Hemodynamic and analgesic aspects in conscoius sedation for chronic subdural hematoma evacuation: a rendomized controlled comparison between magnesium sulphate versus fentanyl

Rania S. Fahmy, Amal A. Elsawy, Maha Mostafa, Ahmed Hasanin, Tarek Radwan, Nasr M. Abdallah

Department of Anesthesia and Critical Care Medicine, Cairo University, Cairo, Egypt

Correspondence to Rania S. Fahmy, MD/PhD, 13 Massara Street, Shoubra, Cairo 11231, Egypt. Tel: +20 127 082 0372; e-mail: ransam98@gmail.com

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Objectives

Subdural hematoma evacuation has been performed under general anesthesia, local anesthesia, and conscious sedation, though the adequacy of any of those techniques on its own is questionable. We aimed to compare the hemodynamic and analgesic effects of magnesium sulfate versus fentanyl as adjuncts to propofol-induced conscious sedation in patients subjected to chronic subdural hematoma (CSDH) evacuation with local infiltration.

Patients and methods

In this randomized controlled trial, we included adult patients with CSDH undergoing evacuation through burr-hole surgery. All patients received continuous infusion of propofol. Patients in the magnesium group (n=16) received magnesium sulfate (loading dose of 50 mg/kg and then continuous infusion at 15 mg/kg/h). Patients in the fentanyl group (n=16) received fentanyl (loading dose: 1 μg/kg and then continuous infusion at 0.5 μg/kg/h). The primary outcome was intraoperative systolic blood pressure. The secondary outcomes included incidence of hypotension and bradycardia, the total dose of propofol, time to awake, and the incidence of postoperative nausea and vomiting.

Results

A total of 32 patients were analyzed. The average intraoperative systolic blood pressure was better maintained in the magnesium group. Furthermore, the incidence of hypotension, nausea, and vomiting was lower in the magnesium group. The time to awake was shorter in the magnesium group. The incidence of bradycardia, total propofol requirements, time to first rescue analgesia, and surgeon satisfaction were comparable between groups.

Conclusion

Magnesium sulfate was associated with a better hemodynamic profile and less incidence of nausea and vomiting in comparison with fentanyl when combined with propofol for conscious sedation during CSDH evacuation. It produced an anesthetic-sparing effect comparable to fentanyl.

Keywords:
burr-hole surgery, chronic subdural hematoma, conscious sedation, fentanyl, magnesium sulfate, propofol

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Introduction

Chronic subdural hematoma (CSDH) is a commonly occurring intracranial hemorrhage that needs evacuation by burr-hole surgery [1]. General anesthesia is more hazardous, especially when considering elderly patients. On the contrary, patients might not be tolerant to local anesthesia solely, which may have a negative effect on the surgical conduct. Local anesthesia with supplementary sedation is a reasonable anesthetic choice for this procedure [2]. Inadequate sedation during this procedure would result in patient movements and noncooperation, which impairs surgical conditions. Patient straining would result in bulging of the brain and hypertension, which increase the risk of cerebral edema, infarction, and postoperative reaccumulation of the hematoma [3].

Drug choice for patient sedation during the evacuation of CSDH would help in optimizing patient comfort and provide good surgical conditions. Being a short-acting, potent anesthetic agent, with excellent recovery, propofol is commonly used for conscious sedation in various procedures.

The most common disadvantages of propofol are respiratory and cardiovascular depression, which are more prominent in elderly patients [4]; hence, using analgesic and sedative adjuvants would help to decrease propofol requirements and minimize its adverse effects.

Fentanyl as a potent opioid has been used as an adjunct to propofol for conscious sedation in awake cranial surgeries [5]. However, the propofol–fentanyl combination poses a higher risk of hypotension [6]. Furthermore, being an opioid, fentanyl increases the possibility of postoperative nausea and vomiting [7], which is a distressing adverse effect that could postpone patient discharge and increase hospital stay.

