

EFFICACY OF INTRAVENOUS MAGNESIUM SULPHATE IN REDUCING INTRAOPERATIVE RESPIRATORY COMPLICATIONS AMONG SMOKERS VERSUS NON-SMOKERS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

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Abstract

Background: Carbon dioxide pneumoperitoneum in general anesthesia laparoscopic cholecystectomy results to significant respiratory complications due to the following reasons. There is decreased lung compliance, increased airway pressures and change in carbon dioxide exhalation. Smoking increases susceptibility to respiratory complications.

Objective: The objective of the present study was to compare the intraoperative respiratory variables and complications in smokers and non-smokers who underwent elective laparoscopic cholecystectomy with intravenous magnesium sulphate administration.

Methods: This was a prospective, randomized, double-blind, placebo controlled comparative study conducted at the Department of Anaesthesiology, Allied Hospital, Faisalabad. A total of 124 patients undergoing elective laparoscopic cholecystectomy were enrolled in the study. Subjects were divided on the basis of smoking and magnesium sulphate/placebo administration. Magnesium sulphate was administered through intravenous route in a dose of 15 mg/kg in 100 mL of normal saline for 15 minutes prior to induction, whereas the placebo group was given an equal amount of normal saline. Respiratory variables intra-operatively such as SpO₂, EtCO₂, peak airway pressure and dynamic compliance were observed. Hypoxemia, hypercapnia, bronchospasm, laryngospasm and respiratory rescue measures were noted. Statistical analysis was done by SPSS software, with p≤0.05 significance level.

Results: The smoking patients exhibited intraoperative respiratory impairment relative to the non-smoking patients especially when in pneumoperitoneum and at pre-extubation times. The smoking patients under

magnesium sulphate had lower SpO₂ but high EtCO₂ and high peak airway pressure relative to the non-smoking patients. There were statistically significant differences in hypoxemia, hypercapnia, bronchospasm and high airway pressure.

Conclusion: The respiratory system of smokers undergoing laparoscopic cholecystectomy surgery is more susceptible than that of nonsmokers. IV Magnesium Sulphate could be considered as an adjunct for respiratory management before and after the procedure; nevertheless, further research with a balanced sample group is needed.

Introduction

Laparoscopic cholecystectomy is a frequently performed operation in gallbladder pathology[1]. Despite the benefits, such as less post-operative pain, shorter hospitalization period, laparoscopic surgery results in significant physiological effects caused by the production of carbon dioxide pneumoperitoneum[2]. Cephalad displacement of the diaphragm, decrease of the functional residual capacity, lungs compliance and rise in airway pressures are caused by increased intraabdominal pressure. In addition, CO₂ absorption could result in raised end tidal CO₂ and ventilation workload[3].

Smoking is an important risk factor for respiratory complications during the perioperative period[4]. Prolonged smoking is associated with inflammatory changes in the airways, increased airway reactivity, decreased mucociliary clearance and susceptibility to respiratory complications under general anesthesia[5]. Consequently, smokers might be at increased risk of bronchospasm, desaturation and airway problems during airway manipulation, pneumoperitoneum and awakening from anesthesia[6].

Magnesium sulphate has become interesting for use as a perioperative adjuvant due to its possible bronchodilator and stabilizer effects[7]. The mechanisms of action of magnesium sulphate include calcium channel blocking and antagonism of NMDA receptors, which might inhibit bronchial smooth muscle contraction and airway hyper-reactivity[8]. Magnesium sulphate has been tested in a number of perioperative situations, but there is a lack of evidence regarding its effect on respiratory functions during laparoscopic

cholecystectomy based on patients' smoking history[9].

Smoking is well known to be a risk factor for perioperative respiratory complications as chronic exposure to smoking leads to changes in the structure and functioning of the respiratory system[10]. Inflammation of the airways, increased reactivity of bronchial smooth muscle, excess secretions, and mucociliary clearance may enhance the reaction of the airways to laryngoscopy, tracheal intubation, and mechanical ventilation[11]. These airway conditions, combined with the additional respiratory stress due to pneumoperitoneum during laparoscopic surgery in patients, put them at higher risk of respiratory events during general anesthesia[12]. There have been some previous findings showing different respiratory results for patients undergoing general anesthesia depending on whether they are smokers or nonsmokers[13]. According to the literature provided in the current thesis, the following has been found concerning smokers versus nonsmokers undergoing general anesthesia: Smokers tend to have lower oxygen saturation, more peri-extubation desaturation, and more episodes of bronchospasm and laryngospasm[14]. Other researchers have also identified increased CO₂ levels and reduced pulmonary function in patients who smoke and undergo laparoscopy[15].

For this reason, the current study was performed to compare the intraoperative respiratory variables and respiratory complications of smoking and nonsmoking patients during elective laparoscopic cholecystectomy and to consider the possible role of magnesium sulphate in improving respiratory functions.

Methodology

Study Design and Setting: It was a prospective randomized double blind placebo controlled comparative trial carried out in operation theatres of the Department of Anesthesiology at Allied Hospital, Faisalabad. The subjects included were patients for elective laparoscopic cholecystectomy under general anesthesia.

Participants: The patients involved in the study ranged from 18 to 65 years of age with ASA Physical Status I-III undergoing elective laparoscopic cholecystectomy. Patients with significant cardiopulmonary illness except for tobacco related changes, difficult airway, pregnancy or emergency surgery were not included. The final SPSS database consisted of 124 patients. The subjects were classified based on their smoking history as smokers or non-smokers and were further divided as per magnesium sulphate or placebo.

