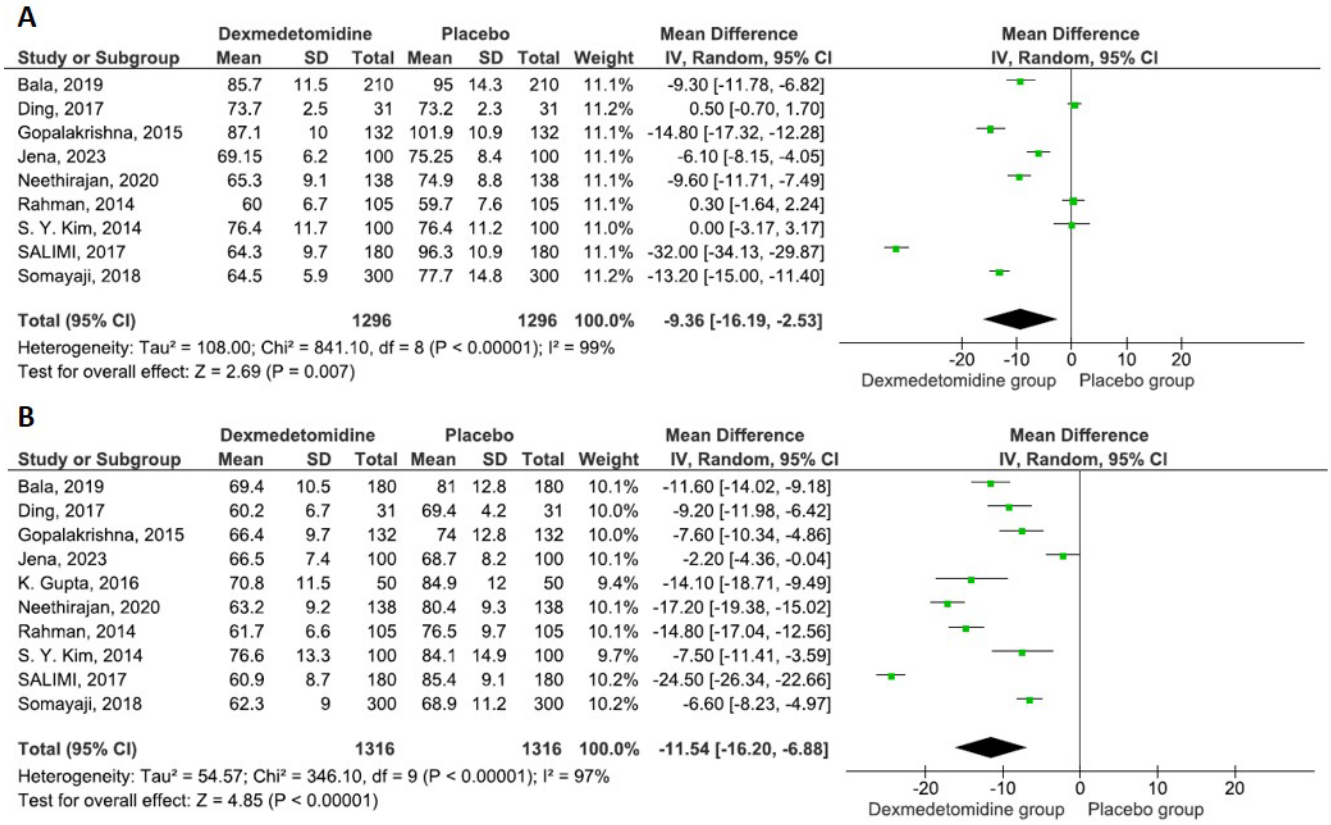


Figure 5. (A) The dexmedetomidine group exhibited a decrease in intraoperative mean arterial pressure with a total number of measurements = 1296 (p = 0.007). (B) There was a difference in heart rate between the groups with a total number of measurements = 1316 (p < 0.00001).

