Role of gabapentin in controlled hypotension for nasal surgeries: a randomized controlled study

Amira A.E. Shaban[a], Hanaa F. Mohammed[a], Amany A.A. El Zaher[b]

Background Providing bleeding control is critically important when microsurgical techniques are used. A mild bleeding can complicate the working in surgical field in nasal surgery so, a bloodless surgical field should be provided. For that purpose, the anesthesiologists should use controlled hypotension anesthetic technique. The aim of this study was to investigate the hypotensive and analgesic effects of gabapentin if combined with nitroglycerin infusion for conduction of hypotensive anesthesia in nasal surgeries.

Patients and methods The present study was carried out at El-Zahraa hospital, Al Azhar University on 40 patients ASA I and II were randomly assigned into two equal groups (n=20). Gabapentin nitroglycerin (GN) group: patients received 1200 mg gabapentin orally 2 h preoperatively. Nitroglycerin placebo group (N): patients received placebo tablet orally 2 h preoperatively. Intravenous nitroglycerin infusion started and titrated for all 40 patients according to the target hypotensive condition (mean arterial pressure range between 55–65 mmHg and heart rate between 60–75 b/min). Intraoperative hemodynamic changes in the form of heart rate (HR) and mean arterial pressure (MAP) were recorded; the total nitroglycerin dose required was recorded; blood loss and quality of surgical field were assessed. Also, visual analog scale (VAS) for pain assessment and total amount of morphine used within 12 postoperative hours were detected for each group.

Results The results showed that the heart rate and the mean arterial pressure were significantly lower in the GN group compared to N group. The total dose of intraoperative nitroglycerin was significantly lower in the GN group compared to N group. GN group provides the lower amount of blood loss and better surgical field exposure compared to N group. The visual analog scale (VAS) values was significantly lower at 30 min and 4 h post-operative while non-significant difference at 1 and 6 h postoperative in the GN group compared with N group. There was a significantly lower in the total morphine consumption for GN group compared to N group.

Conclusion Preoperative oral gabapentin (1200 mg) augments the hypotensive effect of nitroglycerin as it provides dryness of surgical field associated with lower infusion rate of nitroglycerin. Also, it has better analgesic effect with lower narcotic consumption during controlled hypotensive anesthesia for nasal surgeries when compared to the administration of nitroglycerin alone.

Sci J Al-Azhar Med Fac, Girls 2019 3:172–180

The Scientific Journal of Al-Azhar Medical Faculty, Girls
2019 3:172–180

Keywords: controlled hypotension, gabapentin, nitroglycerin

[a]Department of Anesthesia and Intensive Care, Faculty of Medicine, Al Azhar University, [b]Faculty of Medicine, Cairo University, Cairo, Egypt

Correspondence to Dr. Amira Abd El Fattah Shaban, Assistant Professor of Anesthesia and Intensive Care, Faculty of Medicine, Al Azhar University, 116 Hadayek EL-Koba Street, Egypt. Tel: 01009956912; e-mail: amiraabdelfattah390@yahoo.com

Received 25 December 2018 **Accepted** 29 December 2018

Introduction

Functional endoscopic sinus surgery (FESS) is the mainstay of surgical treatment for the sinonasal disease. Because of the limited surgical field and the proximity of the sinuses to critical structures (e.g. eye, skull base, carotid artery, brain), even small amounts of surgical site bleeding can obscure the surgeon's view and lead to rare but devastating and even life-threatening complications.

The benefit of a clear, 'bloodless' surgical field on outcomes in those patients is widely accepted by surgeons and anesthesiologists. Therefore, identifying perioperative measures that decrease excessive intraoperative bleeding to optimize surgical visualization is important to anesthesiologists, surgeons, and patient's outcome [1].

Controlled hypotension is an anesthesia technique that provides a significant reduction of complications resulting from major blood loss, including the risks of hypovolemia, hypoperfusion and those associated with blood transfusion [2].

Techniques of controlled hypotension can be classified into nonpharmacological techniques (positioning, intermittent positive-pressure ventilation, and hyperventilation, etc.) [3], and pharmacological techniques (proper analgesia, anesthesia and muscle relaxants, nitrates, β-adrenergic blockers, α-adrenergic blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors and magnesium sulfate, etc. [4].