Intervention: The patients under the magnesium sulphate treatment were administered magnesium sulphate intravenously at a dosage of 15 mg/kg in 100 ml of normal saline over 15 minutes prior to inducing anesthesia. The patients under the placebo were administered with the same volume of normal saline. General anesthesia was induced on both the groups.

Data Collection: Respiratory parameters such as SpO₂, EtCO₂, peak airway pressures, and dynamic compliance were measured during the procedure. Respiratory complications such as hypoxia, hypercapnia, bronchospasm, and laryngospasm were also noted. Any rescue respiratory therapy measures were documented.

Statistical Analysis: SPSS was used to analyze data. Continuous data were expressed in mean and standard deviation, while categorical data were expressed in frequencies and percentages. Continuous data were compared using independent-samples t-test, while categorical data were compared using either chi-square or Fisher's exact test. One-way ANOVA was also applied when necessary. The level of significance was set at $p \leq 0.05$.

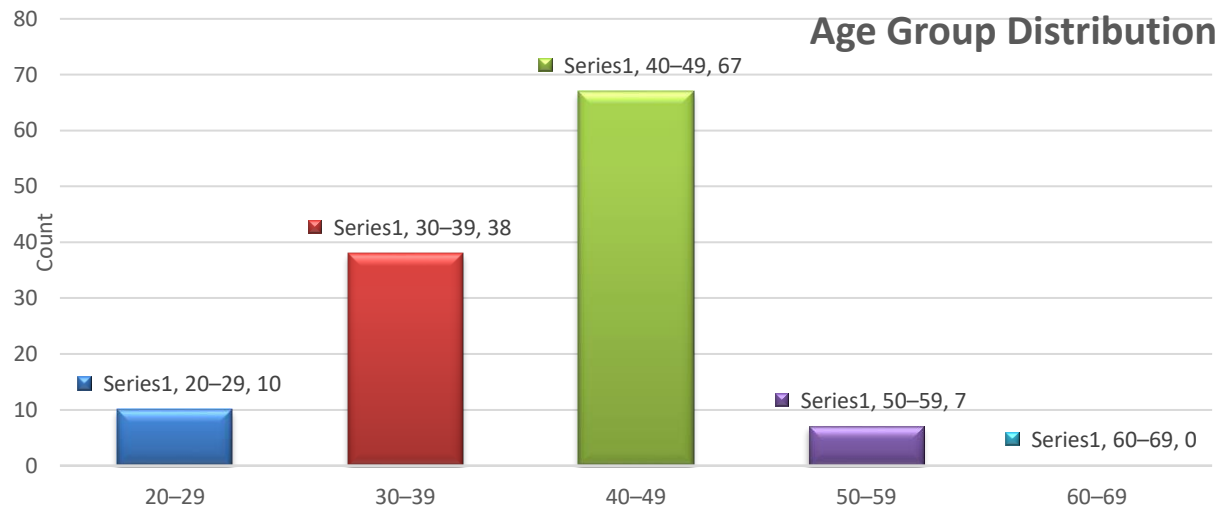
Results

The sample size for the final analysis comprised of 124 patients. Out of this, 64 (51.6%) were smokers while 60 (48.4%) were non-smokers. The average age of participants was 39.92 ± 7.89 years. The number of male patients was 58 (46.8%), while female patients numbered 66 (53.2%). In all, 115 (92.7%) patients were administered magnesium sulphate, while 9 (7.3%) were given placebo. The four study subgroups were non-smokers on magnesium sulphate (n=56), non-smokers on placebo (n=4), smokers on magnesium sulphate (n=59), and smokers on placebo (n=5).

Table 1. Demographic Characteristics of Participants

Characteristic	Overall (N=124)
Age, mean $\pm$ SD (years)	39.92 $\pm$ 7.89
Male, n (%)	58 (46.8%)
Female, n (%)	66 (53.2%)
Smokers, n (%)	64 (51.6%)
Non-smokers, n (%)	60 (48.4%)
Magnesium sulphate, n (%)	115 (92.7%)
Placebo, n (%)	9 (7.3%)

Figure 1. Age Group Distribution



However, most subjects were of the ASA II group. ASA I, ASA II and ASA III had a total number of 38, 57 and 28 subjects, respectively. One participant was unable to be classified due to an ASA classification of 0.

Analysis among the four groups revealed the age means of the participants to range between 39.34 ± 8.68 years for non-smokers on magnesium

sulphate and 45.00 ± 2.45 years for smokers on placebo. The age was not significantly different among the four groups ($p=0.482$). There was a significant difference in gender distribution among the groups ($\chi^2=11.97$, $p=0.007$), while ASA distribution was not significantly different among the groups ($\chi^2=13.64$, $p=0.136$).

