

A Comparison between single-dose pregabalin and magnesium sulfate in induced hypotension during functional endoscopic sinus surgery: A prospective randomized double-blinded study

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Abstract

Background: Functional Endoscopic sinus surgery (FESS) is a surgical intervention during which controlled hypotension can improve visibility. Magnesium sulfate is used for controlled hypotension. Pregabalin is also effective in hypotensive anesthesia.

Objectives: This study aimed to detect the effect of single preoperative oral pregabalin versus intravenous magnesium sulfate to facilitate induced hypotension during functional endoscopic sinus surgery.

Patients and methods: In a randomized, double-blind, prospective study, 60 patients of either sex were divided into 2 equal groups. Group P received an oral pregabalin capsule of 150 mg 30 minutes before general anesthesia. Group M received a single-dose 2 grams of magnesium sulfate 30 minutes before induction of anesthesia. The primary outcome was the total intraoperative consumption of nitroglycerin required to maintain the mean arterial blood pressure (MAP) at the range of 55– 65 mmHg. The secondary outcomes were the quality of the surgical field assessed by the Fromm and Boezaart grading scale, surgeon satisfaction assessed by the five-point Likert scale, and the visual analog pain scores (VAS).

Results: The pregabalin group P showed statistically significant lower nitroglycerine doses (1.3 ± 1.2 mg) compared to group M (3.3 ± 1.5 mg) with a P value of <0.001 . The surgical field quality and the surgeon satisfaction scales showed statistically significant better scores in group P (1.7 ± 0.6 and 5 ± 0.6 respectively) than in group M (3.2 ± 0.9 and 2.1 ± 0.6 respectively) with P values of (0.023 and 0.001 respectively). The VAS showed statistically significant lower scores in group P (1.3 ± 0.9) compared with group M (3.4 ± 0.6) with a p value= 0.001.

Conclusion: A single preoperative pregabalin dose was more effective than magnesium sulfate in reducing the total intraoperative consumption of nitroglycerin. It also provides a dryer surgical field that achieves better surgeon satisfaction and provides postoperative analgesia.

Keywords: Induced hypotension; FESS; Magnesium sulfate; Pregabalin; Single dose.

DOI: 10.21608/svuijm.2022.180059.1470

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Received: 12 December, 2022.

Revised: 17 December, 2022

Accepted: 28 December, 2022.

Published: 7 June, 2023

Cite this article as: Sarah M. Omar Mousa, Eman Gamal Hassan, Khalid Ahmed Abdo. (2023). A Comparison between single-dose pregabalin and magnesium sulfate in induced hypotension during functional endoscopic sinus surgery: A prospective randomized double-blinded study. *SVU-International Journal of Medical Sciences*. Vol.6, Issue 2, pp: 380-388 .

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Introduction

It is the prime concern of every surgeon during functional endoscopic sinus surgery to delineate the anatomy and, thus, the need for a bloodless operative field achieved by induced hypotension, which produces a controlled and safe reduction in arterial blood pressure while preserving organ perfusion by reducing the mean arterial blood pressure (**Tegegne et al., 2021**).

Magnesium sulfate is a well-known hypotensive and premedication agent. It is used in different surgical procedures, as it decreases anesthetic, analgesic, and muscle relaxant requirements (**Rokhtabnak et al., 2017**). Pregabalin is a gamma-aminobutyric acid (GABA) analog. GABA reduces the excitability of the brain neurons, which plays a role in seizures and pain signals transmission (**Naguib et al., 2020**). Pregabalin got approval from the Food and Drug Administration (FDA) in 2004 and is used to treat pain and seizures (**Bidari et al., 2019**).

The study aimed to estimate the effect of single-dose oral pregabalin versus intravenous magnesium sulfate as premedication on total intraoperative nitroglycerin consumption required to maintain the mean arterial blood pressure at 55–65 mmHg during FESS. The quality of the surgical field and surgeon satisfaction were assessed as well.

Patients and methods

Eligibility of the study

After obtaining approval from the Faculty of Medicine, El Minia University ethical committee (55:2021), and written consent from all patients, this study was registered at Clinical Trial Gov. (ID: [NCT05442931](https://clinicaltrials.gov/ct2/show/study/NCT05442931)) and

conducted on 60 patients of both sexes, ASA physical status I or II and scheduled for FESS in the period from July 2022 to November 2022 at El Minia University Hospital.

