



**An-Najah National University**  
**Faculty of Graduate Studies**

# **EFFECT OF INTRAVENOUS MAGNESIUM SULFATE IN ACUTE ASTHMA**

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## **Dedication**

I thank God Almighty and i dedicate this research to the owner of a fragrant biography and enlightened thought, for he had the first credit in attaining higher education (my beloved father), may God prolong his life.

To those who set me on the path of life, made me calm, and took care of me until I become old (my great mother).

I dedicate this achievement to my great and kind husband who has always been beside me and supported me in my period of study.

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It would not be possible to achieve this without the support of my family, especially my parents ,my wonderful husband. This accomplishment would have been impossible without them.

Thanks To everyone who gave me the moral support for the completion of this task.

**Author**

**Abeer Mahameed**

## Declaration

I, the undersigned, declare that I submitted the thesis entitled:

### **EFFECT OF INTRAVENOUS MAGNESIUM SULFATE IN ACUTE ASTHMA**

I declare that the work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

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# **EFFECT OF INTRAVENOUS MAGNESIUM SULFATE IN ACUTE ASTHMA**

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## **ABSTRACT**

**Background:** Acute asthma exacerbations can lead to admission to the emergency room. When these exacerbations do not respond to standard therapy, guidelines recommend administering a single intravenous bolus dose of magnesium sulfate in addition to standard therapy for the management of patients admitted to the emergency room.

**Objective:** This study was conducted to evaluate the effectiveness of magnesium sulfate administered intravenously in combination with standard treatment to patients with acute asthma admitted to emergency room settings in a major governmental hospital in Palestine.

**Methods:** This study was conducted in a quasi-experimental design. Patients in both control and intervention groups were recruited from Al Watani hospital. The patients were recruited during the high season of acute asthma exacerbations. Patients in the control group received standard therapy. Patients in the intervention group received a single intravenous bolus dose of magnesium sulfate in addition to the standard therapy. Demographic and clinical variables of the patients were collected on a data collection sheet. Dyspnea was measured using a modified Borg dyspnea scale.

**Results:** A total of 65 patients were assigned to control ( $n = 32$ ) and intervention ( $n = 33$ ) groups. Patients in both control and intervention groups were similar in terms of demographic and clinical variables before the intervention. There were no significant differences in dyspnea measured before the treatment. Administration of a single intravenous bolus dose of magnesium sulfate in addition to standard therapy was shown to significantly reduce signs of dyspnea as measured in the modified Borg dyspnea scale.

**Conclusion:** Magnesium sulfate administered intravenously in combination with standard treatment to patients with acute asthma admitted to emergency room settings in Palestine might have improved signs and symptoms of dyspnea compared to standard treatment alone.

**Keywords:** Asthma, Exacerbation, Magnesium sulfate, Emergency department.

# **Chapter One**

## **Introduction and Literature Review**

Severe acute asthma, also known as an asthma condition, is a serious medical emergency that requires immediate intervention by medical personnel including bronchodilator therapy and systemic corticosteroids. Sometimes complications of asthma and some cases do not respond to these drugs from dilators and others, so intravenous magnesium sulfate was considered an effective treatment(Agnihotri & Saltoun, 2019).

The economic burden of countries is increasing day by day, and this is due to many reasons, and one of those reasons is the large number of chronic diseases that need a lot of treatment and long hospital occupation, the most common chronic disease is acute Asthma, the needs of treatment for such this disease take long times not just the time also the frequency of the attacks, so one person can suffer from asthma many times in one year, After the investigation, the medical team observe that many cases entering the emergency department suffering from acute respiratory diseases specially asthma (Moore et al., 2007).

Asthma is a common disease that affects all people specifically children, then adults, and affects over 300 million people in the world. Therefore, it is estimated that by the beginning of 2025 numbers of these cases will be around 400 million people all over the world (Pawankar, Canonica, Holgate, & Lockey, 2012).The prevalence rate is from 1-18 percent in most countries. The number of deaths every year reaches about 250,000 people. In the United Kingdom, 60,000 hospitalized cases were diagnosed as asthma every year. Also in Nigeria, Elegbeleye reported a mortality rate of 6% Lagos University in a Teaching Hospital over 9 years(Fanta & Daba, 2016).