Table 2. Comparison of Demographic Characteristics between Study Groups

Variable	Non-smoker + MgSO ₄ (n=56)	Non-smoker + Placebo (n=4)	Smoker + MgSO ₄ (n=59)	Smoker + Placebo (n=5)	p-value
Age, mean $\pm$ SD	39.34 $\pm$ 8.68	41.25 $\pm$ 4.19	39.95 $\pm$ 7.53	45.00 $\pm$ 2.45	0.482
Male, n (%)	20 (35.7)	2 (50.0)	36 (61.0)	0 (0.0)	0.007
Female, n (%)	36 (64.3)	2 (50.0)	23 (39.0)	5 (100.0)	
ASA I, n (%)	23 (41.1)	3 (75.0)	12 (20.3)	0 (0.0)	0.136
ASA II, n (%)	22 (39.3)	0 (0.0)	32 (54.2)	3 (60.0)	
ASA III, n (%)	11 (19.6)	1 (25.0)	14 (23.7)	2 (40.0)	

The respiratory parameters showed more respiratory strain in the smoking population. In patients administered magnesium sulphate, smokers had lower SpO₂ levels as compared to non-smokers at several intra-operative intervals. After the administration of pneumoperitoneum, the SpO₂ level was $96.81 \pm 1.89\%$ for smokers compared to $98.38 \pm 1.58\%$ for non-smokers. The

EtCO₂ level after the administration of pneumoperitoneum for smokers was 43.97 ± 3.68 mmHg while that of non-smokers was 40.59 ± 4.62 mmHg. Peak airway pressure after pneumoperitoneum was also higher among smokers (26.37 ± 5.54) than non-smokers (23.59 ± 3.42).

Table 3. Intraoperative Respiratory Parameters According to Study Group

Parameter	Non-smoker + MgSO ₄	Non-smoker + Placebo	Smoker + MgSO ₄	Smoker + Placebo	p-value
Baseline SpO ₂ (%)	97.80 ± 1.05	98.50 ± 1.00	96.49 ± 1.22	98.20 ± 1.10	<0.001
SpO ₂ post-induction (%)	98.84 ± 1.33	97.00 ± 2.00	97.88 ± 1.43	98.00 ± 1.00	<0.001
EtCO ₂ post-induction (mmHg)	36.77 ± 3.83	37.00 ± 5.23	38.36 ± 4.15	43.00 ± 1.58	0.005
Peak airway pressure post-induction	20.84 ± 3.38	21.00 ± 2.00	23.03 ± 4.33	23.80 ± 2.28	0.015
Dynamic compliance post-induction	23.75 ± 3.96	24.25 ± 2.99	22.93 ± 4.76	25.80 ± 1.92	0.434
SpO ₂ after pneumoperitoneum (%)	98.38 ± 1.58	96.75 ± 1.26	96.81 ± 1.89	97.20 ± 1.64	<0.001
EtCO ₂ after pneumoperitoneum	40.59 ± 4.62	43.50 ± 2.38	43.97 ± 3.68	43.00 ± 2.00	<0.001
Peak airway pressure after pneumoperitoneum	23.59 ± 3.42	21.25 ± 0.50	26.37 ± 5.54	22.00 ± 2.00	0.002
Dynamic compliance after pneumoperitoneum	21.70 ± 3.06	23.50 ± 1.91	21.15 ± 3.74	24.80 ± 1.79	0.080
SpO ₂ before extubation (%)	98.61 ± 1.38	97.75 ± 1.26	97.10 ± 2.14	95.60 ± 0.89	<0.001
EtCO ₂ before extubation	36.00 ± 4.19	36.25 ± 1.89	39.53 ± 4.07	35.80 ± 0.84	<0.001
Peak airway pressure before extubation	22.00 ± 3.24	25.75 ± 3.10	25.15 ± 4.73	27.60 ± 2.70	<0.001
Dynamic compliance before extubation	22.29 ± 4.25	14.75 ± 4.50	21.10 ± 4.79	14.80 ± 1.79	<0.001

