



Research article

Comparative study between magnesium sulphate and L-hyoscyamine on duodenal motility during ERCP under general anaesthesia: A prospective randomized study



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ABSTRACT

Objective: Endoscopic retrograde cholangiopancreatography (ERCP) is a relatively complex procedure as compared with other endoscopy which needs longer duration, duodenal relaxation and good sedation. The aim of this study was to evaluate the efficacy and safety of magnesium sulphate as spasmolytic agent during ERCP under general anaesthesia.

Design: A prospective randomized study.

Setting: Delivery room, operating room and postoperative recovery area.

Patients and method: Patients, who were treated for calculous obstructive jaundice by ERCP were randomized into two groups. The patients were randomized into two groups: G I, patients received 500 mg magnesium sulphate in 100 ml saline 15 min before induction and G II, patients received 0.5 mg L-hyoscyamine sulphate before induction of anaesthesia.

Measurement: The primary outcome was duodenal relaxation during ERCP under general anaesthesia. Secondary outcomes include changes of heart rate, changes in oxygen saturation, time needed for cannulation, procedure difficulty, duration of the procedure, post-procedure complications, and the need of post-procedure analgesia.

Results: Duodenal motility score was found to be 0.85 ± 1.47 in GI and 2.2 ± 3.08 in GII ($P = 0.0001$). The number of patients who had no duodenal contraction was significantly more in GI. The success rate of biliary cannulation is significantly higher in GI than in GII (58 (100%) vs 54 (93.1%), $P = 0.04$). The duration of cannulation was significantly shorter in GI. The number of patients who developed pancreatitis, nausea and vomiting was significantly less in GI. The pulse rate was found to be statistically less in GI at different time follow-ups.

Conclusion: Magnesium sulphate is a safe spasmolytic agent during general anaesthesia that improves the success rate of ERCP and it allows easy completion of the procedure by decreasing the duodenal motility. It decreases the duration of the procedure, subsequently shortens the period of anaesthesia and improves post procedure recovery. It reduces post ERCP pancreatitis, nausea and vomiting.

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1. Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a useful tool for diagnosis and treatment of obstructive jaundice [1–4]. ERCP needs patient cooperation and adequate sedation. Although, some centres are undergoing ERCP with moderate sedation, other centres performed ERCP under deep sedation or general anaesthesia [2,5–8]. The Post ERCP morbidity and mortality rate

were 5–15% and 0.7–1.2%, respectively [2–6]. Lack of cooperation has been found to be one of the leading cause for post ERCP morbidity such as duodenal perforation, bleeding papillotomy, pancreatitis and cholecystitis [2,4,7,8].

Patients undergoing ERCP are at a risk of hypoxia and cardiac problems due to prolonged duration of the procedure, semiprone position, sedation, abdominal distension due to insufflations, medication used to decrease duodenal motility, and associated cardiopulmonary disorder [7,8]. So general anaesthesia during ERCP is better than sedation alone to decrease the risk of hypoxia and cardiac problem [5,6].

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Duodenal contractions during ERCP make papillary cannulation and subsequent manipulation difficult. Pharmacologic drugs that decrease or suppress duodenal motility are often needed during ERCP [9,10]. L-hyoscyamine sulphate is antimuscarinic, anticholinergic agent with antispasmodic effect. L-hyoscyamine sulphate is commonly used to suppress duodenal motility during ERCP with duration of action of 4 h but with some adverse effect. Other centres used intravenous glucagon but it has a short duration of action, expensive and has many side effects including hyperglycaemia, nausea, and vomiting [9].

Magnesium sulphate is a potent **calcium antagonist** that makes relaxation of gastrointestinal tract and may decrease contraction. It has a potent bronchodilatation and so improves oxygenation during ERCP. Also, it has an analgesic effect and decreases the incidence of post ERCP pancreatitis [11].

The aim of this study was to evaluate the efficacy and safety of magnesium sulphate on duodenal motility and its impact on heart rate and oxygen saturation during ERCP under general anaesthesia.