Nitroglycerin (NTG) is an organic nitrate that acts principally on venous capacitance vessels and large coronary arteries to produce peripheral pooling of blood and decreased cardiac ventricular wall tension. However, as the dose of NTG is increased, there is also relaxation of the arterial vascular smooth muscle. NTG can produce pulmonary vasodilation equivalent to the degree of systemic arterial vasodilation [5].

Gabapentin is a second generation anticonvulsant that is effective in the treatment of chronic neuropathic pain. It was, until recently, thought to be useful in acute perioperative conditions. However, a growing body of evidence suggests that perioperative administration of gabapentin is effective in producing attenuation of the hemodynamic response to laryngoscopy and intubation, effective as postoperative analgesic agent, preventing chronic post-surgical pain, and postoperative nausea and vomiting, and delirium [6].

The aim of this study was to assess the effect of preoperative oral gabapentin (1200 mg) on intraoperative blood pressure to induce controlled hypotensive anesthesia for nasal surgeries and decreasing postoperative narcotics' demand.

Patients and methods

This prospective randomized double-blind controlled study was carried out at El-Zahraa hospital, Al Azhar University after ethical committee approval. All patients in the study were informed about the study design and objectives as well as the tools and the techniques.

Forty patients of both sexes with an age ranging from 25 to 35 years, American Society of Anesthesiologists (ASA) I–II physical status were scheduled for elective nasal surgeries under general anesthesia with controlled hypotensive technique.

Patients excluded from this study were those who refused to participate in this study, physical status ASA III or more, known allergy to any drugs used in this study, patients with a medical condition that contraindicated hypotensive anesthesia, such as peripheral vascular disease, cerebrovascular stroke, carotid artery stenosis, previous myocardial infarction, ischemic heart disease, congestive heart failure, limb ischemia, uncontrolled hypertension, raised intracranial tension, preoperative renal disease, hepatic insufficiency, respiratory insufficiency, polycythemia, sickle cell anemia, severe anemia, pregnancy and diabetes mellitus.

All patients were assessed preoperatively by proper history taking, clinical examination, laboratory evaluation, chest radiography, and ECG, and preoperative fasting of a minimum 6 h was ensured before the operation.

At the preoperative visit, all patients were clinically evaluated and instructed about the evaluation of pain using the visual analog scale (VAS) of 0–10 cm (0=no pain and 10=worst possible pain).

The study protocol was explained to the patients, and their written consents were taken. Patients were allocated randomly into two equal groups (20 patients for each group): group GN (gabapentin nitroglycerin group): 1200 mg gabapentin (conventin 400 mg capsules; EVA Pharma, Cairo, Egypt) were received orally 2 h preoperatively and group N (nitroglycerin group): placebo tablets were received orally 2 h preoperatively.

Randomization was achieved by computer-generated table and sealed envelope method wherein pieces of paper with group names written on them were placed in sealed envelopes.

Before initiation of anesthesia a suitable intravenous cannula (22G) was inserted, premedication were achieved as: IV metoclopramide 0.25 mg/kg and IV ranitidine 50 mg.

In the operative room, all patients were monitored with ASA standard monitoring in the form of ECG leads attached to the chest wall, noninvasive blood pressure monitoring and pulse oximetry (oxygen saturation), and capnography (end-tidal carbon dioxide) preoperative parameters were recorded.

Ringer lactate intravenous infusion at a rate of 4–6 ml/kg/h was initiated before induction of anesthesia and continued during anesthesia.

Preoxygenation was started with oxygen 100%; induction of anesthesia was started by intravenous lidocaine 1 mg/kg, propofol 1.5–2.5 mg/kg and fentanyl 1–2 μg/kg, and tracheal intubation was facilitated by atracurium 0.5 mg/kg.

Oral intubation was performed by a suitable size nonkickable tube using a rigid laryngoscopy, followed by cuff inflation, and the oral pack was inserted properly around the endotracheal tube (ETT) to prevent aspiration.

After proper positioning with head up 15°, both groups received intravenous infusion of NTG (nitronal aqueous, 1 mg/ml; Sunny Pharmaceutical, Badr, Egypt), titrated via syringe pump according to target mean arterial blood pressure (MAP) (55–65 mmHg); increment dose of morphine 2 mg was administered intravenously to maintain heart rate (HR) (60–75 beats/min). If tachycardia persisted, propranolol 0.5–1 mg was given slowly over 1 min, and the patient was excluded from the study.