Exclusion criteria

The Patients on pregabalin, gabapentin, anticonvulsants, antipsychotics, or any analgesics within 48 h before surgery were excluded from the study. The Patients with a history of allergy to the study drugs, pregnant or breastfeeding women, hypertensive, suffering from endocrinal disease, bleeding abnormalities, cardiac, hepatic, or renal impairment were excluded.

Study design, randomization, and blinding

The patients were grouped into two equal groups of thirty each in this prospective randomized, double-blind study based on a randomization computer-generated table using Microsoft Excel by a statistician. The grouping paper was put in a sealed opaque envelope to cover the allocation. For blinding, the study medications were prepared and given to the patients by an anesthesiologist other than the investigator, who was blinded to the study drugs half an hour before surgery.

The surgeon was also blind to the study medications. After the study ended, it was revealed that P stood for the pregabalin group (received a tablet of pregabalin 150 mg orally, in addition to 100 ml normal saline IV). Group M was the magnesium sulfate group (received 2 g of magnesium sulfate in 100 ml saline).

Technique

In the preparation room, all patients were cannulated. The study medications were introduced to the patients 30 min before

induction by an anesthetist other than the investigator. Pregabalin 150 mg (LYRICA, Pfizer, USA) orally plus 100 ml saline IV was given to group P patients. Patients in group M received 2 gm magnesium sulfate (Magnesium Sulfate, EIPICO, Egypt) in 100 ml saline infusion over 10 minutes.

In the operating room, the investigator anesthetized all patients with propofol 2 mg/kg, nalbuphine 0.2 mg/kg, and atracurium 0.5 mg/kg. Face mask ventilation was for 3 minutes, then the patient was intubated with the appropriate-sized endotracheal tube. Routine monitoring was applied as ECG, pulse oximetry, and noninvasive arterial blood pressure. Arterial cannulation and invasive arterial blood pressure monitoring were involved as well.

Nitroglycerin (Nitronal 1mg/ml. Pohl-Boskamp, Germany) was infused by an infusion pump (50 mg in 50 ml volume) starting with 0.5µg/kg/min. Surgery was performed in the two groups with a MAP range of 55- 65 mmHg by titration of nitroglycerine infusion. It was maintained until the end of the operation, and the total nitroglycerin consumption (mg) was recorded.

During the operation, blood loss was recorded, and the surgeon blinded to the study medications was asked to evaluate his satisfaction by the 5-point Likert scale (5: excellent, 4: Good, 3: Satisfactory, 2: Poor, and 1: Very poor). The surgeon estimated intraoperative bleeding by rating the amount of bleeding based on Fromm and Boezart's scale for the evaluation of operative field visibility during the surgery, demonstrating 0: no bleeding, 1: slight bleeding, (blood evacuation is not necessary); 2: slight

bleeding, (some blood should be evacuated); 3: light bleeding, (blood should be frequently evacuated as the operative field is visible only briefly after the evacuation); 4: average bleeding, (blood should be often evacuated as the operative field is visible only immediately after the evacuation); and 5: active bleeding, (constant blood evacuation is needed as bleeding often exceeds the evacuation resulting in rendering the surgery nearly impossible). One hour postoperatively, the visual analog pain score, Ramsay sedation score, and Aldrete recovery score were recorded. We followed up on the lab investigations in the first 24 h, and the patient's discharge date from the hospital was also recorded.

Sample size calculation

The count of participants required in each group in this study was calculated after data was collected from a pilot study. The mean intraoperative nitroglycerin consumption was 0.57±0.05 in the pregabalin group and 0.65±0.1 µg/kg/min in the magnesium sulfate group.

In each group, a sample size of 27 patients will be needed to provide 95% power for the t-test at 5% significance. It had been increased to 30 patients for better accuracy.

The sample size was calculated using the PASS program (Power Analysis and Sample Size Calculation) by NCSS, LLC, USA (Mazy and Abo-Zeid, 2020).

Statistical analysis

The data analysis was done using the IBM SPSS 28.0 statistical package software (IBM; Armonk, New York, USA). The data normality was tested using the Kolmogorov-Smirnov test. Data were expressed as

mean±SD, minimum, and maximum range for quantitative measures, in addition to both number and percentage for categorized data. The student t-test for the parametric data and the Mann-Whitney U test for the non-parametric data were used to compare two independent groups. The dependent sample t-test was used for dependent non-parametric data. The Chi-square or the exact Fisher's tests were used to compare the categorical variables. A p-value < 0.05 was considered significant.