Regarding some statistics around 10% of the world's population suffers from asthma. In the United States, disease burden has increased by 15% over 20 years, and 5% of those cases are categorized as severe asthma, hospitalized adult asthmatic patients require ventilator support in between 3% and 16% of cases(R. K. Chakraborty & Basnet, 2021).

Asthma is best defined as a chronic disease that enrolled inflammation of the pulmonary airways and bronchial hyper-responsiveness that consequences in the clinical presence

of a lower airway obstruction that is reversible in usual. Physiologically, bronchial hyper-responsiveness is known as diminished bronchial airflow after bronchoprovocation with methacholine or histamine. Other causes and triggers that provoke airway obstruction include cold air, exercise, viral upper respiratory infection, cigarette smoke, and respiratory allergens (Fireman, 2003).

According to the etiology, asthma is divided as the following:

1. Allergic Asthma: This kind of asthma usually starts since childhood.
2. Infective or Intrinsic Asthma: Related with upper respiratory tract or bronchial infections.
3. Emotional Asthma: comes with stress and psychological issues.
4. Occupational asthma: usually from the area of working, such as dust (Dahat, 2021).

Asthma is an emergency that needs very rapid treatment because that may lead to obstructions of the airflow during exacerbations which leads to life-threatening respiratory failure. Initial and emergency treatment requires oxygen,  $\beta_2$  stimulants. For patients who are not responding to this standard treatment, magnesium sulfate may be an option of treatment (Duong, Zeki, & Louie, 2017).

Asthma has many risk factors that trigger the disease and exacerbate its symptoms, these factors could be prevented or overwhelmed such as reducing smoking and environmental smoke disclosure; decreasing air pollution and occupational exposures; decrease the body weight to avoid obesity; improving fetal-maternal health; breastfeeding; childhood vaccinations; and reducing social inequalities (Beasley, Semprini, & Mitchell, 2015).

Magnesium is a chemical compound that helps maintain cellular balance in the body due to it is a cofactor in many enzymatic reactions, a salt of formula  $\text{MgSO}_4$ , consisting of magnesium cations  $\text{Mg}^{2+}$  that make 20.19% of the mass and sulfate anions  $\text{SO}_4^{2-}$ . It is a solid white crystalline, soluble in ethanol. Magnesium is an essential mineral and is common in biological environments as it is one of the soil components (Long & Romani, 2014).

Magnesium has many benefits and usage, but it has some uses that were not yet clearly understood, specifically in asthma, but research has shown how it works, magnesium prevents the release of acetylcholine from the nerve limbs by adjusting and modifying the flow of calcium ion causes bronchiectasis (Long & Romani, 2014).

Additionally, magnesium rather than stabilize T cells it could prevent their activation, and prevents the degradation of mast cells, and therefore limits the production of inflammatory mediators as it motivates the production of nitric oxide and prostacyclin, and may reduce the intensity of asthma restoration (De Sanctis et al., 2015).

Mostly Acute Asthma patients can be stabilized and treated in an emergency department or an equal care setting. According to the recommendations of the Global Initiative for Asthma (GINA), patients with severe exacerbations, all should initially be given oxygen,  $\beta_2$  agonists, anticholinergic, and corticosteroids, the onset of bronchodilation effect may happen within minutes by using inhalers with  $\beta_2$  agonists or within hours as in corticosteroids. In some cases, the standard treatment (Ipratropium or cortisone) maybe inefficient so Magnesium sulfate can be as a therapeutic option for those patients who do not respond to these initial therapies, Although magnesium sulfate is really beneficial in acute asthma in patients who are not responded  $\beta_2$  agonists and systemic corticosteroids, its use remains restricted in pediatric emergency settings (Saadeh, 2020).

Although the use of magnesium sulfate is common in obstetrics, acute asthma and others, it has side effects like hypermagnesemia-induced lethargy, diminished reflexes (diminished deep tendon reflexes), muscle weakness, paralysis of the respiratory muscles, paralytic ileus, and even cardiac arrest have always been of concern. significant hypermagnesemia is generally uncommon with normal renal function(Arumugam, Takkellapati, & John, 2021).

Acute magnesium toxicity is unusual. Magnesium toxicity can present in several ways, This toxicity is due to magnesium's effect on blocking calcium and potassium channels, both extracellular and intracellular. Calcium gluconate treats hypermagnesemia through direct antagonism of magnesium at the site of action(A. Chakraborty & Can, 2021).