Maintenance of anesthesia was achieved by intermittent positive-pressure ventilation with adjusted tidal volume and respiratory rate according to body weight, and target end-tidal carbon dioxide by capnography was 30–35 mmHg, isoflurane 2%, and atracurium was given at a dose 0.1 mg/kg every 20 min

At the end of surgery, inhalation anesthesia was discontinued, and, after attempts of spontaneous respiration, reversal of neuromuscular blockade was carried out by intravenous atropine 0.01–0.02 mg/kg and intravenous neostigmine 0.04–0.08 mg/kg. The oral pack was removed, and then awake removal of ETT was carried out.

Finally, after ensuring safe airway, normal respiration, and stable hemodynamics, the patient was transferred to the postanesthetic care unit. Postoperative analgesia was provided using 2 mg intravenous bolus injections of morphine; the incremental bolus dose of morphine was increased to 3 mg if analgesia was inadequate according to the VAS.

The surgeon and anesthesiologist recording the data were blinded to which group the patient belonged.

The primary outcome of the study was to evaluate the efficacy of gabapentin in controlled hypotensive anesthesia to reach the target MAP, which is the main outcome variable in this study.

The following parameters were used to conclude its efficacy:

(1) Hemodynamic changes (MAP and HR) recorded at the baseline value then every 5 min for 2 h intraoperatively and in the immediate postoperative period.
(2) NTG dose used intraoperatively.
(3) Quality of surgical field according to Fromme *et al.* score (Table 1).

Table 1 Fromme *et al.* scale for quality of surgical field assessment [7]

Grade of scale	Description of surgical field
5	Massive uncontrollable bleeding
4	Bleeding, heavy but controllable, that significantly interferes with dissection
3	Moderate bleeding that moderately compromises surgical dissection
2	Moderate bleeding, a nuisance but without interfering with accurate dissection
1	Bleeding, so mild it was not even a surgical nuisance
0	No bleeding, virtually bloodless field

The secondary outcomes of the study were as follows:

(1) The assessment of postoperative pain by VAS for 12 h.
(2) Postoperative requirements of morphine (mg) within 12 h.

Sample size calculation

On the basis of the previous study sample size, estimation based on initial pilot observations indicated that ~20–23 patients should be included in each group, in order to ensure a power of 0.80 for detecting clinically meaningful reductions in HR and systolic arterial pressure by 10–20%. An α error was assumed to be 0.05 [8].

Statistical analysis

Data were collected, revised, coded and entered into the statistical package for social science (SPSS Inc., Chicago, IL, USA) version 22. The quantitative data were presented as mean, SD and ranges, when their distribution was found to be parametric, while nonparametric data were presented as median with interquartile range. Qualitative variables were presented as number and percentages.

The comparison between groups with regard to qualitative data was carried out by using the χ^2-test.

The comparison between two independent groups with quantitative data and parametric distribution was carried out by using the independent *t*-test.

The confidence interval was set to 95%, and the margin of error accepted was set to 5%. Hence, the *P*-value was considered significant at the level of less than 0.05.

Results

There was no statistically significant difference ($P>0.05$) between the two studied groups with

Table 2 Comparison between the two studied groups with regard to demographic and operative data

	Gabapentin nitroglycerin group (*N*=20)	Nitroglycerin group (*N*=20)	Test value	*P*-value
Age (years)				
Mean±SD	28.55±3.66	29.4±3.25	0.776[a]	0.442
Range	24–35	25–35		
Sex				
Female	7 (35.0)	7 (35.0)	0.000[b]	1
Male	13 (65.0)	13 (65.0)		
Body weight (kg)				
Mean±SD	72.1±12.87	73.05±11.74	0.244[a]	0.809
Range	49–90	53–90		
Height (cm)				
Mean±SD	168.8±8.49	166.55±8.97	0.815[a]	0.420
Range	156–180	153–181		
BMI				
Mean±SD	25.23±4.07	26.43±5.21	–0.810a	0.423
Range	19.14–33.6	19.9–36.1		
American Society of Anesthesiologists				
I	14 (70.0)	15 (75.0)	0.125b	0.723
II	6 (30.0)	5 (25.0)		
Mallampati				
I	9 (45)	12 (60)	0.902	0.342
II	11 (55)	8 (40)		
Type of surgery				
Septoplasty	10 (50.0)	9 (45.0)	0.144	0.931
Rhinoplasty	5 (25.0)	6 (30.0)		
Functional endoscopic sinus surgery	5 (25.0)	5 (25.0)		
Duration of surgery (min)				
Mean±SD	92.25±21.37	99±19.1	1.053	0.299
Range	60–120	60–120		