Magnesium sulfate is a multiuse drug with favorable anesthetic and analgesic effects owing to its N-methyl-D-aspartate receptor antagonistic action in the central nervous system. Besides, it was found to have a sedative effect, which was thought to be a resultant of central nervous system depression [8]. Furthermore, it alters hemodynamic response to stress due to its inhibitory effect on catecholamines release as well as its vasodilatory and antiarrhythmic effects [9].

After thorough literature search, magnesium sulfate infusion as adjunct to propofol sedation during cranial surgery for CSDH through burr-hole surgery has not been investigated before. This study aimed to assess and compare the hemodynamic and analgesic of magnesium sulfate versus fentanyl for conscious sedation in patients undergoing evacuation of subdural hematoma with local infiltration.

Patients and methods

This randomized, triple-blinded, controlled study was conducted after Institutional Research Ethics Committee approval (N28-2018) and after clinical trial registration (NCT03854812). The study involved patients with CSDH subjected to evacuation through burr-hole surgery under local infiltration during the period from March to October 2019. The patients undergoing the operative procedure or their proxy provided a written informed consent after thorough explanation of the surgical and anesthetic procedures.

The study included patients undergoing unilateral CSDH, above the age of 50 years, ASA physical status I and II, and Glasgow coma scale ranging 14–15. Patients presenting with any of the following were excluded from the study: bradycardia (<50 bpm), ischemic heart disease, heart block of the second and third degree, opioid addiction or habituation, dependance on sedative-hypnotic drugs for more than 6 months, allergy to study drugs, and neuropsychiatric diseases. In addition, patients with predicted difficult airway, defined as Ganzouri score more than 4 [10], and patients with a history of obstructive sleep apnea were also excluded. Patients with unconventional surgical procedure or with inadequacy of local anesthesia were excluded from the study. Randomization was achieved by a computer-generated sequence of codes. The patient, surgeon, and outcome assessor were blinded to the patient group.

Anesthetic management

Upon arrival to the operating room, standard monitors were applied. Oxygen supplementation at FiO_2 of 0.35 was achieved. Bispectral index (Covdien BIS VISTA by Aspect medical systems) was used to assess the conscious level during the operation.

The magnesium group (n=16) received a loading of 50 mg/kg in 100 ml of normal saline over 15-min of magnesium sulfate [magnesium sulfate 100 mg/ml (0.41 mmol/ml)], followed by continuous infusion at 1 ml/kg/h of 15 mg/ml solution [11].

The fentanyl group (n=16) received a loading of 1 μg/kg of fentanyl (fentanyl 50 μg/ml by Hamelin Pharmaceuticals, Hamelin, Germany) in 100 ml of normal saline over 15-min followed by continuous infusion starting at 1 ml/kg/h of 0.5 μg/ml solution.

To achieve a Ramsay sedation scale (RSS) [9] of 3 (respond to command), both groups were given a bolus dose of propofol (0.5–1.5 mg/kg), and an additional dose of propofol (0.2 mg/kg) was given if the target RSS of 3 was not achieved. The propofol was then given as a continuous infusion (1–2.5 mg/kg/h) to a target intraoperative BIS reading ranging from 60 to 80.

After reaching RSS of 3, the surgeon infiltrated the surgical site with local anesthetic (bupivacaine–lidocaine–epinephrine) 5 min before surgical incision. Following burr-hole craniotomy, the dura was anesthetized with pledgets soaked in lidocaine; 5 min afterward, the dura was incised, and the hematoma was evacuated. Sedative infusions were discontinued after skin closure.

Distressing patient movements during the operation (defined as movements which may impact the surgical procedure such as winding the upper and/or lower extremities and head movement) [2] were first addressed by comforting the patients and supporting them. If there was no response and the movements persisted, 0.5 mg/kg of propofol was given as a bolus dose followed by increasing the propofol infusion rate to 2.5 mg/kg/h to retain the target BIS score ranging from 60 to 80.