Renal clearance is the main determinant of free serum magnesium, as closely all levels above normal is quickly excreted in the urine. Therefore, the maximum serum level throughout therapy depends more on the rate of infusion and not on the total dose or duration of the infusion(Jose E Irazuzta, Fatima Paredes, Viviana Pavlicich, & Sara L Domínguez, 2016).

Asthma is treated by 4 steps, alternating from mild to intensive managements, depending on the severity; each step includes an suitable dose of an inhaled corticosteroid, which may differ from low to high. Long-acting beta2-agonists, leukotriene receptor antagonists, sustained-release theophylline, and long-acting muscarinic antagonists are suggested, regarding anti-immunoglobulin E antibodies and other biologics, and oral steroids are used for very severe and persistent asthma related to allergic reactions. Inhaled  $\beta_2$ -agonists, aminophylline, corticosteroids, adrenaline, oxygen therapy, and other methods are used as needed during acute exacerbations(Nakamura et al., 2020).

Asthma in pregnancy may be different by the phase(stage). The 1st trimester is well tolerated in asthmatic women, with infrequent acute episodes. The symptoms and episodes of exacerbations have been mainly happened between gestation weeks 17 and 36.asthmatic women, lean towards experience less symptoms and less numerous asthma exacerbations during weeks 37 to 40 of pregnancy. The crucial aim of asthma therapy in pregnancy is to preserve sufficient oxygenation of the fetus preventing hypoxic events in the mother. Inhaled Corticosteroids are the support of controller therapy during pregnancy. Studies shown that cortisone does not affect the baby, there is no significant increased risk of congenital malformations and has very few side effects on the delivery stages(Namazy & Schatz, 2018).

Barriers to asthma control can include any of the following: viral infections, obesity, and tobacco smoke exposure(Namazy & Schatz, 2018).

As we know the respiratory symptoms and signs for asthma are unfortunately similar to other respiratory disease , the most critical and new one is COVID-19, which is a pandemic that we live with it from 2020,viruses commonly trigger asthma exacerbations, overrepresentation can occur since severe acute respiratory syndrome



coronavirus 2 , activates asthma exacerbations, that's make asthma as a risk feature for COVID-19 mortality and morbidity (Abrams, W't Jong, & Yang, 2020).

Oxygen should be given to those cases because most of them develop hypoxemia, high flow nasal cannula oxygen therapy developed recently, in which oxygen at a definite concentration combined with high-flow gas is directly transported to patients through a non sealed nasal cannula. This O<sub>2</sub> therapy has been evaluated by many studies and can be applied to patients with acute hypoxemic respiratory failure and respiratory failure without tracheal intubation, thus effectively improving oxygenation. However, few studies have confirmed the efficacy of high flow nasal cannula in treating bronchial asthma(Geng, Batu, You, Tong, & He, 2020).

Having severe asthma interferes with the health-related quality of life of patients. The concept of health-related quality of life involves physical, mental, emotional, and social domains. Rather, it emphasizes the impact health status has on quality of life, over and above the direct measures of morbidity and mortality. Currently, many public health messages erroneously suggest that asthmatic individuals can live normal, unaffected lives free of asthma symptoms (McDonald, Hiles, Jones, Clark, & Yorke, 2018).

### **1.1 Problem statement**

Asthma is one of the most common chronic diseases, causes significant increase in morbidity and mortality, and has resulted in a public health load. Asthma affects 1.6 million people and is responsible for approximately 183,000 hospital admissions every year in United States. unfortunately, the poor quality emergency department may be responsible for up to one-third of these deaths (Pate et al., 2021). Acute asthma is a medical emergency that must be quickly diagnosed and treated, airflow blocks during exacerbations can be severe, resulting in life-threatening respiratory failure.

### **1.2 significant of study**

The importance of the topic comes from the researcher hospital experience that magnesium becomes one of the drugs used for the treatment of many disorders, and thus leads to reducing the mortality rate and the costs especially in Palestine there is a shortage in the medical fields, so if the treatment of asthma by mgso<sub>4</sub> in ER can help in curing the patients and facilitate their early discharge will save the costs and the humane medial recourse that are needed to follow up such of these cases, also this can save the

beds leading to more and more patients can utilize the medical service, so this study could be adopted by the ministry of health and being a policy to be used in the management of acute asthma.