Results

The current study included 60 patients randomly allocated into two equal groups of thirty patients each, as shown in the Consort flow chart (**Fig.1**). There had been no statistically significant differences between the study groups as regards demographic data, ASA classification, weight, and the duration of the surgery, as shown in (**Table .1**). The patients in the two groups showed statistically insignificant differences as regards hemodynamic data (heart rate, blood pressure, and oxygen saturation) throughout the study period.

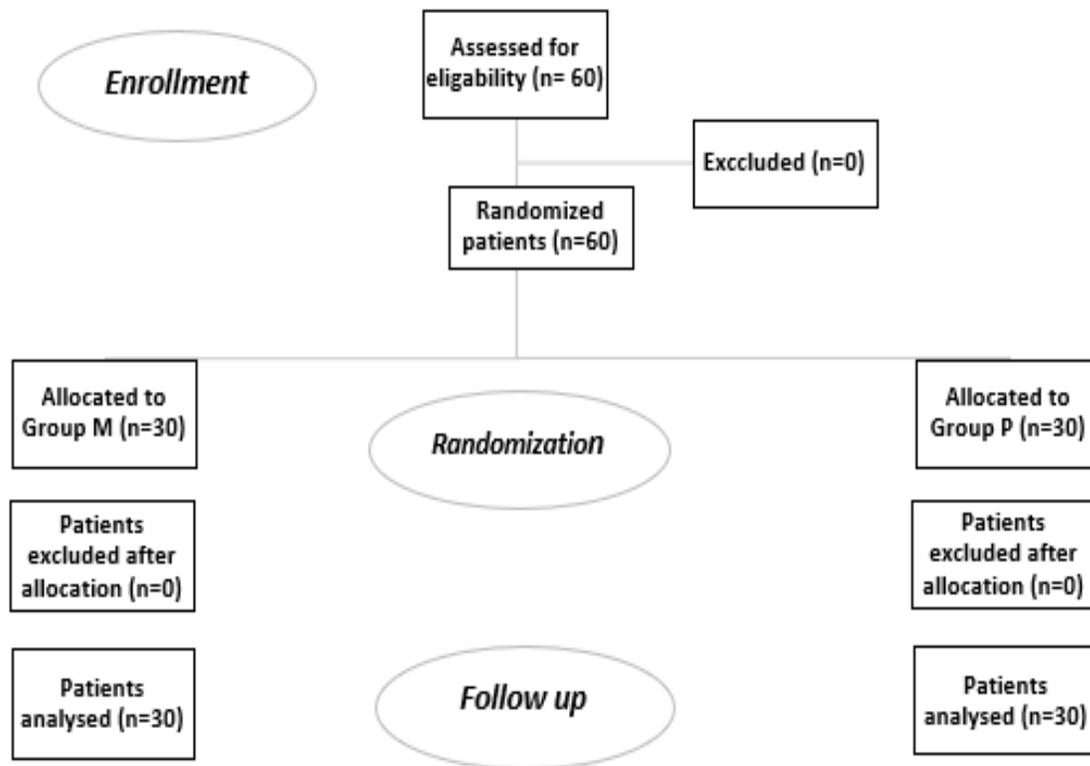


Fig.1. Consort flow chart

Table 1. The demographic and operative data of the two groups

Variables	Group P (N=30)	Group M (N=30)	P value
Age yr (mean±SD) Range	37±11.6 (18-60)	37±13.2 (18-65)	00.992
Sex (n. %) Male Female	14 (46.7%) 16 (53.3%)	16 (53.3%) 14 (46.7%)	1.0
ASA classification (n. %) I II	26 (86.7%) 4 (13.3%)	24 (80%) 6 (20%)	00.488
Body weight Kg (mean±SD) Range	75±11.6 (60-110)	73.6±10.2 (50-100)	00.629
Duration of surgery min (mean±SD) Range	83±23.9 (50-120)	85.7±19.5 (60-120)	0.638

SD: standard deviation -yr: years -n: number -%: percentage. - min: minutes Numerical data are expressed as mean ± standard deviation and range. Categorical data are presented as numbers (percentages). Student's t-test for continuous variables and Chi-square (χ^2) test for categorical variables.

(Table.2) and (Fig.2) show that total nitroglycerin consumption in milligrams was significantly less in group P when compared with group M, with a P value <0.001.