[a]Independent *t*-test. [b]χ^2-test.

regard to the demographic and operative data (Table 2). The following observations were made:

Mean arterial pressure changes (mmHg)

There was a statistically highly significant decrease in MAP ($P<0.01$) in the GN group compared with the N group all through 20–60 min of the intraoperative recorded measures. There was a statistically significant decrease in the recorded measured MAP ($P<0.05$) in the GN group compared with the N group at post-ETT time, 10, 15, 65, 70, 75, 95, 100, 105, 110, and 120 min. There is no significant change at this 3 period of the study difference ($P>0.05$) between the two studied groups at preoperative, 5, 80, 85, and 90 min of the intraoperative and in the immediate postoperative period (Fig. 1).

Heart rate changes (beats/min)

There was a statistically highly significant increase in recorded HR ($P<0.01$) in the N group compared with the GN group at 5–75 min and 110–120 min of the intraoperative period. There was significant decrease in HR (*P*-value <0.05) in the GN group compared to the N group at post ETT time, 80–105 min of the intraoperative recorded heart rate. There was a statistically nonsignificant difference ($P>0.05$) between the two studied groups at preoperative HR only (Fig. 2).

Intraoperative total dose of nitroglycerin (μg)

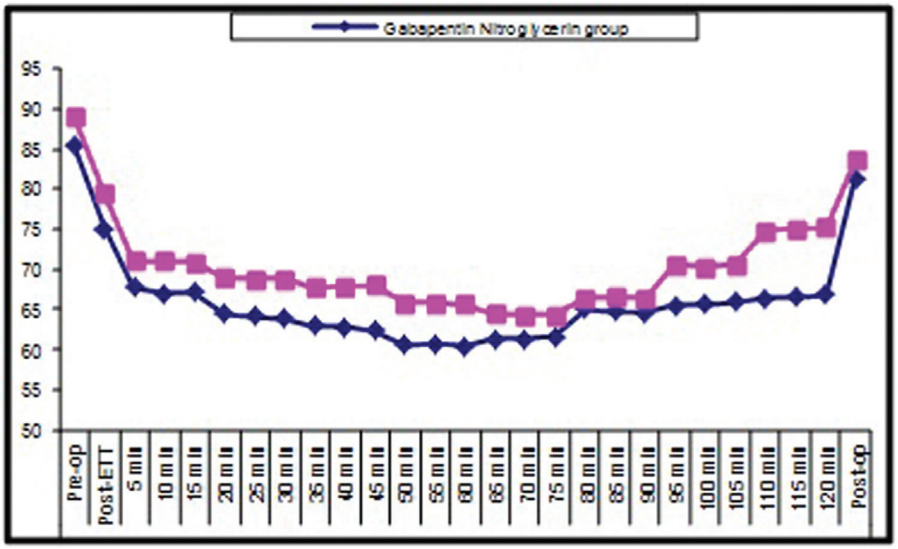
There was a statistically highly significant increase in the total received NTG dose to conduct hypotensive anesthesia ($P<0.01$) in the N group (2706.00 ±651.99 μg) compared with the GN group (1292.25 ±398.63 μg) (Table 3).

Quality of surgical field

There was a statistically highly significant ($P<0.01$) difference between the two studied groups with regard to quality of surgical field according to Fromme *et al.* scale, as it was of better quality for the GN group compared with the N group.