2. Patients and Method

2.1. Patients

Patients, who were treated for calcular obstructive jaundice by ERCP at Gastroenterology Surgical Center, Mansoura University, Egypt, during the period from November 2014 to June 2015, will be eligible for the study. Exclusion criteria included patients less than 18 years or above 60 years, patients with severe cardiovascular disease, Respiratory, metabolic and endocrine diseases, patients with BMI above 30 kg/m² patients with impaired renal or hepatic function or patients with anatomical deformities that will hinder the procedure.

Informed consent was obtained from all patients to be included in the study, after a careful explanation of the nature of the disease and possible treatment with its complications. The study was approved by the Institutional Review Board (IRB).

2.2. Pre ERCP assessment

All patients subjected to careful history taking, clinical examination (age, sex, medical diseases, symptoms and signs), laboratory investigation (complete blood count, liver functions, creatinine, serum amylase, and coagulation profile), radiological investigations (abdominal ultrasound, magnetic resonance cholangiopancreatography MRCP, and abdominal computerized tomography) and Cardiopulmonary assessment by ECG, chest X ray and ECHO in selected cases.

On arrival to the operating theatre, canula [18–20 G] was inserted for all patients and infusion of lactated ringer solution at a rate of 2–4 ml/kg/h for fluid deficits and maintenance supply.

2.3. Randomization

Patients enrolled in the study were randomized into two groups using the closed envelope method. The envelopes were drawn and opened by a nurse not otherwise engaged in the study in the operating room. The patients were randomized into two groups: Group I, patients received 500 mg magnesium sulphate in 100 ml saline 15 min before induction and Group II, patients received 0.5 mg L-hyoscyamine sulphate before induction of anaesthesia.

2.4. Procedure

Anaesthetic plan was the same for both groups. All patients were induced by propofol at a dose of 1.5–2 mg/kg I.V. bolus

followed immediately by a continuous propofol infusion via a syringe pump in a descending schedule rate [15–20 mic g/kg/min]. Tracheal intubation was facilitated by administration of atracurium 0.5 mg/kg and controlled mechanical ventilation to keep Etco₂ around 35 mmHg; patients will be handled in prone position; and at the end of the procedure anaesthesia will be discontinued and the residual of neuromuscular blockade was reversed with neostigmine 0.04 mg/kg plus atropine 0.02 mg/kg.

2.5. Data collected and definitions

Routine intraoperative monitoring for heart rate using lead II ECG, non invasive mean blood pressure, pulse oximetry and capnography will be recorded every 5 min. Anaesthesia time [time from induction till discontinuation of propofol infusion] was recorded.

Duodenal motility will be recorded according to this scale as follows: [1] no contraction, [2] less than 5 cont./min, [3] 5–10 cont./min, [4] 11–15 cont./min and [5] continuous contraction [9,12]. Cannulation time is time needed from endoscope introduction till cannulation of the papilla of Vater Procedure difficulties will be assessed on a scale 1–4 with the following: grade [1] a successful procedure that lasted less than 30 min, grade [2] 30–60 min, grade [3] more than 60 min and grade [4] unsuccessful procedure [9–11].

Postoperative analgesia according to verbal rating score will be assessed. Postoperative sedation score will be assessed. Postoperative concomitant complications will be recorded as nausea, vomiting, bleeding, pancreatitis and cholangitis.

2.6. Assessments

The primary outcome was duodenal relaxation during ERCP under general anaesthesia. Secondary outcomes include changes of heart rate, changes in oxygen saturation, time needed for cannulation, procedure difficulty, duration of the procedure, post-procedure complications, and the need of post-procedure analgesia.

Descriptive data were expressed as means and standard deviations or as median with ranges for continuous data. Categorical variables were described using frequency distributions. A *P* value < .05 was considered statistically significant. Comparison of variables was done by independent Student's *t*-test for continuous variables and Chi-square test for categorical variables. Statistical analysis was done with the help of SPSS v. 17.