Figure 2. Intraoperative Respiratory Outcomes

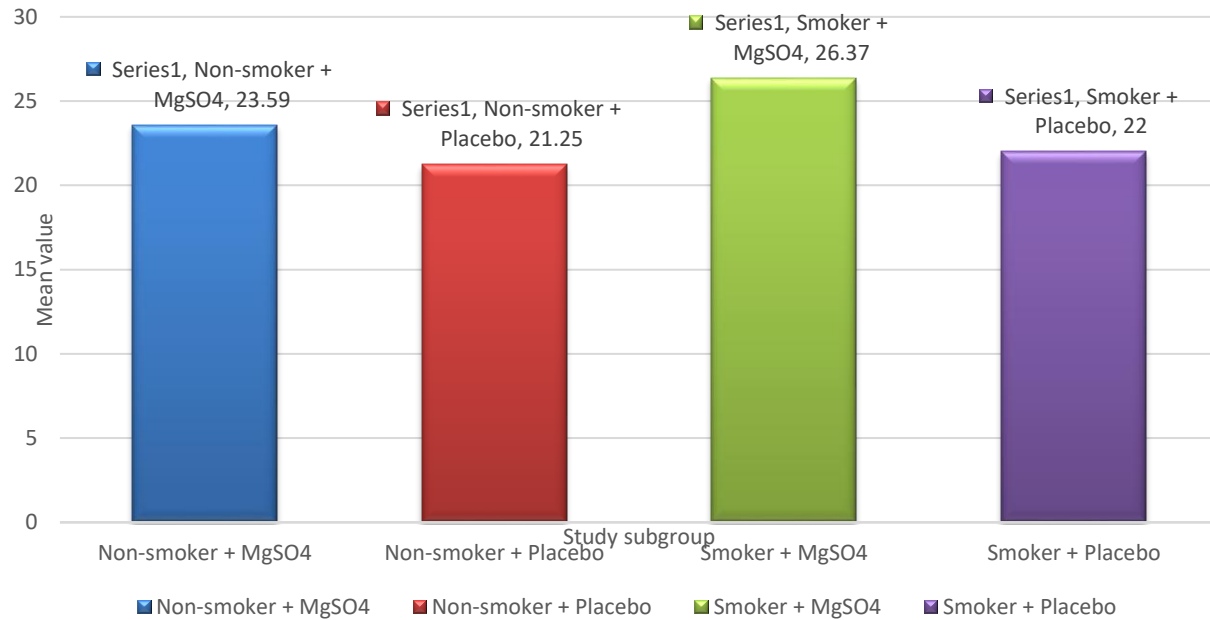


Figure 3. SpO₂ at Pneumoperitoneum

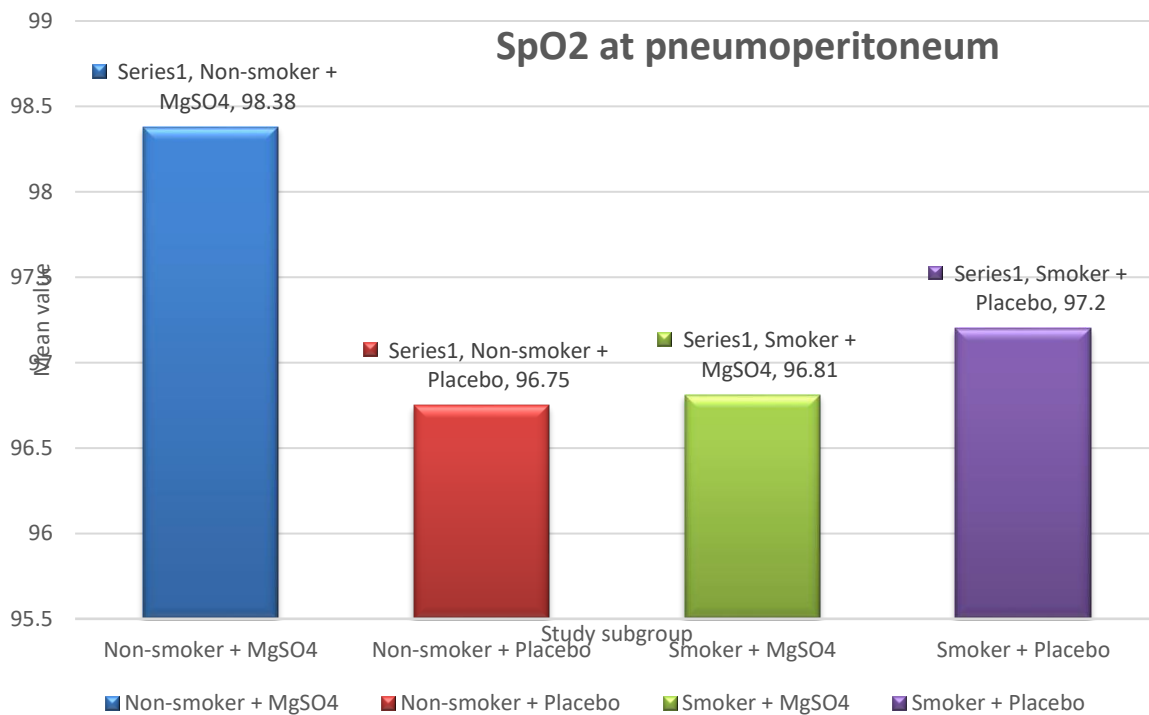


Figure 4. Carbon Dioxide / EtCO₂ Outcomes

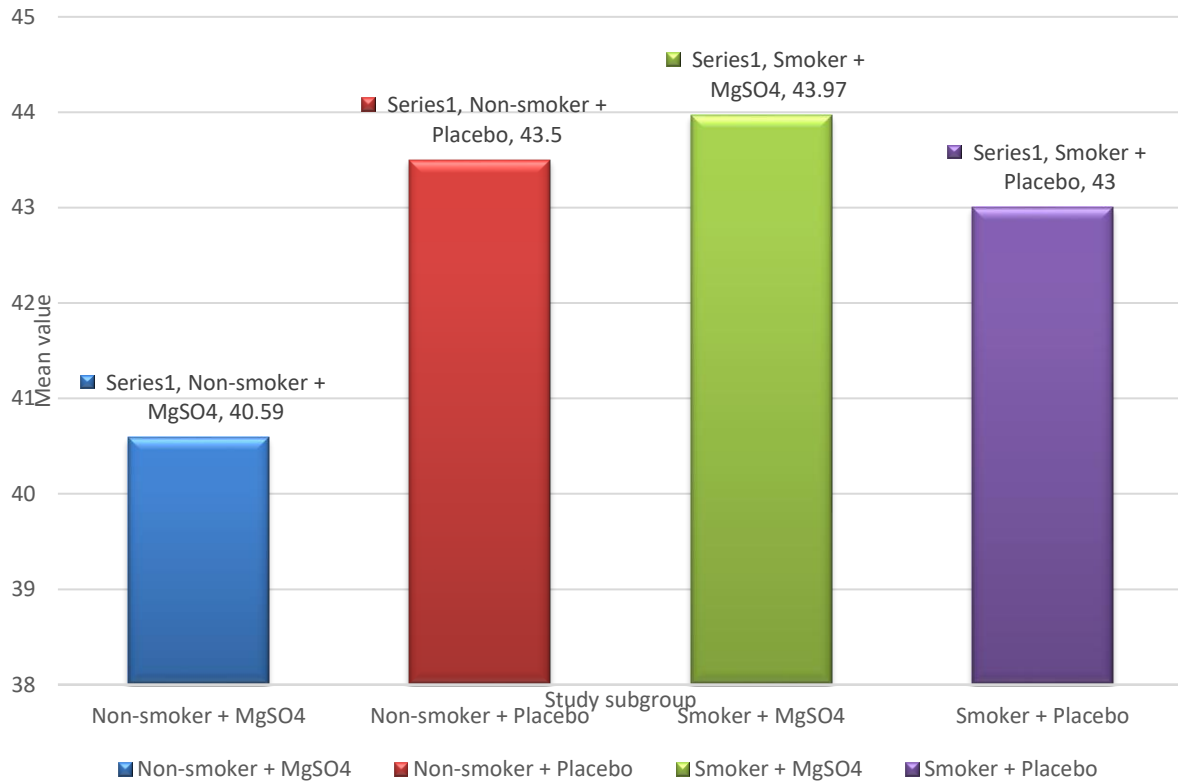


Figure 5. Airway Resistance and Dynamic Compliance



Respiratory complications during surgery comprised hypoxemia in 37 patients, hypercapnia in 53 patients, bronchospasm in 26 patients, laryngospasm in 12 patients, and increased airway pressure in 58 patients. Significant differences were noted between the groups in hypoxemia

($p < 0.001$), hypercapnia ($p < 0.001$), bronchospasm ($p = 0.017$), and increased airway pressure ($p < 0.001$). There was no statistically significant difference for laryngospasm between the groups ($p = 0.146$).

Table 4. Intraoperative Respiratory Complications

Complication	Non-smoker + MgSO ₄	Non-smoker + Placebo	Smoker + MgSO ₄	Smoker + Placebo
Hypoxemia, n (%)	3 (5.4%)	0 (0.0%)	29 (49.2%)	5 (100.0%)
Hypercapnia, n (%)	16 (28.6%)	0 (0.0%)	37 (62.7%)	0 (0.0%)
Bronchospasm, n (%)	6 (10.7%)	2 (50.0%)	18 (30.5%)	0 (0.0%)
Laryngospasm, n (%)	4 (7.1%)	2 (50.0%)	6 (10.3%)	0 (0.0%)
Increased airway pressure, n (%)	18 (32.1%)	2 (50.0%)	38 (64.4%)	0 (0.0%)