Hypertensive episodes occurring when systolic blood pressure more than 25% from baseline were managed by giving nitroglycerine (0.1–10 μg/min), whereas hypotensive episodes occurring when systolic blood pressure less than 25% from baseline were managed by giving ephedrine (5 mg). Postoperative pain intensity was assessed using the visual analog scale (VAS), and ketorolac (30 mg) was administered if the VAS exceeded 3.

Outcomes

Intraoperative blood pressure may increase owing to sympathetic stimulation ensuing from pain and anxiety. Sympathetic stimulation results in increased systemic vascular resistance with systolic and diastolic hypertension [12,13]. On the contrary, intraoperative systolic hypertension is thought to increase the incidence of postoperative hematoma in cranial surgeries [14]. Hence, the primary outcome was chosen as the average intraoperative systolic blood pressure. The secondary outcomes included incidence of hypotension, hypertension, bradycardia, tachycardia, total ephedrine, nitroglycerine, and atropine dose, the total amount of propofol utilization, the total number of intraoperative patient's movements, and time to awake (defined as the time from discounting drug infusion to regain of baseline conscious level).

Heart rate and systolic blood pressure were recorded at baseline; after induction of conscious sedation; at skin incision; at 1, 2, 5, 10, and 15 min after skin incision; and then every 15-min intraoperative. Postoperatively, the heart rate and systolic blood pressure were recorded at 15, 30 min, 1, 2, 3, and 6 h.

After the conclusion of the surgery, surgeon satisfaction score was assessed as follows: 1 denoting extremely dissatisfied surgeon, 2 denoting that the surgeon is not satisfied but can manage, 3 denoting that the surgeon is satisfied, and 4 denoting an extremely satisfied surgeon.

RSS was recorded at 15, 30, and 60 min postoperatively. VAS was recorded at 15, 30 min, 1, 2, 3, and 6 h postoperatively. Time to first rescue analgesia in the first 24 h following the surgery and the incidence of postoperative nausea and vomiting were also recorded.

Sample size calculation

Our primary outcome was average systolic blood pressure during the intraoperative period. In a pilot study on six patients, the average intraoperative systolic blood pressure was 110±10 mmHg. The sample was calculated by means of MedCalc (14.10.2) software to detect a mean difference of 10% (i.e. 11 mmHg) between both groups. A minimum number of 28 patients (14 patients per group) were needed to achieve a study power of 80% and an alpha error of 0.05. The number of envelopes was increased to 32 to compensate for possible dropouts.