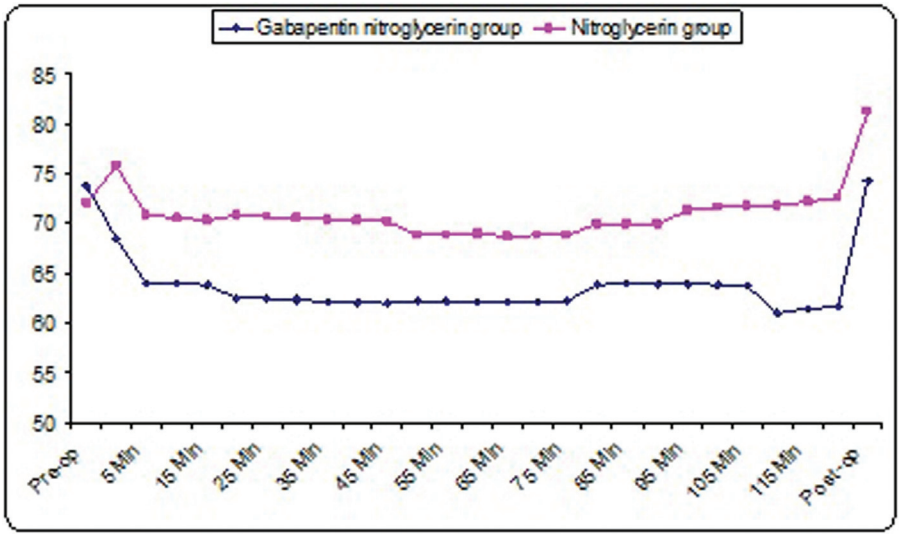
Quality of surgical field according to Fromme *et al.* scale was graded as follows: Grade 1, mild bleeding that

Figure 1



Comparison between the two studied groups with regard to mean arterial blood pressure. ETT, endotracheal tube.

Figure 2



Comparison between the two studied groups with regard to heart rate (beats/min).

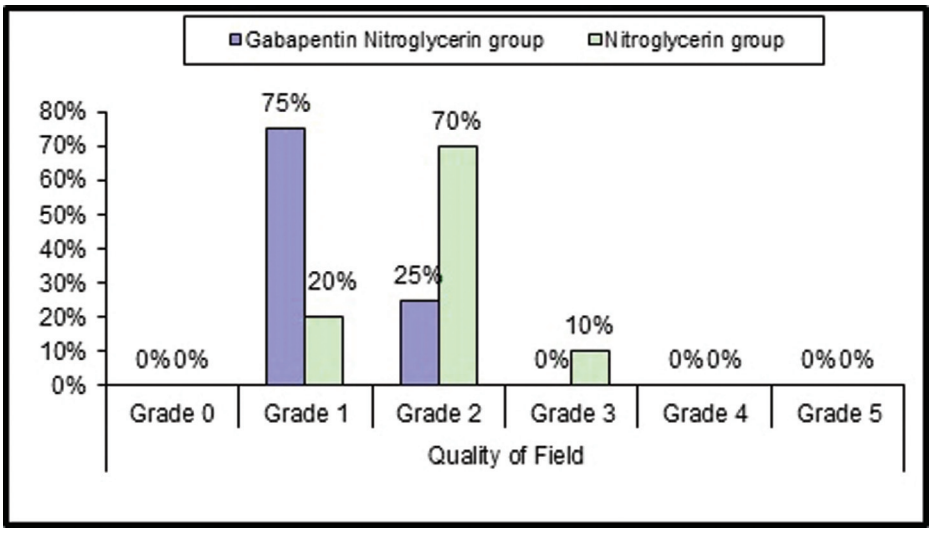
Table 3 Comparison between the two studied groups with regard to intraoperative total nitroglycerin dose (μg)

	Gabapentin Nitroglycerin group (*N*=20)	Nitroglycerin group (*N*=20)	Test value[a]	*P*-value
Nitroglycerin dose (μg)				
Mean±SD	1292.25±398.63	2706.00±651.99	8.273	0.000

P>0.05, NS. *P*<0.05, significant. *P*<0.01, highly significant. [a]Independent *t*-test.

did not affect surgical dissection for 75 and 20%; grade 2, moderate bleeding that did not interfere with surgical dissection for 25 and 70%; and grade 3, moderate bleeding that interfered with surgical dissection for 0 and 10% in the GN group and the N group, respectively. There was no patient associated with grade 4, heavy or grade 5, massive bleeding in both groups (Fig. 3).

Figure 3



Comparison between the two studied groups with regard to the quality of surgical field according to Fromme *et al*. scale.

Table 4 Comparison between the two studied groups with regard to the postoperative total dose of morphine required

Postoperative morphine (mg)	Gabapentin nitroglycerin group (*N*=20)	Nitroglycerin group (*N*=20)	Test value[a]	*P*-value
Mean±SD	3.30±1.26	4.25±1.48	−2.183	0.035

P>0.05, NS. *P*<0.05, significant. *P*<0.01, highly significant.
[a]Independent *t*-test.