Figure 6. Bronchospasm

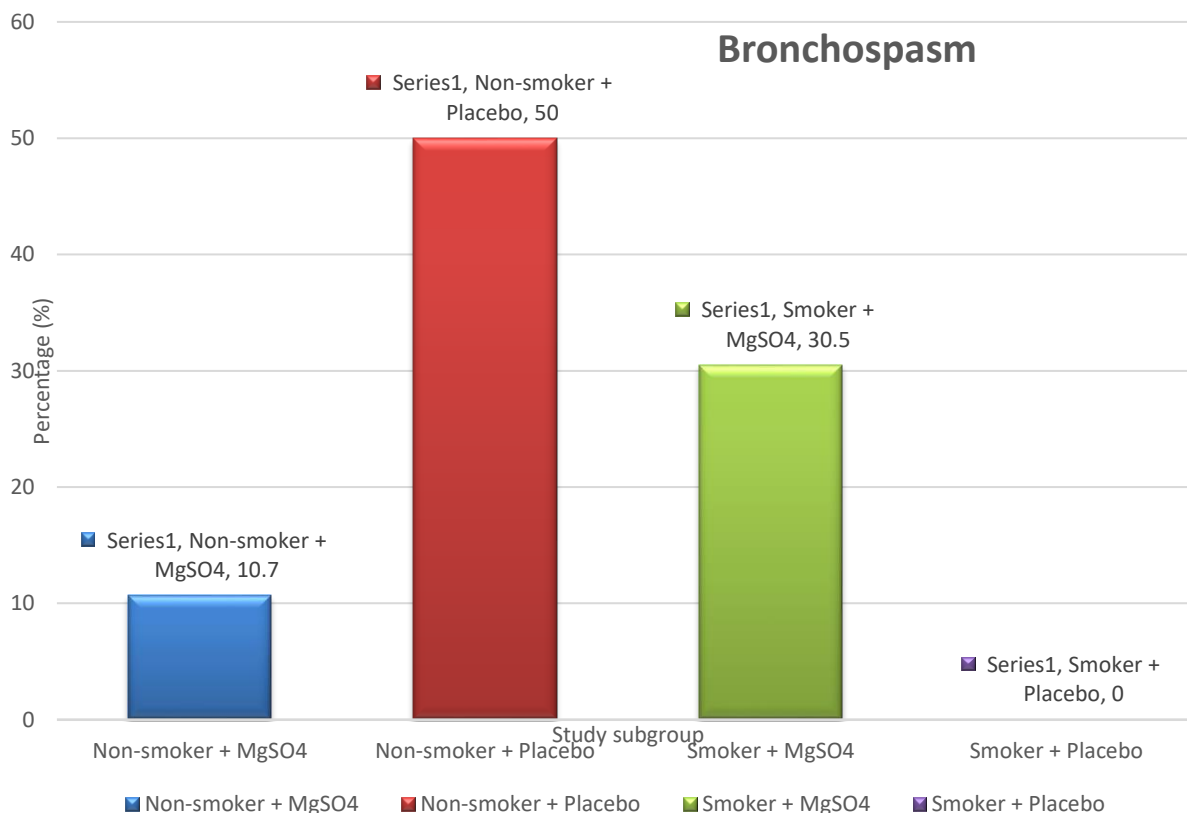


Figure 7. Laryngospasm

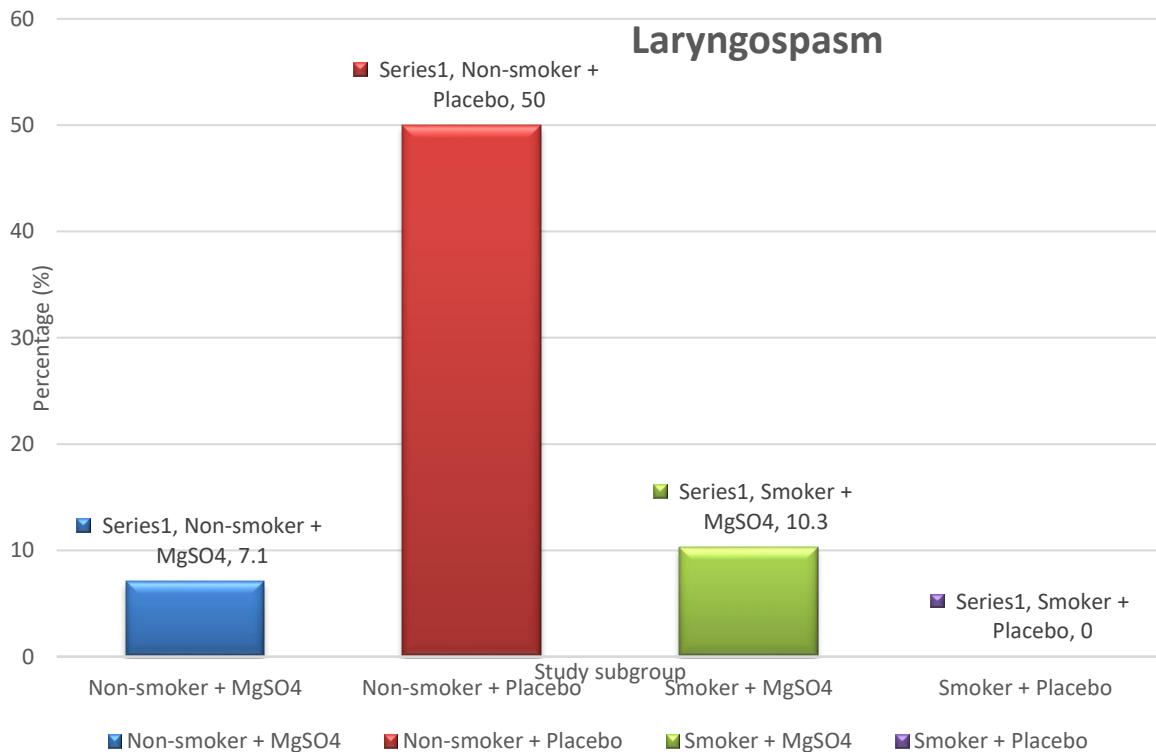