Statistical analysis

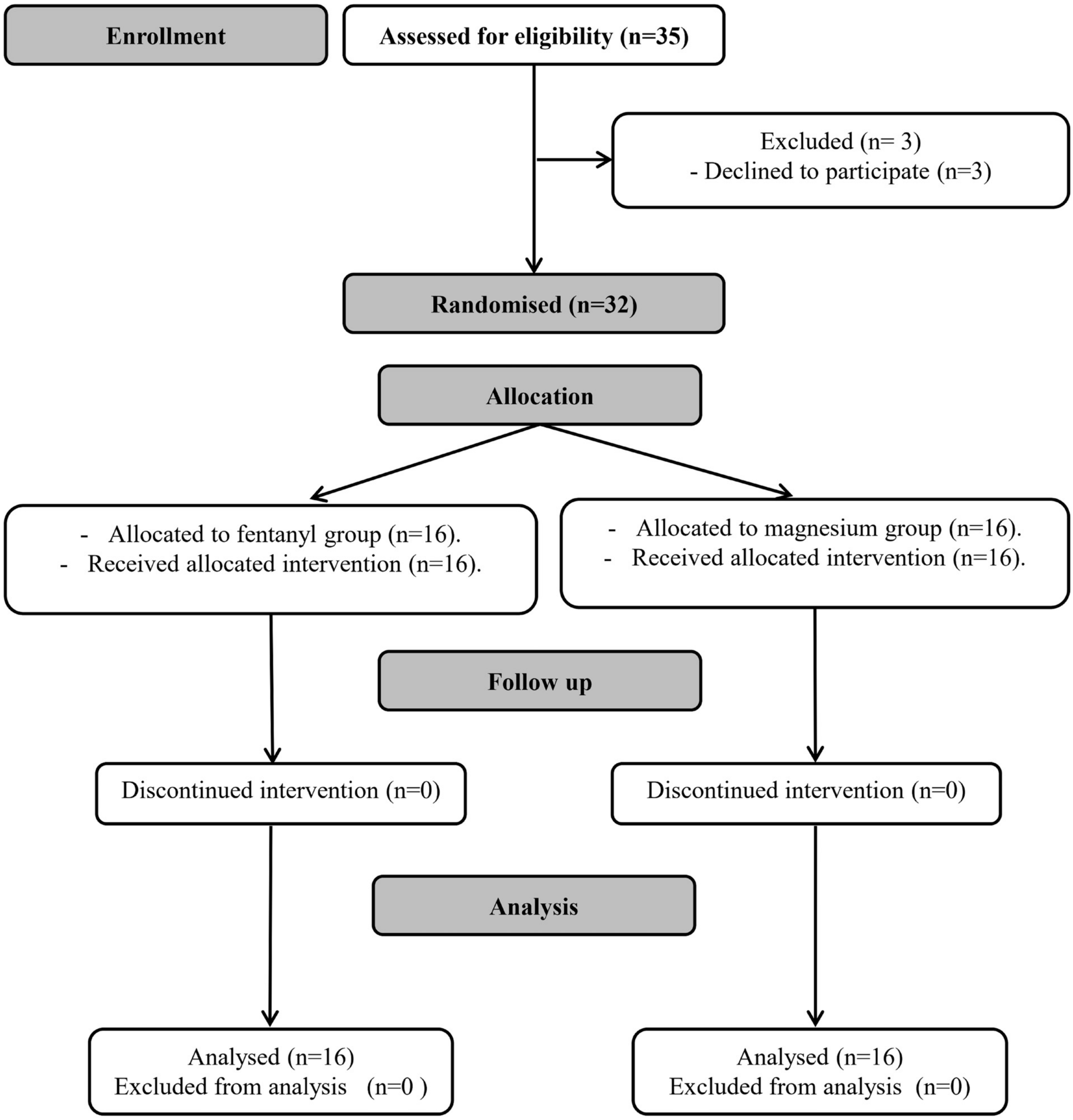
Statistical analysis was done using SPSS, version 23 (IBM Corp., Armonk, New York, USA). Categorical data were presented as frequency and were analyzed using the χ^2 test. Continuous data were checked for normality using the Shapiro–Wilk test. Normally distributed data were expressed as means (SDs), and skewed data were expressed as medians (interquartile range). Unpaired continuous data were analyzed using the unpaired Student's *t* test or the Mann–Whitney *U* test as appropriate. When evaluating repeated measures, a two-way repeated measure analysis of variance was used to assess drug (between-group factor) and time (repeated measures). We analyzed the repeated measures for 60 min intraoperatively (shortest intervention time). The Bonferroni test was used to adjust for multiple comparisons. A *P* value less than 0.05 was considered significant.

Results

A total of 35 patients with CSDH were screened for eligibility. Three patients were excluded due to refusal to participate in the study and 32 patients were included (16 patients in each group). None of the included patients required conversion to general anesthesia, and all of the 32 patients were available for the final analysis (Fig. 1). Upon analysis, the demographic data and the baseline hemodynamics were comparable between groups (Table 1).

The average intraoperative systolic blood pressure was higher in the magnesium group than in the fentanyl group. Furthermore, the incidence of hypotension and ephedrine consumption was lower in the magnesium group than in the fentanyl group (Table 2). In both groups, systolic blood pressure readings were lower

Figure 1



Patients' enrolment flow chart.