Postoperative total dose of morphine requirements (mg)

There was a statistically significant increase in the postoperative morphine required ($P<0.05$) in the N group compared with the GN group for 12 h, as it was 4.25±1.48 for the N group and 3.30±1.26 for the GN group (Table 4).

Assessment of postoperative pain by visual analog scale

There was a statistically highly significant increase of pain according to VAS ($P<0.01$) in the N group compared with the GN group at 12 h postoperatively, as it worsened for the N group (3.05 ±0.83) compared with the GN group (2.15±0.75).

There was no difference between the two studied groups at 12 h postoperatively, as all patients were pain-free (Table 5 and Fig. 4).

Discussion

Controlled hypotensive anesthesia technique during nasal surgeries is considered to be mandatory, as they are performed in a narrow and confined space; hence, bleeding during these surgeries reduces visibility. This may lead to undesirable events such as prolongation of surgery and anesthesia time, increasing the possibility of complications and increased surgical stress [9].

This study was designed to assess the role of gabapentin in controlled hypotension anesthesia for nasal surgeries as regard intraoperative hemodynamic changes, total dose of nitroglycerin administered intraoperative, the quality of surgical field, postoperative pain assessment (VAS) and postoperative morphine demand. No patient was excluded after inclusion to study. All patients were able to complete the entire study and their data were included in the final analysis.

As regards the hemodynamic change, this study showed that there was a significant decrease in the MAP and HR ($P<0.05$) in the GN group compared with the N group.

This in agreement with Raghavendra *et al.* [10], who concluded that both NTG and esmolol (ESM) were safe and effective in providing optimal operating conditions, but ESM is superior because it provides superior surgical dryness at a higher MAP and reduces the surgical blood loss more than NTG. The absence of reflex tachycardia caused by baroreceptors' mediated response secondary to hypotension was the added advantage of ESM over NTG.

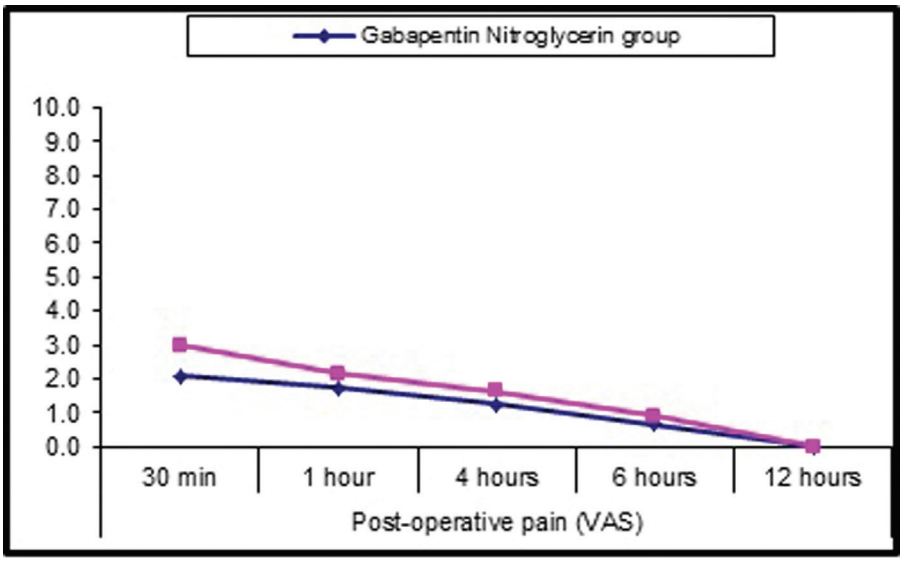
The same results were obtained by Rabie and Gomaa [11] who aimed to assess the effect of gabapentin (1200 mg) in patients with supratentorial brain

Table 5 Comparison between the two studied groups with regard to postoperative pain assessment by visual analog scale

Postoperative pain (VAS)	Gabapentin nitroglycerin group (*N*=20)	Nitroglycerin group (*N*=20)	Test value[a]	*P*-value
30 min				
Mean±SD	2.10±0.79	3.00±0.73	–3.758	0.001
Range	1–3	2–4		
1 h				
Mean±SD	1.75±0.72	2.15±0.67	–1.823	0.076
Range	1–3	1–3		
4 h				
Mean±SD	1.25±0.55	1.65±0.59	–2.223	0.032
Range	0–2	1–3		
6 h				
Mean±SD	0.65±0.49	0.90±0.55	–1.515	0.138
Range	0–1	0–2		
12 h				
Mean±SD	0.00±0.00	0.00±0.00	–	–
Range	0–0	0–0		

VAS, visual analog scale. $P>0.05$, NS. $P<0.05$, significant. $P<0.01$, highly significant. [a]Independent *t*-test.