3. Result

3.1. Patients data

The study flow chart is shown in Fig. 1. Of 336 consecutive patients seen during the study period who had CBD stones, only 116 patients who had CBDS were included in the study. These patients were randomly divided into two groups: Group I, patients received 500 mg magnesium sulphate in 100 ml saline 15 min before induction and Group II, patients received 0.5 mg L-hyoscyamine sulphate before induction of anaesthesia. 220 patients were excluded from the study as present in Fig. 1.

3.2. Pre ERCP data

Demographic data were comparable in both groups as regards age, sex, serum bilirubin, CBD diameter, and presence of DM. The pre ERCP data of the both randomized groups are presented in Table 1.

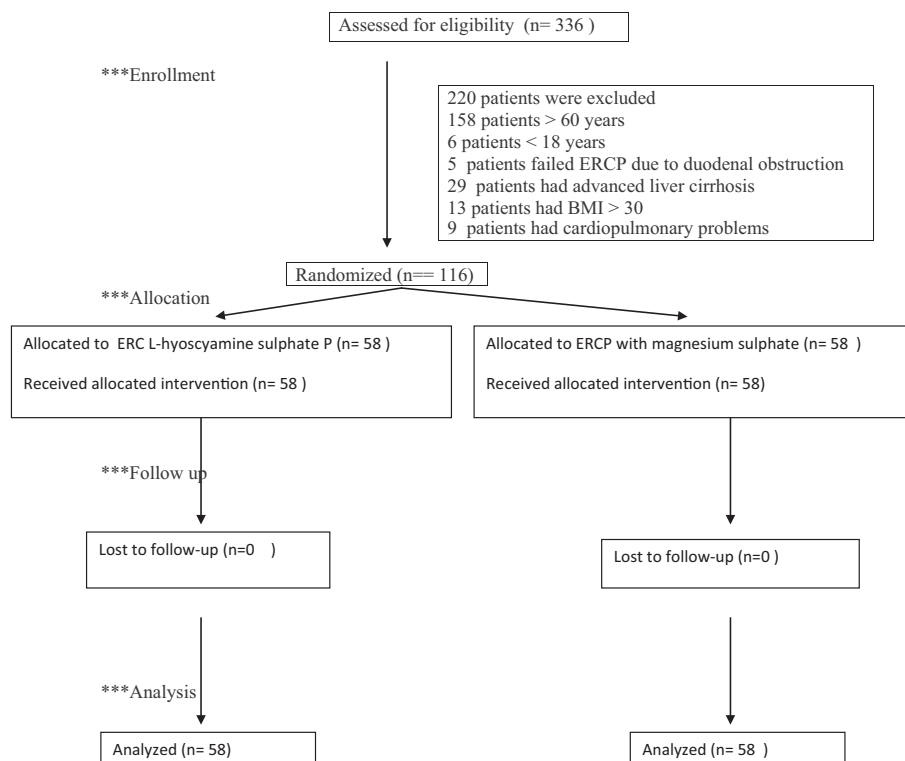


Figure 1. Flow diagram of the progress through the phases of a randomized trial (i.e., enrolment, intervention allocation, follow-up, and data analysis).

Table 1
Demographic data.

	Magnesium sulphate group	L-hyoscyamine sulphate group	P value
Median age	43 (22–59)	45 (22–59)	0.33
Sex			
Male	11 (19%)	13 (22.2%)	0.65
Female	47 (81%)	45 (77.6%)	
BMI	23.9 (19–30)	24.3 (18–30)	0.56
Diabetes (DM)	4 (6.9%)	3 (5.2%)	0.69
Median serum bilirubin (mg/dl)	3.05 (0.6–10.3)	3.25 (0.5–12.8)	0.66
Serum amylase (U/L)	78 (45–155)	77 (40–150)	0.35
Median CBD diameter (mm)	13 (9–25)	13 (8–24)	0.24
Number of CBD stone			
Single	46 (79.3%)	47 (81%)	0.82
Two	12 (20.7%)	11 (19%)	
CBD stone size	10 (2–15)	10 (2–15)	0.6

3.3. During ERCP

Duodenal motility score was found to be 0.85 ± 1.47 in magnesium sulphate group and 2.2 ± 3.08 in L-hyoscyamine group which was statistically significant. Also, the number of patients who had no duodenal contraction was significantly more in magnesium sulphate [Table 2](#).