Table 1 Demographic data and baseline hemodynamics

	Fentanyl group (*N*=16)	Magnesium group (*N*=16)	*P* value
Age (years)	63 (8)	61 (8)	0.501
Weight (kg)	78 (9)	77 (7)	0.825
Male sex	10 (63)	11 (69)	1
GCS	15 (14, 15)	15 (14, 15)	1
Baseline HR (bpm)	89 (10)	88 (11)	0.842
Baseline SBP (mmHg)	149 (16)	152 (15)	0.517

Data are presented as mean (SD), median (quartiles), and frequency (%). GCS, Glasgow coma scale; HR, heart rate; SBP, systolic blood pressure.

than the baseline reading intraoperatively and then became comparable to the baseline reading postoperatively (Fig. 2).

The heart rate was generally lower than the baseline reading in both groups (Fig. 3). Furthermore, intraoperative heart rate and incidence of bradycardia were comparable between both groups (Table 2). None of the included patients had hypertension, tachycardia, or seizure.

Intraoperative persistent movements, the need for propofol top-up, total propofol requirements, time to first rescue analgesia, and surgeon satisfaction were comparable between both groups. (Table 2).

The time to be awake was likely to be shorter in the magnesium group than in the fentanyl group [median (quartiles): 30 (19, 60) min and 60 (30, 60), respectively, *P* value: 0.057]. The incidence of postoperative nausea and vomiting was lower in the magnesium group than in the fentanyl group [three (19%) patients and 16 (100%) patients, respectively, *P* value <0.001]. (Table 2).

Table 2 Intraoperative and postoperative outcomes

	Fentanyl group (*N*=16)	Magnesium group (*N*=16)	*P* value
Average intraoperative SBP (mmHg)	118 (8)	127 (9)	0.003
Incidence of hypotension	16 (100)	11 (69)	0.043
Ephedrine consumption (mg)	13 (10, 15)	4 (0, 10)	0.005*
Incidence of bradycardia	5 (31)	4 (25)	1
Persistent movements	2 (1, 2)	3 (1, 3)	0.063
Frequency of propofol top-up	2 (1, 3)	3 (1, 3)	0.131
Total propofol requirement (mg)	436 (96)	466 (71)	0.324
Time to be awake (min.)	60 (30, 60)	30 (19, 60)	0.057
Time to rescue analgesia (min)	60 (60, 120)	60 (60, 120)	1
Surgeon satisfaction	3 (2, 4)	2 (2, 3)	0.239
Postoperative nausea and vomiting	16 (100)	3 (19)	<0.001*

Data are presented as mean (SD), median (quartiles), and frequency (%). SBP, systolic blood pressure. *Statistical significance.