Figure 4



Comparison between the two studied groups with regard to postoperative pain assessment (VAS).

tumors undergoing craniotomy under general anesthesia. The HR, MAP and intracranial pressure decreased significantly with gabapentin, as compared with the placebo group.

Another study carried out by Mausumi *et al.* [12] concluded that gabapentin (900 mg) premedication provided perioperative hemodynamic stability compared with the placebo group during laparoscopic surgery.

In contrast to this study's results, Farnoush *et al.* [13] found that premedication with 900 mg gabapentin did not affect the hemodynamic changes induced by laryngoscopy in patients undergoing septorhinoplasty.

As regards the dose of NTG needed intraoperatively, this study showed that there was a statistically highly significant increase in the total received dose of NTG ($P<0.01$) in the N group compared with the GN group.

In agreement with our study results, Mahmoud *et al.* [14] found that the gabapentin group required significantly lower infusion rates and total doses of a hypotensive agent (sodium nitroprusside) than the placebo group in elective FESS operations.

Furthermore, these results run parallel to the results obtained by Marouf and Khalil [15] who found that the pregabalin group showed better surgical field, a lower overall dose of NTG administered intraoperatively,

and less postoperative pain and morphine requirements in FESS operations.

As regards the quality of surgical field according to Fromme *et al.* scale, we found that there was a statistically highly significant difference between the two studied groups ($P<0.01$), as the quality of the surgical field was better for the GN group compared with the N group.

In the same line with results of this study, Prasant *et al.* [9] reported that the quality of the surgical field was better in cases with induced hypotension technique compared with normotensive technique.

In the same line with our study, Darius and Juozas [16] proved that the visibility of the surgical field during endoscopic rhinosurgery was better with hypotensive anesthesia technique induced by NTG and captopril compared with the normotensive technique.

As regards postoperative assessment of pain according to VAS and the total morphine dose (mg) administered during 12 h since arrival to postanesthetic care unit, this study showed that there was a statistically significant difference between the two studied groups as postoperative pain scale (VAS) was worse for the N group compared with the GN group. Moreover, the total postoperative opioid (morphine) requirement through 12 h was higher in the N group compared with the GN group.

In the same line with our study results, Chandra *et al.* [17] found that patients who received a pre-emptive dose of gabapentin (600, 900, and 1200 mg) had lower VAS scores at all time points than patients who received gabapentin 300 mg, with lower fentanyl consumption used for postoperative pain relief after single-level lumbar discectomy.

In agreement with this study, Ajit *et al.* [18], in their review, found that gabapentin reduces acute pain and opioid consumption after breast cancer surgery.

Moreover, our study is in line with the study carried out by Ferdi *et al.* [19], who aimed to evaluate the analgesic effect of single-dose preoperative gabapentin (600 mg) on postoperative pain and morphine consumption after cardiac surgery. They found that oral gabapentin given before cardiac surgery significantly reduced postoperative morphine consumption and postoperative pain.

The same results were obtained by Chetna *et al.* [20]. They found that patients in the gabapentin group had statistically significant lower pain score and significantly less tramadol consumption until 24 h postoperatively compared with the placebo group in upper abdominal surgeries.

Conclusion

Preoperative oral gabapentin (1200 mg) augments the hypotensive effect of nitroglycerin as it provides dryness of surgical field associated with lower infusion rate of nitroglycerin. Also, it has better analgesic effect with lower narcotic consumption during controlled hypotensive anesthesia for nasal surgeries when compared to the administration of nitroglycerin alone.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Valentine R, Wormald PJ. Carotid artery injury after endonasal surgery. *Otolaryngol Clin North Am* 2011; **44**:1059–1079.