Figure 8. Hypercapnia

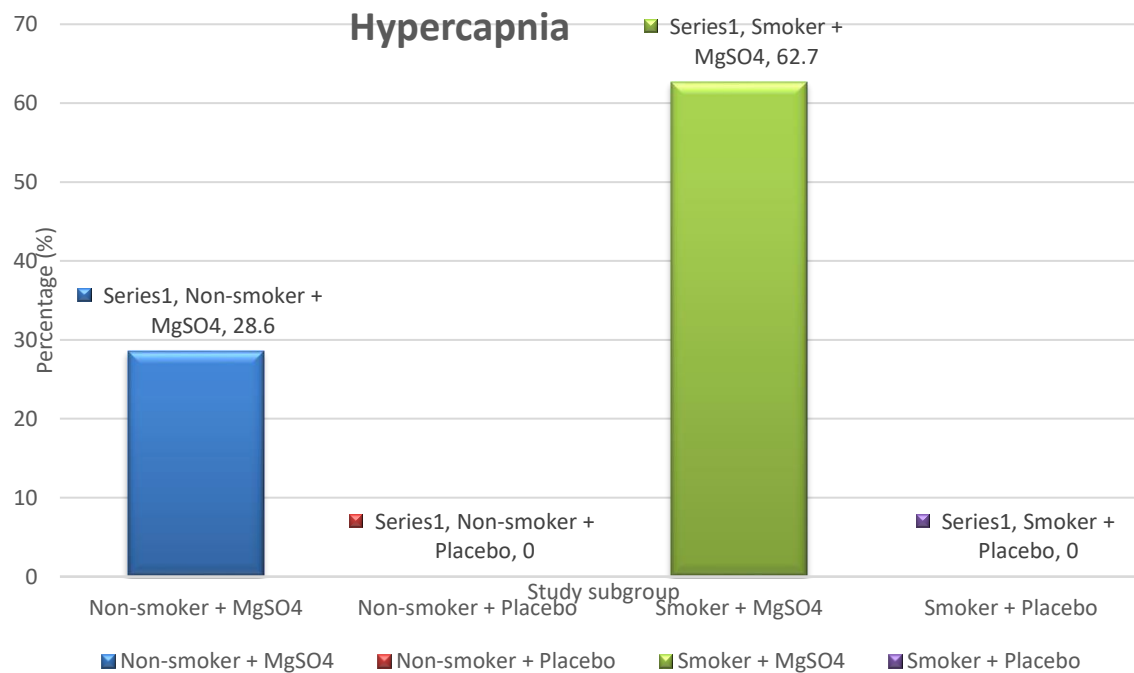
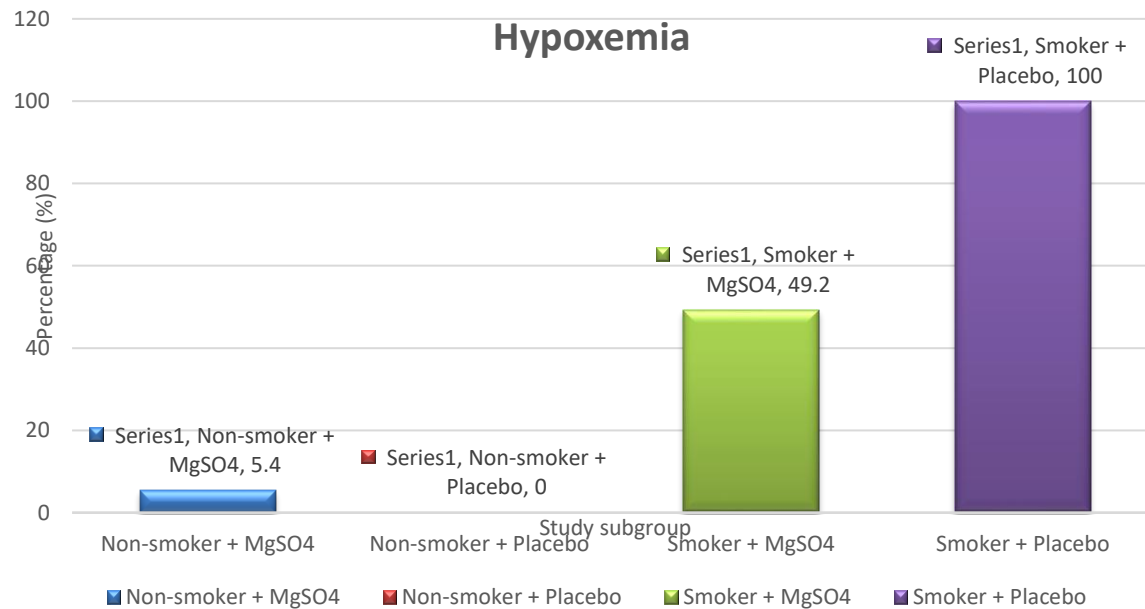