From the moral and the patient view , it is great if we can alleviate and decrease the suffering of the asthma patients, due to it is acute event and every minute can be decreased will help the patient to get rid of this bad experience.

Regarding the statistics, worldwide asthma affects around 300 million people, and this number is predictable to reach 400 million by 2050. In Palestine, the prevalence rate of asthma in children living in villages, cities, and refugee camps were 17.1%, 8.8%, and 9.4%, respectively(El Bilbeisi, Albelbeisi, Hosseini, & Djafarian, 2019).

### **1.3 Aim of study**

The aim of present study is to assess the effectiveness of intravenous magnesium sulfate in minimizing the patient's symptoms of acute asthma in the emergency setting in Palestine.

### **1.4 Research question**

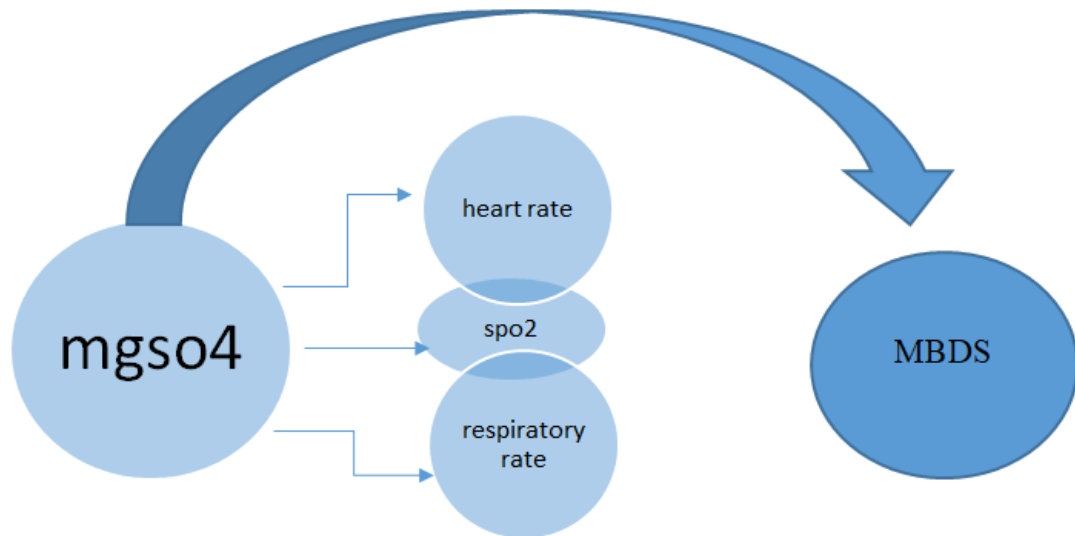
- Does intravenous magnesium sulfate effective in treating adult Acute Asthma in the emergency setting?
- Do demographic and characteristics of patient with acute asthma affect the mg treatment outcome?
- Does the use intravenous magnesium sulfate affect the patients length of stay time in ER?

### **1.5 Research hypothesis**

**Null hypothesis:** There no benefit from adding intravenous magnesium sulfate to standard treatment of adult acute asthma.

**Alternative hypothesis:** There is a benefit from adding intravenous magnesium sulfate to standard treatment of adult acute asthma.

## 1.6 Conceptual Framework



## 1.7 Variables

### Independent variables:

- Mgso4
- Demographic characteristics ( age , gender , weight ) .

### Depended Variables:

- Spo2 .
- respiratory rate .
- Blood pressure.
- pulse.
- modified borg dyspnea scale (MBDS) .

Interval: the interval of variables should be within normal range for all dependent variables:

- Spo2: 95-100 .
- Respiratory rate: 12-24 rate /hour .
- Blood pressure: 110/60-150/95mmhg`.
- Pulse: 60-100 beat /minute .
- MBDS it should be within normal range 1/10.

### **1.8 definition of related term**

**Mgso4:** A small colorless crystal Unbounded physiological serum magnesium (Mg), directly bound to ionized Mg, produces a transient block of N-methyl-D-aspartate receptor calcium channels with subsequent muscle relaxation. Preventing calcium from entering the airway interferes with the contraction of smooth muscles, causing bronchiectasis (Irazuzta & Chiriboga, 2017).