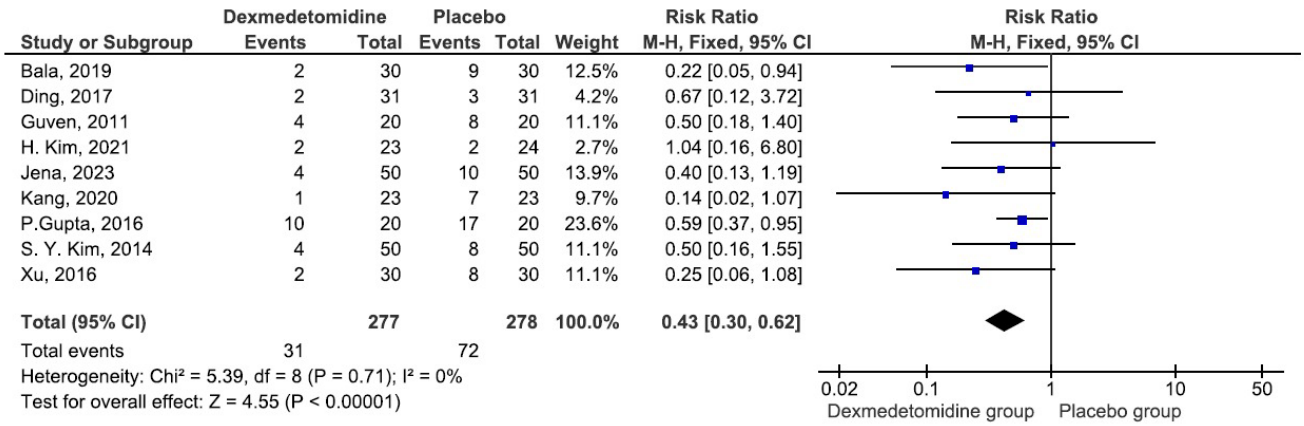


Figure 6. The incidence of postoperative pain was significantly reduced in the dexmedetomidine group ($p < 0.00001$).

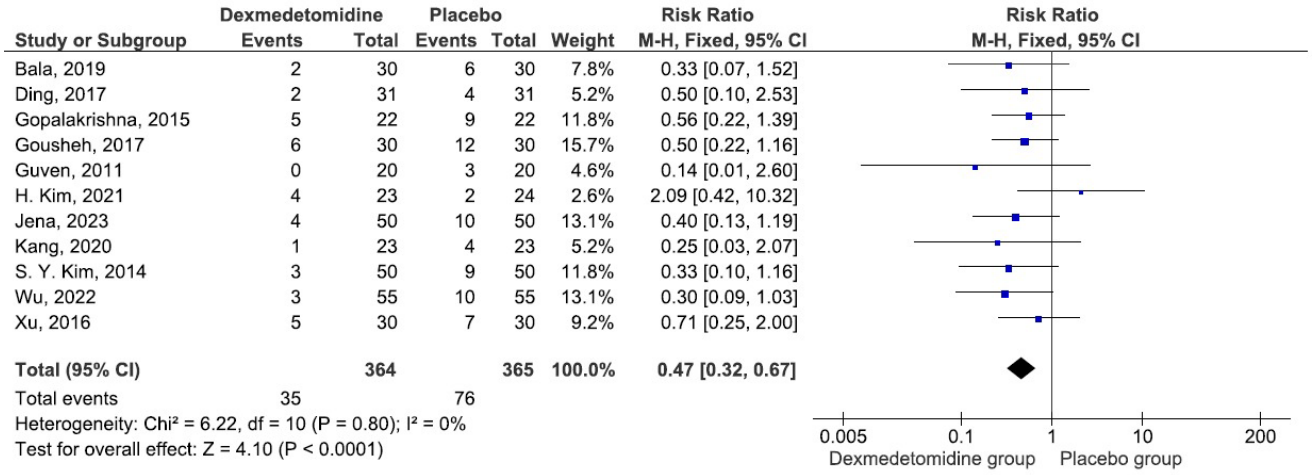


Figure 7. The risk of postoperative nausea and vomiting decreased in the intervention group ($p < 0.0001$).

Septoplasty can also be performed as an endoscopic surgical modality [44]. However, due to the anatomical characteristics of the nasal septum, bleeding can be less problematic, especially after the surgeon correctly identifies the plane over the mucoperichondrium [45,46], not carrying the same weight as pure endoscopic sinus modalities. Only one of the assessed articles exclusively included septoplasty cases [15]. When this study was excluded in a subgroup analysis of exclusive endoscopic modalities (ESS and TSS), there was no significant change in blood loss or improvement in the surgical field. Although this analysis is based on the exclusion of a single article, it suggests that dexmedetomidine has a lesser impact on septoplasty compared to ESS and TSS.

Restricted and extensively vascularized cavities, such as the nose and paranasal spaces, can be rapidly filled with blood within a matter of seconds during most procedures, and endoscopic sinus surgery does not allow for simultaneous use of surgical instruments and blood aspiration [41] and thus requires a halt to conduct suction. Consequently, bleeding can have a progressive and detrimental impact, resulting in a prolonged OT [47]. Our data suggests that dexmedetomidine reduces the OT, which can be seen as an indirect indication of an improved surgical field, as described by Fromme et al. [23] and Boezaart et al. [2] a clear surgical field requiring less aspiration, resulting in fewer interruptions during the surgery.