Figure 9. Hypoxemia



Rescue respiratory management was more often needed among smoking patients administered magnesium sulphate. Usage of bronchodilator was needed in 20 (33.9%) smokers, whereas in non-smoking patients, the value was 6 (10.7%). Increased PEEP was needed in 38 (64.4%)

smokers, whereas in non-smokers, the figure was 15 (26.8%). Ventilator changes were needed in 41 (69.5%) smokers, whereas in non-smokers, the value was 21 (37.5%). The reported p-values were 0.007 for bronchodilator use and <0.001 for both increased PEEP and ventilator adjustment.

Table 5. Rescue Treatment Requirements

Rescue intervention	Non-smoker + MgSO ₄	Non-smoker + Placebo	Smoker + MgSO ₄	Smoker + Placebo	Overall p-value
Bronchodilator, n (%)	6 (10.7%)	2 (50.0%)	20 (33.9%)	0 (0.0%)	0.007
Increased PEEP, n (%)	15 (26.8%)	1 (25.0%)	38 (64.4%)	0 (0.0%)	<0.001
Ventilator adjustment, n (%)	21 (37.5%)	0 (0.0%)	41 (69.5%)	0 (0.0%)	<0.001

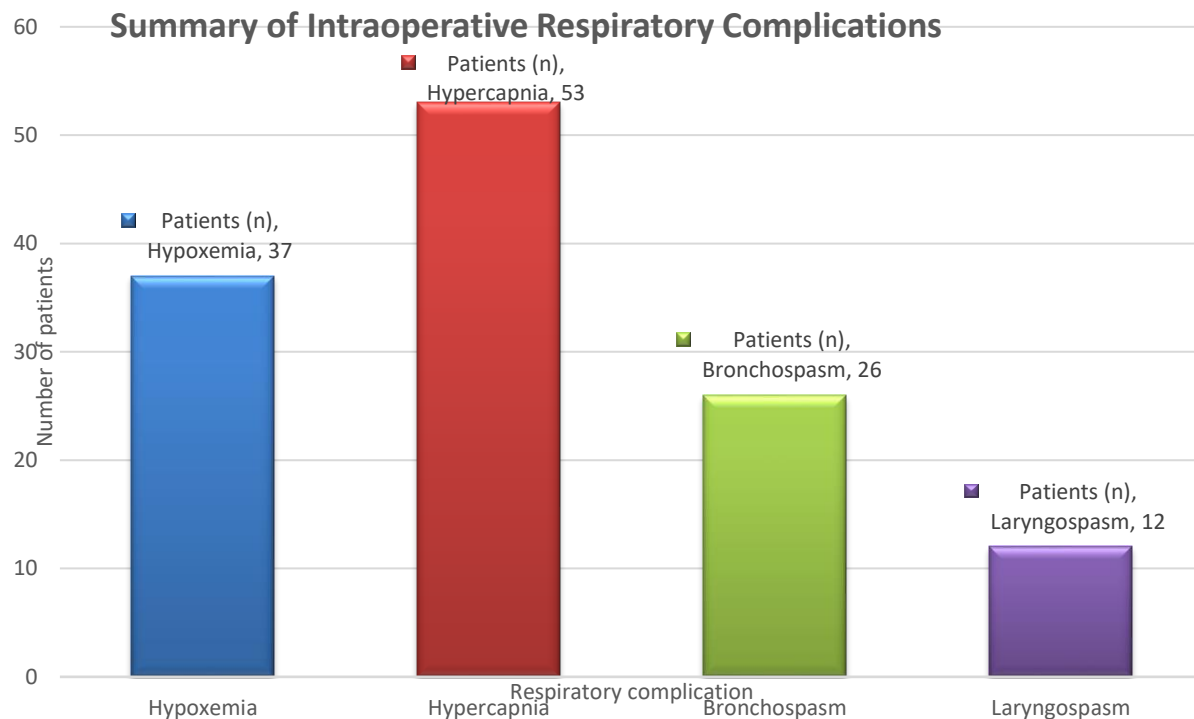
Recovery was also variable between the various groups in the study. The average recovery time was 13.93 ± 5.37 minutes, whereas the average PACU time was 58.67 ± 18.89 minutes. Recovery time was statistically significantly different between the