**Asthma:** is a multifactorial, chronic inflammatory disease of the airways, cause a variable degree of air-flow obstruction and bronchial hyper-responsiveness, narrowing and inflammation of the small airways in the lungs leads to asthma symptoms, which can be cough, wheeze, shortness of breath and chest tightness, and it is usually revisable(Myers & Tomasio, 2011).

**Emergency department:** known as an emergency room, emergency ward or casualty department, is a medical treatment facility specializing in emergency medical and surgical care , the acute care of patients who present without a prior appointment(Weiss, Wier, Stocks, & Blanchard, 2014).

**Modified borg dyspnea scale:** is a 0 to 10 graded numerical score used to assess dyspnea as described by the patient throughout submaximal exercise and is usually administered during six-minute walk testing. Most common and frequently used to assess the disease severity in Pulmonary arterial hypertension, asthma and COPD (Banerjee et al., 2017).

## 1.9 literature review

Magnesium is one of the most common electrolytes in the human body and its role is well known in human biology. The researchers focused on studying its role as assistance or even therapy for many conditions, some of them are life threatening. However, One of the most critical facts regarding Mgso4 researches is about the right therapeutic dose. A slow iv bolus of 2 g of Mgso4, given not less than 20 min , appears to be the preferred dose in most investigations to minimize the side effects of a rapid administration while exploiting its full potential. Up to now the use of Mgso4 in the ED has entered the daily routine in the treatment of many conditions(Carroll & Lenney, 2007).

Mgso4 use was recommended by many protocols and guideline in cases of acute refractory asthma status, and its uses has now entered clinical practice. Nebulized Mgso4 seems to have no particular benefit in moderate asthma exacerbations, but intravenous use may reduce the need for hospital admission in adult the patients presenting to the ED with severe asthma exacerbations. Moreover, a randomized trial of Alansari tried to determine the utility of intravenous use of Mgso4 in acute bronchiolitis when added to supportive care, but it does not seem to provide any particular benefit, although Kan would seem to encourage the use of inhaled Mgso4 in the same state, in addition to standard therapy(Mohammed & Goodacre, 2007).

In 2017 the researcher did a research on the effect of Mgso4 in bronchitis asthma, but the result was contradictory that IV magnesium did not provide benefit for patients with acute bronchiolitis and may be harmful(Alansari, Sayyed, Davidson, Al Jawala, & Ghadier, 2017).

In 2019 the researcher applied a research use mgso4 in ER for multiple cases, some cases have asthma coming to ER, after giving the therapeutic dose from mgso4, the bronchus was dilated, and allow patients who breath more o2, and decreasing the effort of breathing and dyspnea also most of them was discharged from ER(Gilardi et al., 2019).

In 2014, similar research on the use of magnesium to treat chronic diseases, particularly the crisis in the elderly, and medical records were reviewed in that year and it was found after the procedure to give magnesium that giving it in the emergency room reduces the

patient's admission to the hospital, as they noticed that the patient's admission to the hospital causes Psychological situation and increases his sickness, and this in itself does not help with treatment, and to be discharged from the hospital helps the patient to recover seriously (Kew, et al., 2014).

The medical records were reviewed and according to statistics it was found that 10% suffer from asthma and that half of them do not respond to treatment and did not admitted to the hospital (Green et al., 2016).

In 2012 retrospective study was reviewed by many specific databases, mainly on the use of magnesium in the dealing of severe asthma. The researchers determined after conducting a review of the records that magnesium has very little toxicity compared to other drugs that have been already used in asthma, it is preferred to be used on many treatments and this shows it is better to use intravenously than to use it with a nebulizer, and this has been proven by review, and there are many patients who have benefited from magnesium therapy(Song & Chang, 2012) .

Quasi-randomized trials of Ten samples were identified 4 of these patients with asthma, who had given mgso4 iv, and 4 patients with asthma were given mgso4 nebulizer. The meta-analysis showed that iv magnesium sulfate is an effective treatment, clear and extraordinary results of intravenous magnesium were observed, as it showed effective results, specifically children, as their lung function improved and symptoms of asthma decreased compared to those who did not use magnesium, but the use of nebulizer for magnesium didn't show any effective results for them (Su, Li, & Gai, 2018).