In endonasal surgeries, controlled hypotension is defined as a reduction to 65 to 55 mmHg, or 30% in MAP baseline, and is one of the most employed techniques to control bleeding (48). The use of vasodilators, such as sodium nitroprusside, for this purpose may result in reflex tachycardia and increased cardiac output, which can exacerbate vasodilation and local bleeding [49]. However, centrally acting presynaptic α2 agonists, such as dexmedetomidine, decrease HR and cardiac contractility, which reduces cardiac output and MAP, improving blood loss and surgical field scores [48-51].

In ESS, studies have shown that dexmedetomidine reduces MAP and HR effectively, counterbalancing the instability caused by nociceptive effects arising from the surgical process [21,24,37,38].
In our study, the pooled analysis demonstrated a reduction in intraoperative MAP and HR. However, five of the evaluated studies did not achieve the target values (65 to 55 mmHg) or found no difference in MAP between the groups [18,24,27,28,36]. Nevertheless, four of these studies still identified a reduction in blood loss volume in the dexmedetomidine group. These findings suggest that, in addition to hypotension, reduction and stabilization of HR achieved with dexmedetomidine is an independent factor contributing to intraoperative haemostatic control. These results align with recent literature [52,53].

Controlled hypotension maintenance by opioids, nitroglycerin, inhalable agents, or beta-blockers associated with surgical stimulus in the nasal cavity, triggers a cascade of stress responses by accumulation of catecholamines inciting nociception, and activates the sympathetic nervous system increasing postoperative morbidities like agitation, nausea, emesis, respiratory depression, pruritus, reflex tachycardia and hyperalgesia [21,54,55]. As a highly selective α2-specific agonist, dexmedetomidine has sedative, anaesthetic, opioid-sparing, and sympatholytic properties [56]. There is substantial evidence demonstrating the capacity of dexmedetomidine to control postoperative side effects, particularly agitation from general anaesthesia in children, postoperative pain, and the need for antiemetics [57-62]. Our findings are consistent with the literature, suggesting that the sympatholytic and anaesthetic effects of dexmedetomidine, beyond intraoperative bleeding control, provide postoperative support to patients by reducing the risk of pain, nausea, and vomiting. In contrast, prolonged sedation is one of the most common side effects of this drug [16,19,21,27,31,32,36].

Study limitations

Most notably, the inclusion of studies with different doses of dexmedetomidine, anaesthesia drugs and doses, vasoactive drugs, and underlying morbidity resulted in high heterogeneity in the primary outcomes. Only six studies [15,16,18,27-29] reported the use of pre-surgical topical vasoconstrictors and/or anaesthetics, such as infiltration of adrenaline/lidocaine or topical application of an adrenaline-soaked pack. Whether the use of these agents could influence the relative efficacy of dexmedetomidine vs. placebo is unclear; however, it is unlikely that these topical agents would favor either intervention group due to the predominantly blinded nature of the included studies.
This heterogeneity hindered the precise quantification of the effects of dexmedetomidine on these variables. However, heterogeneity was eliminated when matching doses of dexmedetomidine were grouped with similar anaesthetic drugs in a subgroup analysis of the primary outcome (intraoperative bleeding).
Lastly, most studies included in this review had exclusion criteria that prevented the evaluation of the benefits of dexmedetomidine in patients with chronic cardiac and pulmonary diseases. As a result, the effects of dexmedetomidine on this patient profile remain unclear.

Conclusion

The results of this meta-analysis, which included 1386 patients, highlight that the use of dexmedetomidine compared to placebo leads to better control of intraoperative bleeding. This control results in improved visualization of the surgical field, increased surgeon satisfaction, reduced surgical duration, and lower postoperative morbidities. There was elevated heterogeneity in the outcomes, likely related to methodological differences between studies and different doses of dexmedetomidine. Nevertheless, these findings support the implementation of dexmedetomidine as a first-line anaesthetic adjuvant for endonasal surgeries in patients without cardiac and pulmonary complications.

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Authorship contribution

RG and JH conducted a manual search to identify any additional relevant studies. RG, AL, and MD extracted the data based on predefined search criteria and performed the statistical analysis. RG and PQ completed the risk of bias assessment. RG led the writing of the article, with assistance from JH and MD, AL performed the final review of the article before submission.

Conflict of interest

There are no conflicts of interest from any of the authors.

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Rodolfo Baptista Giffoni
Universidade Estadual de Feira de Santana
Feira de Santana
Bahia
Brazil

Tel: +5527999044838
E-mail: rodolfo.giffoni1@gmail.com