The success rate of biliary cannulation is significantly higher in magnesium sulphate group than in L-hyoscyamine group (58 (100%) vs 54 (93.1%), $P = 0.04$) [Table 2](#).

The duration of cannulation was significantly shorter in magnesium sulphate and also the total duration of anaesthesia is less in magnesium sulphate group [Table 2](#).

3.4. Post ERCP outcomes

Post ERCP recovery status significantly differed in both groups at different time points after ERCP as shown in [Table 3](#).

The number of patients who developed pancreatitis was significantly more in L-hyoscyamine and all patients managed conservatively and discharged after resolution of pancreatitis.

The number of patients who developed nausea and vomiting was significantly more in L-hyoscyamine and they responded to antiemetic drug and antilucer.

3.5. Changes in pulse rate, blood pressure and oxygen saturation

The most frequent adverse effect of L-hyoscyamine is tachycardia. The pulse rate was found to be statistically lower in magnesium sulphate at different time follow-ups (at the beginning of ERCP, after 5 min, and after 10 min) [Table 4](#).

No significant difference was seen between both groups as regards oxygen saturation, and mean blood pressure at different time of procedures [Table 4](#).

Table 2
ERCP in both groups.

	Magnesium sulphate group	L-hyoscyamine sulphate group	P value
Success rate of cannulation	58 (100%)	54 (93.1%)	0.04
Mean duodenal motility/min	0.85 ± 1.47 (0–8)	2.2 ± 3.08 (0–12)	0.0001
Duodenal motility			
No contraction	47 (81%)	34 (58.5%)	0.03
Less than 5 cont./min	7 (12.1%)	16 (27.6%)	
5–10 cont./min	4 (6.9%)	7 (12.1%)	
Continuous contraction	0	1 (1.7%)	
Median duration needed till cannulation (min)	3.5 (0.5–12)	6 (1–15)	0.0001
Number of pancreatic cannulation	0.12 ± 0.46 (0–2)	0.29 ± 0.87 (0–4)	0.18
Anaesthetic period (min)	30 (16–55)	38 (20–89)	0.08
Endoscopist satisfaction			
Satisfied	52 (89.7%)	46 (79.3%)	0.12
Not satisfied	6 (10.3%)	12 (20.7%)	
Outcome of ERCP			
Failed cannulation	0	4 (6.9%)	0.21
CBD clearance	53 (91.4%)	50 (86.2%)	
Failed clearance of CBDS and stent application	5 (8.6%)	4 (6.9%)	

Table 3
Post procedure outcomes in both groups.