This study conducted in Asuncion, Paraguay evaluated the efficacy of a high-dose prolonged magnesium sulfate infusion in patients with severe asthma , using Prospective, randomized, open-label study , they took all patients who were not improved after 2 hrs. of standard therapy for asthma. Participants were randomized to receive magnesium sulfate, 50 mg/kg over 1 hour (bolus) or high-dose prolonged magnesium sulfate infusion of 50 mg/kg/hr for 4 hours (max, 8.000 mg/4 hr). Patients were monitored for cardiorespiratory complications. They assessed Asthma severity via asthma scores and peak expiratory flow rates at 0-2-6 hours. 38 patients were joined, 19 in each group. There was a statistical significant in the patients discharged at 24 hours. in the high-dose prolonged magnesium sulfate infusion group was shorter in the period

of staying in hospital. The costs in the high-dose prolonged magnesium sulfate infusion group was 1/3 lower than the bolus group, there were no interventions or discontinuations of magnesium sulfate due to adverse events(Jose E Irazuzta et al., 2016).

This study adopted an idea that if serums electrolyte levels affect asthma progression in both chronic and acute events, by using a prospective cross-sectional study they divide the participants into two groups, group 1 that involved 50 patients existing with chronic stable asthma and group 2 that involved 50 consecutive patients existing with acute severe asthma, serum level of electrolytes (Mg, Na, K, Ca). The results was hypomagnesemia and hypocalcemia were found to be the two most common electrolyte disturbances in patients with chronic stable asthma and acute asthma exacerbation. Therapeutic agents used to treat patients with chronic asthma have a role on abnormal electrolyte levels(Mohammad, Abdulfttah, Abdulazez, Mahmoud, & Emam, 2014).

Regarding the quality of life for patients with asthma was observed by a study that took a random sample and cross-sectional method was applied on 160 patients ,they observe that 68.75% have complaint of active wheezing chest, 68.75% take their medications regularly, while 25% patients take their drugs infrequently, and when needed due to asthma attack, whereas 6.25% patients never take their medications(Naveed, Hameed, Sharif, Qamar, & Abbas, 2016).

This study applied in Finland attempted to know the incidence of allergic and non-allergic asthma, the questionnaire for 4173 responded subjects included questions on atopic status, asthma and age at asthma diagnosis. Median ages that diagnosis of allergic and non-allergic asthma were (19 and 35 years) The incidence of allergic asthma is peak in early childhood and gradually decreases with aging . while the incidence of non-allergic asthma is low until it peaks in late adulthood. After approximately 40 years of age, most of the new cases of asthma are non-allergic(Pakkasela et al., 2020).

This study attempted to assess the effects of ipratropium inhaler vs. placebo on clinical outcomes of serious asthma in critically ill children, using a double blinded, placebo-controlled, pilot randomized controlled trial done in a pediatric ICU at a quaternary care center , 30 participants 15 in each group were randomized to receive either ipratropium bromide nebulizer or an equivalent volume of nebulized 0.9% saline, they found that

was no significant difference in median duration of albuterol between the intervention group (17.5 [10.3-22.1] hours) and placebo group, the length of stay in hospital or in pediatric intensive care unit was similar for both groups , Side effects were rare and happened with similarly and equally between both groups, so finally ipratropium was not associated with decreased duration of high intensity albuterol or shortened length of stay when compared to placebo(Murphy et al., 2020).

Randomized controlled trials including 896 asthmatic adults or children assigned to investigate the efficacy of  $\text{MgSO}_4$  inhaler administered in acute asthma on pulmonary functions and numbers of admissions, patients were  $\text{MgSO}_4$  nebulizer alone or in combination with  $\beta_2$ -agonist. The result assume that magnesium sulfate inhaler is suggested only after someone suffering an asthma attack has been given bronchodilators, steroids and has failed to respond sufficiently to them(C. Powell et al., 2012).



## **Chapter Two**

### **Methodology**

This chapter presents an overview of the research methodology that were used for this study. It includes: study design, setting, population, inclusion and exclusion criteria, sample size and sampling process, ethical consideration, project Time table , Data collection procedure , Data Collection and Data analysis plan .

#### **2.1 Study design**

This study conducted as a prospective, quasi-experimental . This design adopted due to its strength on the hierarchy of scientific evidence, having less bias chances and more powerful accurate result(Murad, Asi, Alsawas, & Alahdab, 2016a).