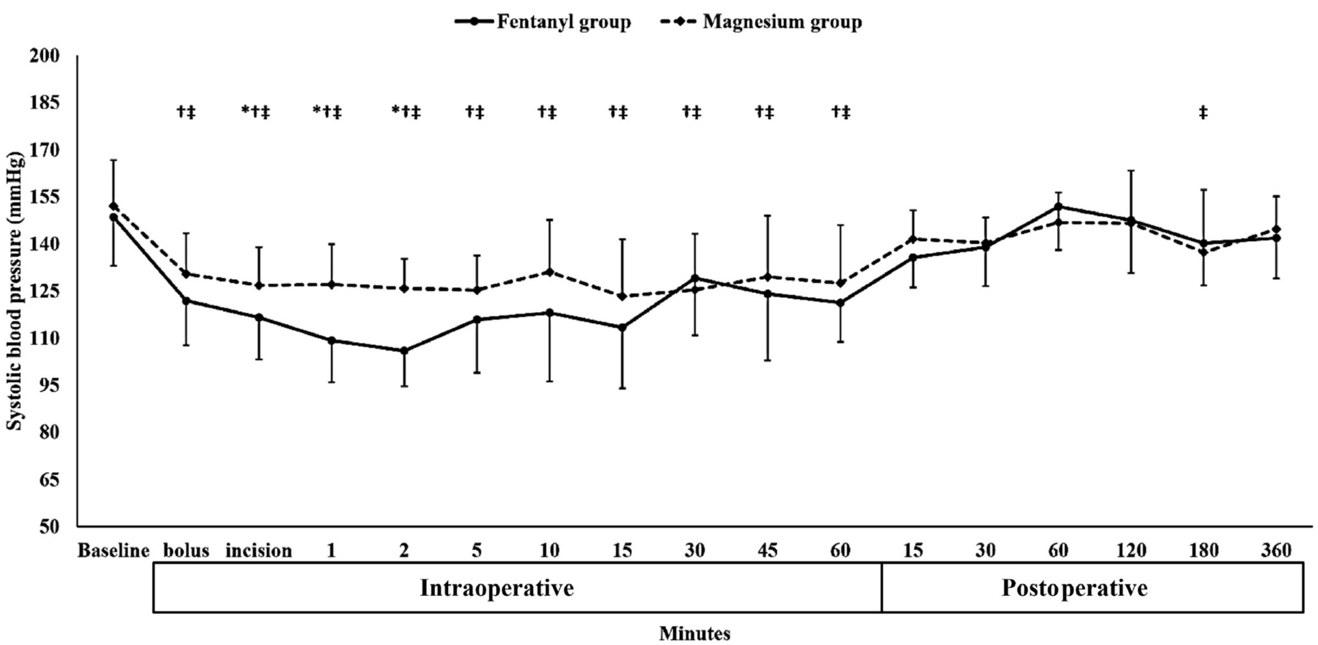
RSS was lower in the magnesium group than in the fentanyl group at 15 min postoperatively, and then it was comparable between both groups at 30 and 60 min postoperatively. The postoperative VAS score was comparable between both groups at all time points of assessment.

Discussion

We report that magnesium sulfate infusion provided a more favorable hemodynamic profile and lower incidence of nausea and vomiting during conscious sedation for CSDH evacuation in comparison with fentanyl infusion. Besides, magnesium sulfate provided a propofol-sparing effect comparable to fentanyl.

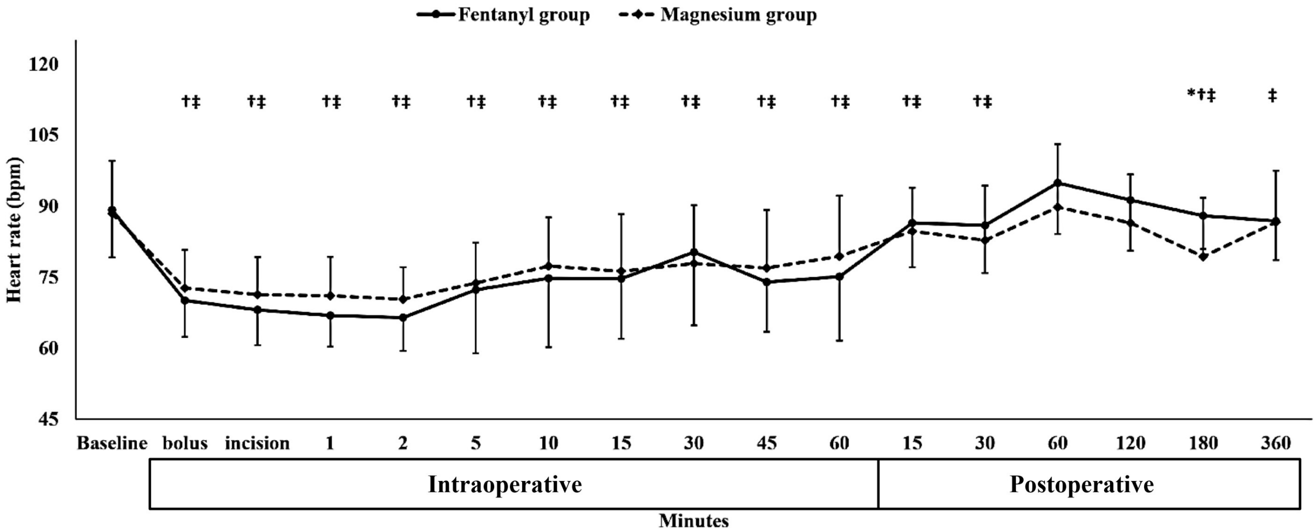
Magnesium sulfate has sedative and analgesic properties when combined with different anesthetics, and its use was associated with anesthetic sparing during general anesthesia and sedation [9]. Few studies have demonstrated the sedative effects of magnesium as an adjuvant during procedural sedation. They showed positive outcomes regarding its sparing effects on propofol [15], sedatives, and narcotics [16]. Nevertheless, our study is the first to