	Magnesium sulphate group	L-hyoscyamine sulphate group	P value
<i>Post ERCP status at the end of procedure</i>			
1. Awake, anxious	0	3 (5.2%)	0.002
2. Awake, cooperative	0	2 (3.4%)	
3. Awake, respond to command only	0	5 (8.6%)	
4. Asleep, brisk response	4 (6.9%)	7 (12.1%)	
5. Asleep, sluggish response	14 (24.1%)	21 (36.2%)	
6. Asleep, no response	40 (69%)	20 (34.5%)	
<i>Post ERCP status after 10 min</i>			
1. Awake, anxious	0	4 (6.9%)	0.0001
2. Awake, cooperative	6 (10.3%)	2 (3.4%)	
3. Awake, respond to command only	4 (6.9%)	18 (31%)	
4. Asleep, brisk response	9 (15.5%)	24 (41.4%)	
5. Asleep, sluggish response	30 (51.7%)	10 (17.2%)	
6. Asleep, no response	9 (15.5%)	0	
<i>Post ERCP status after 30 min</i>			
1. Awake, anxious	19 (32.8%)	33 (56.9%)	0.01
2. Awake, cooperative	18 (31%)	18 (31%)	
3. Awake, respond to command only	15 (25.9%)	4 (6.9%)	
4. Asleep, brisk response	6 (10.3%)	0	
5. Asleep, sluggish response	0	3 (5.2%)	
6. Asleep, no response	0	0	
<i>Post ERCP status after 60 min</i>			
1. Awake, anxious	0	0	0.0001
2. Awake, cooperative	42 (72.1%)	55 (94.8%)	
3. Awake, respond to command only	14 (24.1%)	0	
4. Asleep, brisk response	2 (3.4%)	3 (5.2%)	
5. Asleep, sluggish response	0	0	
6. Asleep, no response	0	0	
Number of patients need analgesic	7 (12.1%)	9 (15.5%)	0.12
Nausea and vomiting	5 (8.6%)	15 (25.9%)	0.01
Serum amylase	79.5 (49–1200)	80 (60–1200)	0.3
Number of patients developed Pancreatitis	2 (3.4%)	8 (13.8%)	0.05
Median serum bilirubin (mg/dl)	2 (0.6–9.4)	2 (0.6–9.5)	0.55

Table 4
Changes in pulse rate, blood pressure, oxygen saturation.

	Magnesium sulphate group	L-hyoscyamine sulphate group	P value
<i>Pulse rate (beat/min)</i>			
Pre ERCP pulse rate	75 (60–94)	74 (60–94)	0.9
Pulse rate at the beginning of ERCP	84 (64–99)	92 (80–102)	0.0001
Pulse rate after 5 min	83 (69–110)	96 (78–120)	0.0001
Pulse rate after 10 min	81 (62–105)	92 (82–120)	0.0001
<i>Mean blood pressure (mmHg)</i>			
Pre ERCP mean blood pressure	90 (67–108)	87 (69–104)	0.15
Mean blood pressure at the beginning of ERCP	89 (68–101)	90 (68–104)	0.93
Mean blood pressure after 5 min	86 (65–104)	87 (65–102)	0.57
Mean blood pressure after 10 min	88 (70–106)	88 (69–105)	0.97
<i>Oxygen saturation</i>			
Pre ERCP oxygen saturation	99 (98–100)	99 (98–100)	0.9
Oxygen saturation at the beginning of ERCP	100 (98–100)	99 (98–100)	0.87
Oxygen saturation after 5 min	100 (98–100)	100 (99–100)	0.85
Oxygen saturation after 10 min	100 (98–100)	100 (99–100)	0.65

4. Discussion

Endoscopic retrograde cholangiopancreatography (ERCP) is commonly used in diagnosis and management of biliary and pancreatic diseases. ERCP is a relatively complex procedure as compared with other endoscopy and needs a longer duration. During ERCP duodenal motility has a great impact on the outcome as it makes hard to cannulate the papilla and other manipulations [11]. Spasmolytic drugs are widely used during ERCP for reduction or inhibition of duodenal motility and to make the papillary cannulation easy. For this aim, drugs such as glucagon and L-hyoscyamine sulphate are widely used [9,10,12–15].

ERCP needs patient cooperation, which requires adequate sedation and pain relief. Patients undergoing ERCP have been found to be more irritable than those undergoing a routine gastrointestinal

endoscopy. Irritability and lack of cooperation have been found to be one of the causes for post-ERCP morbidity such as pancreatitis and visceral perforation [16,17]. ERCP is a prolonged manoeuvre, and hence adequate sedation and patient co-operation are the cornerstones for its successful completion. Although majority of ERCPs are performed under moderate sedation, others do it under deep sedation or general anaesthesia. Hypoxia is an inherent risk associated with sedation. Patients undergoing ERCP are at a risk of oxygen desaturation due to various causes including the prone position, associated cardiopulmonary disorder, prolonged duration, sedation used, and other drugs used. Drugs-induced respiratory depression has been found to be the most common leading cause of endoscopy-related mortality and morbidity. There has been no evidence regarding the safest and the most effective method of sedation [6]. In our centre, in recent years we routinely perform ERCP under general anaesthesia and endotracheal intubation and these allow safe ERCP and improve the results markedly [3].