#### **2.2 study Population**

The target population are all adult patients with acute asthma who met the inclusion criteria and coming to be treated in ER of Al Watni governmental hospital.

#### **2.3 Study site and setting**

This study conducted in the ER at Al -Watani Governmental Hospital, Which is a referral Palestinian government hospital for medical cases in the West Bank , it's number of beds is 55, this hospital was build up in 1888 in the era of the Ottoman Empire that is located in Nablus city that have a population around 415,000 according to Palestinian Central Statistical Organization.

#### **2.4 study period**

It implemented in the period between August 2020 until December 2021.

#### **2.5 sample size**

The sample size is 60 patients in both groups , based on effect size (.42) (Kendrick, Baxi, & Smith, 2000), power of 0.80 and alpha level of 0.05 that calculated by G power.

Also extra 5 participants was taken to overcome the withdrawal.

## **2.6 inclusion & exclusion criteria**

### **Inclusion criteria:**

- Patients have acute asthma .
- Patient above 18 years ago .
- Patient who are living in Nablus west bank , and available at the study period .

### **Exclusion criteria:**

- Patients who have renal diseases.
- Patients who have liver diseases.
- Patients who have other respiratory diseases.
- Patient have allergy to mgso4.
- Patient who have cardiac disease.
- Patient none available at the time of data collection.

## **2.7 Sampling technique**

Convenience method was applied as any patient enter to ER who met the inclusion criteria and suffering from asthma and who agree to join the study , in co-operation with the medical doctor and the emergency team, patients assigned to conventional group without randomization, they suggested also that if the conventional (control) group does not respond to traditional treatment , they will be transferred to interventional group.

## **2.8 study tool**

To achieve the study objectives, the assessment tool used. It includes :

- The first section consisted of demographic information, including diagnosis, gender, and age.

- The second section consisted of a checklist to record the value of heart rate, respiratory rate, oxygen saturation (SaO<sub>2</sub>), BP and temperature.
- The third part consisted of a modified borg dyspnea scale checklist for observing before, during and after intervention.

## **2.9 reliability**

A study showed that a significant correlation existed between the change in MBDS, from pretreatment to post treatment scores ( $r = -.42$ ,  $P < 0.001$ ). so The MBDS is a valid and reliable assessment tool for dyspnea. Patients who used the MDBS evaluated it with a high degree of satisfaction on the ease of use and found that the language in this scale adequately stated their dyspnea(Kendrick et al., 2000).

In this study the researcher did Test-retest, cronbach's alpha = 0.912

## **2.10 validity**

Three faculty doctors at An-Najah National University, from different department expert were consulted and they agreed to review my assessment tool with little editing .

## **2.11 Protocol of study**

When the patient was admitted to ER suffering from shortness of breath due to asthma exacerbation and met the inclusion criteria, consent form and demographic data were taken but if the patient was irritable the researcher take the data from the family, then connected to cardiac monitor ( BP, o<sub>2</sub> saturation, HR, temperature and RR ), vital signs and MBDS recorded and connected to o<sub>2</sub> therapy, iv access obtained, after that examination by the doctor and confirming that the patient is in a state of asthma exacerbation.

- Control group: ipratropium and albuterol in addition to corticosteroids administered to patient as the policy of the hospital as the following 0.5mg of ipratropium, 2.5 mg of albuterol mixed with normal saline 0.9%, in addition to hydrocortisone 200mg iv, after 30 min vital signs and MBDS recorded.

- Intervention group: was given ipratropium, albuterol and corticosteroids as the control group then after 30min MBDS and vital signs recorded and given 2g of mgso4 over 20min iv bolus ,at the end of mgso4 ,vital signs and MBDS were recorded.

The duration from admission to discharge from the ER recorded at the end of treatment.

If the patient does not respond the treatment was admitted to ICU for further management and unfortunately not taken in this study.

Note: Regarding the separation of the patient to control or intervention group was left to the medical doctor and according to the status of the patient. If the patient does not respond to traditional treatment by the nebulizers of (ipratropium and albuterol ) in addition to corticosteroids, directly treated with mgso4 and considered as an interventional group.