Figure 2



Systolic blood pressure. *Significance between the two groups, † significance in relation to baseline reading in the fentanyl group, and ‡ significance in relation to baseline reading in the magnesium group.

Figure 3



Heart rate. *Significance between the two groups, †significance in relation to baseline reading in the fentanyl group, and ‡significance in relation to baseline reading in the magnesium group.

evaluate the use of magnesium sulfate during the evacuation of CSDH and explored its hemodynamic effects in this subset of patients.

The use of fentanyl-propofol during induction of anesthesia was associated with a considerable risk of postinduction hypotension [17,18], but there were no data, to the extent of our knowledge, about the hemodynamic effect of simultaneous infusion of both drugs for conscious sedation in CSDH. The high incidence of hypotension in the fentanyl group is mostly owing to its negative inotropic effect [19], which is more potent in elderly patients [20]. Magnesium sulfate has a well-known vasodilatory effect; however, its use as an adjuvant to general anesthesia was associated with modest hypotension, and it has no cardiac inhibitory effect [21].The incidence of nausea and vomiting was lower in the magnesium sulfate group compared with the fentanyl group. Fentanyl, like other opioids, has a direct stimulation on the chemoreceptor-triggering zone, which in turn stimulates the vomiting center in the medulla [22].

Conscious sedation for evacuation of CSDH is an increasingly used regimen; however, the risk of patient movement could be hazardous if the operative site, which is the head, is moving or if the movement impaired the surgical field. Hemodynamic fluctuations present another challenge, which increase the risk of progressive neurologic deficit [23]. CSDH commonly occurs in elderly patients whose limited physiologic reserve of the vital organs represents another challenge [24]. Our findings introduce magnesium sulfate as an adjuvant to propofol during CSDH evacuation with many advantages over fentanyl. The study has some limitations: (a) it is a single-center study, (b) the use of one dose of each drug, (c) lacking the assessment of patient satisfaction, and (d) missing to report the incidence of postoperative shivering. Future studies should evaluate other doses and other drug combinations.

In conclusion, magnesium sulfate infusion was associated with more hemodynamic stability and less incidence of nausea and vomiting compared with fentanyl in patients undergoing conscious sedation for CSDH evacuation surgery. Magnesium sulfate as well produced an anesthetic-sparing effect comparable to fentanyl infusion when combined with propofol.

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Contribution details: Rania S. Fahmy has actively participated in the concept and design of the study; literature search; data collection and interpretation; statistical analysis; and manuscript preparation, editing, and revision. Amal A. Elsawy has actively participated in the design of the study; literature search; data collection and interpretation; and manuscript preparation, editing, and revision. Maha Mostafa has actively participated in the design of the study; literature search; data collection and interpretation; statistical analysis; and manuscript preparation, editing, and revision. Ahmed Hasanin has actively participated in the design of the study; literature search; data collection and interpretation; statistical analysis; and manuscript preparation, editing and revision. Tarek Radwan has actively

participated in the concept and design of the study; literature search; data interpretation; and manuscript preparation, editing, and revision. Nasr M. Abdallah has actively participated in the concept and design of the study; literature search; data collection and interpretation; and manuscript preparation, editing and revision. The manuscript has been read and approved by all the authors, all requirements for authorship have been met, and each author believes that the manuscript represents honest work.

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Conflicts of interest
There are no conflicts of interest.

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