Spasmolytic drugs widely used during ERCP for reduction or inhibition of duodenal motility may affect the patients who are under anaesthesia [13–15]. The impact of spasmolytic agent on pulse, blood pressure, oxygen saturation and duodenal motility must be monitored by anaesthesiologist.

L-hyoscyamine is an antimuscarinic, anticholinergic agent with antispasmodic properties so, it is widely used during ERCP to reduce the duodenal motility and subsequently allow easy cannulation and decrease the duration of procedure and time of anaesthesia. It has some anticholinergic adverse effects on the heart leading to tachycardia, xerostomia, and urinary retention. Therefore, it should be used with precaution in cases with bronchial asthma, thyrotoxicosis, and heart disorders [13–15].

The spasmolytic effect of magnesium in humans has been found in a few cases, including a patient receiving parenteral magnesium sulphate for tocolysis, and in patients on magnesium laxatives for chronic constipation; the effect was increased secondary to calcium channel blocker use. Magnesium has a nonspecific calcium channel blocker effect, so its action may be increased by calcium channel blockers and hypocalcaemia, and can be partially reversed with calcium injection [18–20]. In this study the use of magnesium sulphate during ERCP induces more duodenal relaxation and decreases duodenal contraction as well as has inhibitory effect on sphincter of Oddi more than in L-hyoscyamine. So, it makes papillary cannulation easier after magnesium sulphate administration. No adverse effect was reported for magnesium sulphate. It decreases the incidence of post ERCP pancreatitis.

Lahoti et al. [11] performed a prospective randomized study that included 308 patients who were randomized to receive intravenous glucagon or intravenous L-hyoscyamine during ERCP. L-hyoscyamine was found to be slightly less effective on duodenal motility and had more side effect at 2 h after ERCP. However, this did not lead to procedure difficulty or success. L-hyoscyamine is much less expensive than glucagon, and L-hyoscyamine has been shown to have similar efficacy to glucagon. Hui and Ostroff [20] in a randomized study, reported that L-hyoscyamine was associated with more xerostomia and tachycardia, but did not affect the procedures and the success rates were the same.

Post-anaesthesia recovery has to be adequate before the patient can be shifted to the ward. Smooth recovery was affected by many factors including duration of procedure, distention of the abdomen, complications after ERCP, haemodynamics, oxygen saturation, Post-operative nausea, retching and vomiting and medication such as spasmolytic agent. Propofol is known to have antiemetic effect. Subhypnotic doses of propofol (0.5 mg/kg) have been found to prevent nausea and retching for 6 h post-procedure [6,21]. In this study, the recovery is more smooth in magnesium sulphate group

because the duration of anaesthesia is shorter than in L-hyoscyamine group.

The present prospective randomized study is subject to one limitation. The sample size was small and not calculated. Further prospective randomized studies with larger sample sizes are required to confirm these results.

5. Conclusion

ERCP is a relatively complex procedure as compared with other gastrointestinal endoscopies and requires a longer duration. Magnesium sulphate is a safe spasmolytic agent during general anaesthesia that improves the success rate of ERCP and it allows easy completion of the procedure by decreasing the duodenal motility. It decreases the duration of the procedure, subsequently shortens the period of anaesthesia and improves post procedure recovery. It reduces post ERCP pancreatitis.

Author contributions

Emad El Hefnawy **designed the research**. Emad El Hefnawy and Ayman El Nakeeb **performed the research**. Emad El Hefnawy and Ayman El Nakeeb **analysed the data**. Emad El Hefnawy and Ayman El Nakeeb **wrote the paper**.

Conflict of interest

We have no conflict of interest to declare.

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