Table 2. Total intraoperative nitroglycerin consumption

Variables	Group P (N=30)	Group M (N=30)	P value
Total nitroglycerin dose (mg) mean±SD Range	1.3±1.2 (1-5)	3.3±1.5 (3-6)	<0.001*

SD: standard deviation, mg: milligram, N: number. The numerical data are expressed as mean ± standard deviation and range. Independent sample t-test for comparison between the 2 groups. * p-value considered significant at <0.05.

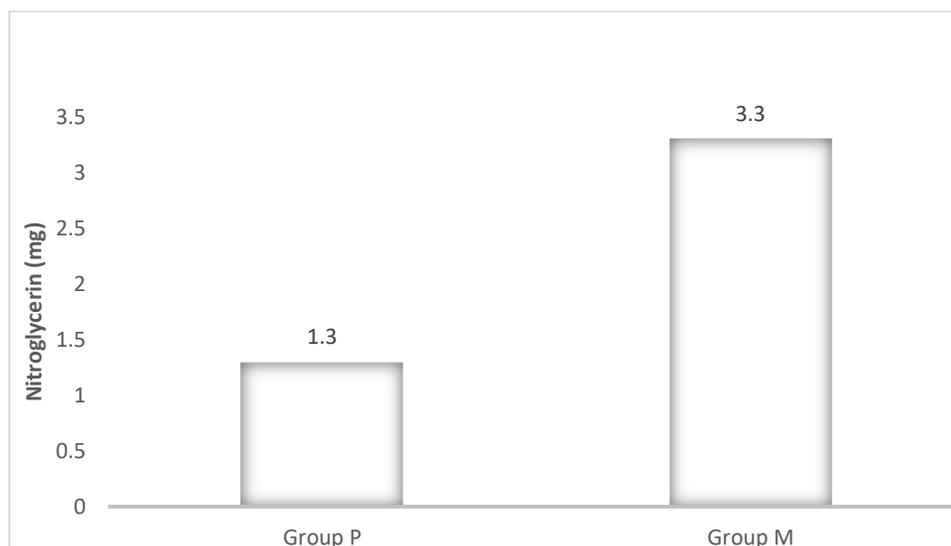


Fig.2. Total Nitroglycerin consumption

(Fig.3) shows the Fromm and Boezaart scale for evaluating operative field visibility during the surgery in the two groups. There was statistically significantly better field visualization in group P, with scores ranging (1-2) 1.7 ± 0.6 for group P and (1-5) 3.2 ± 0.9 for group M, with a P value = 0.023.

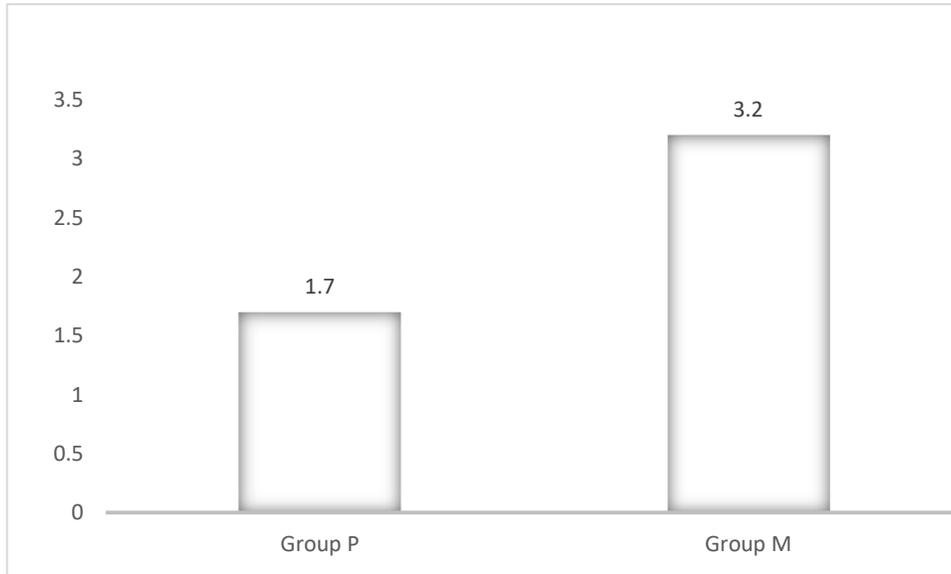


Fig.3. Fromm and Boezaart scale mean scores

The five- points Likert scale scores to evaluate the surgeon’s satisfaction are shown in (Fig.4) The range is (3-6) 5 ± 0.6 for group P and (2-3) 2.1 ± 0.6 for group M with a P value = 0.001 (the surgeon was more satisfied in group P).