2 Pineiro-Aguilar M, Somoza-Martin JM, Gandara R, *et al.* Blood loss in orthognathic surgery: a systematic review. *J Oral Maxillofac Surg* 2011; **69**:885–892.

3 Sutherasan Y, Vargas M, Pelosi P. Protective mechanical ventilation in the non-injured lung: review and meta-analysis. *Crit Care* 2014; **18**:211.

4 Degoute CS. Controlled hypotension: a guide to drug choice. *Drugs* 2007; **67**:1053.

5 Thomas M, Sebastian S, Andreas D. Organic nitrates: update on mechanisms underlying vasodilation, tolerance and endothelial dysfunction. *Vascul Pharmacol* 2014; **63**:105–113.

6 Gottrup H, Juhl G, Kristensen AD. Chronic oral gabapentin reduces elements of central sensitization in human experimental hyperalgesia. *Anesthesiology* 2004; **101**:1400–1408.

7 Fromme GA, MacKenzie RA, Gould AB, Lund BA, Offord KP. Controlled hypotension for orthognathic surgery. *Anesth Analg* 1986; **65**:683–686.

8 Fassoulaki A, Melemeni A, Paraskeva A, Petropoulos G. Gabapentin attenuates the pressor response to direct laryngoscopy and tracheal intubation. *Br J Anaesth* 2006; **96**:769–773.

9 Prasant MC, Kar S, Rastogi S, *et al.* Comparative study of blood loss, quality of surgical field and duration of surgery in maxillofacial cases with and without hypotensive anesthesia. *J Int Oral Health* 2014; **6**:18–21.

10 Raghavendra TR, Yoganarasimha N, Shivakumar A, *et al.* Deliberate controlled hypotension in functional endoscopic sinus surgeries: a comparative study between nitroglycerin and esmolol. *Karnataka Anaesth J* 2016; **2**:54–58.

11 Soliman R, Zohry G. Assessment of the role of gabapentin in patients with supratentorial tumors undergoing craniotomy under general anaesthesia: a double-blind randomized study. *J Neuroanaesthesiol Crit Care* 2017; **4**:147–154.

12 Mausumi N, Santanu B, Debasis G, *et al.* A randomized double-blind placebo-controlled clinical study on the effects of gabapentin premedication on hemodynamic stability during laparoscopic cholecystectomy. *J Anaesthesiol Clin Pharmacol* 2012; **28**:4.

13 Farnoush F, Soudabeh H, Neda E, *et al.* A survey on the effect of oral gabapentin on hemodynamic changes during direct laryngoscopy and

tracheal intubation and intraoperative bleeding in patients undergoing septorhinoplasty. *Anesth Pain Med* 2015; **5**:e29705

14 Mahmoud HM, Adel MF, Karim YKH. Preoperative gabapentin augments intraoperative hypotension and reduces postoperative opioid requirements with functional endoscopic sinus surgery. *Egypt J Anaesth* 2012; **28**:189–192.

15 Marouf HM, Khalil NK. Effect of preoperative pregabalin on induced hypotension and postoperative analgesia with functional endoscopic sinus surgery. *J Anesth Clin Res* 2017; **8**:12.

16 Darius Č, Juozas I. Application of controlled arterial hypotension in endoscopic rhinosurgery. *Medicina* 2003; **39**:9.

17 Chandra KP, Deepa VN, Pramod JG, *et al.* Evaluation of the optimal preemptive dose of gabapentin for postoperative pain relief after lumbar discectomy, a randomized, double-blind, placebo-controlled study. *J Neurosurg Anesthesiol* 2005; **17**:65–68.

18 Ajit SR, James SK, Jasneet D, *et al.* Preoperative pregabalin or gabapentin for acute and chronic postoperative pain among patients undergoing breast cancer surgery: a systematic review and meta-analysis of randomized controlled trials. *J Plast Reconstr Aesthet Surg* 2017; **70**:1317–1328.

19 Ferdi M, Özge K, Murat S, *et al.* Effects of single-dose gabapentin on postoperative pain and morphine consumption after cardiac surgery. *J Cardiothorac Vasc Anesth* 2010; **24**:808–813.

20 Chetna AJ, Rashida J, Manoj K. Pre-emptive use of gabapentin for post-operative pain relief in upper abdominal surgeries. *Indian J Pain* 2014; **28**:2.