four groups ($p < 0.001$), as was PACU time ($p = 0.011$). In magnesium treatment group, smokers had a longer recovery and PACU time than non-smokers.

Table 6. Recovery and PACU Outcomes

Outcome	Non-smoker + MgSO ₄	Non-smoker + Placebo	Smoker + MgSO ₄	Smoker + Placebo	p-value
Recovery time (min)	11.61 ± 4.83	15.00 ± 0.82	15.95 ± 5.42	15.20 ± 0.45	<0.001
PACU stay (min)	52.59 ± 16.60	60.00 ± 24.49	63.73 ± 18.84	66.00 ± 25.10	0.011

Figure 10. Summary of Intraoperative Respiratory Complications



Discussion

In the current study, it was shown that there were higher respiratory risks during surgical operations among smokers undergoing laparoscopic cholecystectomy when compared to non-smokers. The findings were most pronounced during pneumoperitoneum and prior to extubation. In the group of patients who were administered magnesium sulphate, smokers had significantly low oxygen saturation, high EtCO₂ and high airway pressures when compared to non-smokers. Reduced SpO₂ levels seen among smokers might be due to lack of respiratory reserve and changes in airway due to smoking. The rise in levels of EtCO₂ in smokers indicates an increase in carbon dioxide load in pneumoperitoneum. The insufflation of carbon dioxide will cause an

increased absorption of carbon dioxide via the peritoneum, while the increased intra-abdominal pressure will affect the movements of the diaphragm and the mechanisms of breathing. The combination of both processes might be harder to compensate in patients with decreased respiratory reserve. There were also differences in peak airway pressure in smokers who had gone through pneumoperitoneum. It corresponds to increased airway resistance and decreased respiratory compliance. The physiological issues related to pneumoperitoneum and airway hyperreactivity in smokers are also described in the thesis literature review. It was determined that there were differences in hypoxemia, hypercapnia, bronchospasm, and increased airway pressure. There were no differences in laryngospasm among

the participants of the study. The use of bronchodilators was also more pronounced among smokers as well as increased PEEP and ventilator adjustments were observed. Thus, smoking status was found to be clinically important as it can indicate the need for more intensive intraoperative respiratory management. Magnesium sulphate can protect airways due to its bronchodilatory effects and relaxation of smooth muscles. Literature review done in the thesis demonstrated the presence of respiratory or airway benefits of magnesium sulphate under various anaesthetic procedures. However, the current findings should be carefully considered. The final dataset included 115 patients receiving magnesium sulphate and only 9 patients treated with placebo. Out of 4 subgroups only 4 non-smokers and 5 smokers used placebo. Thus, the current research can provide good descriptive data on the differences in respiratory outcomes of smokers and non-smokers, but due to the low number of patients in placebo groups, it is hard to make conclusions about the independent effect of magnesium sulphate on airways. Overall, it can be stated that smokers under laparoscopic cholecystectomy still remain a high-risk respiratory group.

Conclusion

Respiratory challenges were more prevalent in smokers undergoing laparoscopic cholecystectomy compared to non-smokers especially during pneumoperitoneum and before extubation. The SpO₂ levels were low in the smokers while EtCO₂ and peak airway pressure were high among the smokers and needed more respiratory intervention. Smokers may benefit from magnesium sulphate in respiratory management during surgery but this study does not show enough evidence due to the very small placebo groups for both magnesium sulphate and control groups. More randomized trials should be done with adequate sample sizes.

Limitations

- This study was done in a single center, and therefore there could be limitations in generalizing the results to other settings.
- There were very small sample sizes in placebo group because there were 4 non-smokers and 5 smokers taking placebo. This will make the statistics weak for comparing treatments.
- The population under investigation was undergoing laparoscopic cholecystectomy, and thus the results cannot be generalized to other surgeries.
- The study mostly looked at intra-operative and early recovery findings, but did not have comprehensive follow-up of the respiratory system after surgery.
- There were no smoking characteristics such as duration and pack-years of smoking taken into consideration in group comparison.
- The study period and location may affect external validity.

Recommendations

- The future research must use a greater sample size with balanced magnesium sulphate and placebo groups.
- The future research must conduct multicenter randomized control trials to increase the generalizability of results obtained from the research.
- The future research must consider the degree of smoking intensity, duration and pack-years in their respiratory outcome evaluation.
- Postoperative respiratory outcomes must be considered in order to see if there is a significant difference in respiratory outcomes after the surgery.
- The future research must have respiratory outcomes well defined and standardized criteria for rescue intervention.
- Various dose and protocol of magnesium sulphate should be considered to find the best perioperative approach.
- Future research must examine whether the respiratory effect of magnesium sulphate varies according to smoking severity and respiratory risk.

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