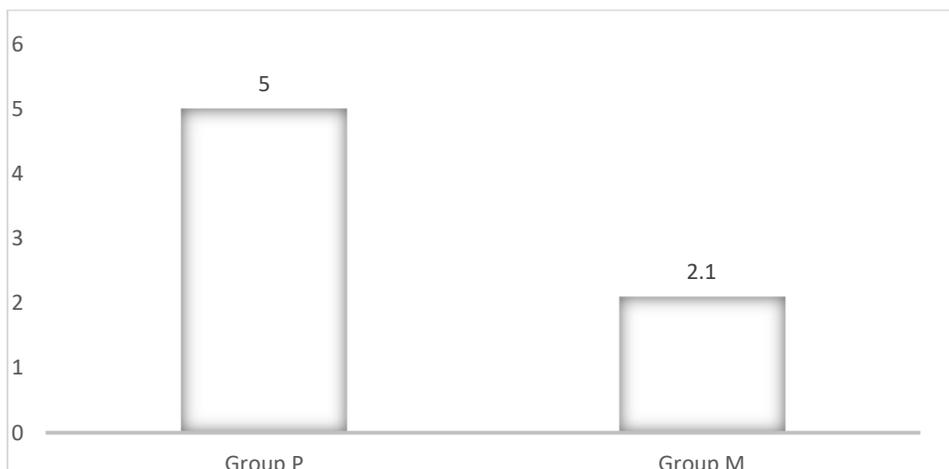


Fig.4. The five-point Likert scale mean scores in the study groups

The postoperative pain scores assessed by the visual analog pain scale were statistically

significantly less in group P compared to group M with a p-value < 0.05, as shown in (Fig.5).

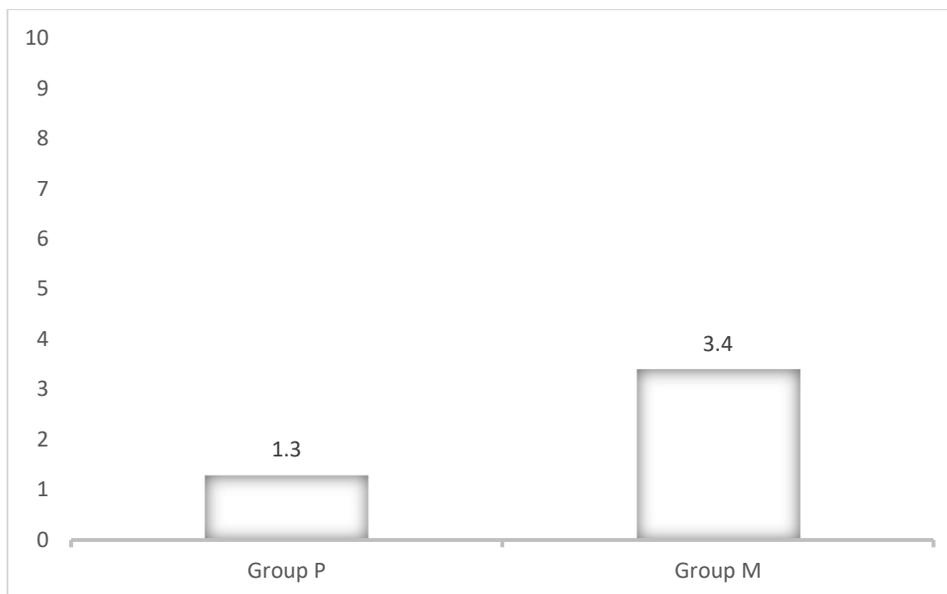


Fig.5. The visual analog pain scores in the study groups

The Ramsay sedation and Aldrete recovery scores showed statistically insignificant differences between the study groups. The lab investigations in the first 24 h and the patient's discharge date were comparable between the two groups with a p-value >0.05.

Discussion

The present study revealed that preoperative oral pregabalin is more effective than intravenous magnesium sulfate in facilitating induced hypotension during FESS evaluated by the total intraoperative consumption of nitroglycerin required to maintain the MAP at the range of 55– 65 mmHg, with better operative field visibility evaluated by the Fromm and Boezaart scale and higher surgeon's satisfaction scores assessed by the Likert scale.

These results were supported by **Marouf and Youssef (2017)**, who studied 80 patients ASA I-II who underwent FESS in

randomized research. Patients were divided into 2 groups. They received either placebo capsule group C or pregabalin capsule 150 mg group P 1 h preoperatively.

During surgery, MAP was maintained between 55-60 mmHg by intravenous nitroglycerin infusion. They recorded the quality of the surgical site and the overall dose of NTG used. In their study, the pregabalin group P showed better quality of the surgical site and a lower overall amount of NTG used than the control group C.

Elsayed (2020) achieved the same results in his double-blind, randomized clinical study, including 80 ASA I-II patients scheduled for dacryocystorhinostomy under local anesthesia. The study enrolled two groups, either receiving a 300mg pregabalin capsule in the first group or a placebo capsule in the control group one hour before surgery. Mean

arterial blood pressure was maintained with nitroglycerin infusion. The visibility of the operative field was assessed by the Fromm and Boezaart scale and the total requirement of nitroglycerin administration. The pregabalin group showed better field visualization and less total dose of nitroglycerin required than the control group.

The results of **Hadavi et al. (2022)** in their prospective, randomized, double-blinded placebo-controlled trial on 105 patients who underwent rhinoplasty, were randomly allocated into three groups. Patients in group A received 300 mg pregabalin before anesthesia, those in group B received intravenous Mg sulfate 30 mg/kg, and group C received a placebo capsule. Pain severity and sedation score were assessed and compared. In this study, the Mg sulfate and placebo groups showed higher pain scores in the postoperative period compared to the pregabalin group ($p < .001$); this is the same as our result. Unlike our results, the Ramsay sedation score was significantly decreased in the pregabalin group compared to the other groups ($p < .001$). It is explained by the higher pregabalin dose used by **Hadavi et al. (2022)** 300mg versus 150mg, used in our study.

Conclusion

Preoperative oral pregabalin decreased the total dose of intraoperative nitroglycerin, improved the quality of the surgical site, and caused perfect surgeon satisfaction during FESS without unusual complications.

Study's limitations

The study did not compare different doses of pregabalin to detect the exact amount that gives the maximum beneficial effects with the most negligible side effects. However, this may be a point for further investigation

References

- **Bidari A, Moazen-Zadeh E, Ghavidel-Parsa B, Rahmani S, Hosseini S, Hassankhani A. (2019).** Comparing duloxetine and pregabalin for the treatment of pain and depression in women with fibromyalgia: an open-label randomized clinical trial. *Daru: journal of Faculty of Pharmacy, Tehran University of Medical Sciences*, 27(1): 149–158.
- **Elsayed A. (2020).** Effect of Pre-emptive Pregabalin on Deliberate Hypotension, Postoperative Pain, and Analgesic requirements for Patients Undergoing Dacryocystorhinostomy Surgery under Local Anesthesia. *Journal of Anesthesia and Intensive Care Medicine*, 11:110-114.
- **Hadavi SMR, Eghbal MH, Kaboodkhani R, Alizadeh N, Sahmeddini MA. (2022).** Comparison of pregabalin with magnesium sulfate in the prevention of remifentanyl-induced hyperalgesia in patients undergoing rhinoplasty: A randomized clinical trial. *Laryngoscope Investigative Otolaryngology*, 7 (5): 1360- 1366.
- **Marouf H , Youssef N. (2017).** Effect of Preoperative Pregabalin on Induced Hypotension and Postoperative Analgesia with Functional Endoscopic Sinus Surgery. *Journal of Anesthesia & Clinical Research*, 8: 10- 15.
- **Mazy A, Abo-Zeid M. (2020).** Pregabalin effects on hypotensive anesthesia during spine surgery. *Research and Opinion in Anesthesia and Intensive Care*, 7. 161-166.
- **Naguib I, Ali N, Elroby F, Elghobashy M, Abdallah F. (2020).**

Ecologically evaluated and FDA-validated HPTLC Method for Assay of Pregabalin and Tramadol in Human Biological Fluids. *Biomedical Chromatography*, 35(4).

- **Rokhtabnak F, Djalali Motlagh S, Ghodraty M, Pournajafian A, Maleki Delarestaghi M, Tehrani Banihashemi A, et al. (2017).** Controlled Hypotension During Rhinoplasty: A Comparison of Dexmedetomidine with Magnesium Sulfate. *Anesthesiology and Pain Medicine*, 7: 6- 13.
- **Tegegne SS, Gebregzi AH, Arefayne NR. (2021).** Deliberate hypotension as a mechanism to decrease intraoperative surgical site blood loss in a resource-limited setting: a systematic review and guideline. *International Journal of Surgery Open*, 1; 29:55-65.