## **2.12 Statistical Analysis**

The data saved into a computer and be analyzed using SPSS program. - Microsoft office programs (such as Excel and Word software) and other software used for data analysis and interpretation like (ANCOVA statistical test, Chi-squared test and Partial Eta Squared)

## **2.13 Ethical considerations**

Approval from the institutional review board (IRB) was obtained from An-Najah National University IRB committee. The Palestinian Ministry of Health facilitation letter was taken to allow for data collection from the clinical field in Al Watni Governmental hospital. Prior to participation a written consent obtained from the participants or their families for those patients with decreasesd LOC or were unable to take the decision. The project was explained to potential participants before they consent to participate in the study. Anonymity and confidentiality were secured. Also the participants informed that they can withdrew from the research at any time without giving any reason.

## **Chapter Three**

### **Results**

#### **Introduction**

The purpose of present thesis is to assess the effectiveness of intravenous magnesium sulfate in treating patient with acute asthma in the emergency setting in Palestine. Furthermore, figure out the most indication of magnesium sulfate effective in treating adult Acute Asthma in the emergency setting. Finally, to assess the relationship between demographic and characteristics of patient with acute asthma and the magnesium treatment outcome

#### **Demographic characteristics of patient with acute asthma:**

The proportion of males and females was close (54.8% & 45.2%) among the participants in the study of acute asthma patients, but the proportion of males was slightly higher among the participants in the interventional group (62.1%) compare with conventional group (48.5%), but this had no statistical significance ( $p$  value= 0.28). The highest percentage among the participants was from the age group between 35 and 50 years of age, and few of them work in the private sector (9.5%).

The percentage of the uneducated was about 40%, and the income group between 2500 and to 3500 is the most common (39.1%). Although there was some differences regarding the above mentioned characteristics between interventional and conventional groups but these differences had no statistically significant differences (  $p$  values > 0.05). for more data see table 3.1.

**Table 3.1***the participants demographic characteristics of patient with acute asthma*

		Group			$X^2$	Df	Sig.
		Total	Interventional	Conventional			
Gender	Male	35(54.8%)	18(62.1%)	16(48.5%)	1.15	1	.284
	Female	28(45.2%)	11(37.9%)	17(51.5%)			
Age (years)	< 20	5(7.8%)	1(3.2%)	4(12.1%)	4.54	3	.209
	20-34	18(28.1%)	7(22.6%)	11(33.3%)			
	35-49	36(56.3%)	19(61.3%)	17(51.5%)			
	> 50	5(7.8%)	4(12.9%)	1(3.0%)			
Occupation	Governmental	17(27.0%)	9(29.0%)	8(25.0%)	.143	2	.931
	Private	6(9.5%)	3(9.7%)	3(9.4%)			
	Other	40(63.5%)	19(61.3%)	21(65.6%)			
Educational level	Not educated	26(40.6%)	15(48.4%)	11(33.3%)	2.68	2	.261
	Basic level	30(46.9%)	14(45.2%)	16(48.5%)			
	High level	8(12.5%)	2(6.5%)	6(18.2%)			
Social status	Single	19(29.7%)	5(16.1%)	14(42.4%)	6.00	2	.050
	Married	40(62.5%)	24(77.4%)	16(48.5%)			
	Divorced	5(7.8%)	2(6.5%)	3(9.1%)			
Economic status	< 1500	13(20.3%)	8(25.8%)	5(15.2%)	3.46	3	.326
	1500 -2499	20(31.3%)	7(22.6%)	13(39.4%)			
	2500 -3499	25(39.1%)	14(45.2%)	11(33.3%)			
	> 3500	6(9.4%)	2(6.5%)	4(12.1%)			

Table No3.2 reflects that there are small differences in the measurements of hemodynamic parameters between the interventional and conventional groups, for example, the heart rate was slightly higher among the participants in the interventional group compared to the conventional group (90.8 & 84.7 BPM), as well as in relation to the number of respirations and systolic pressure, where the readings were higher in the interventional group compared with the conventional (26.8 & 132.4 vs. 25.9 & 127.8), while the diastolic pressure was higher in the conventional group compared to the interventional group (80.8 & 77.8 mmHg), but all those differences had no statistical significance and were within the normal range.

As for the oxygen saturation and temperature, the readings were equal between the two groups (81.5 & 36.6 C<sup>0</sup> vs. 80.2 & 36.4C<sup>0</sup>), interventional and conventional, but it was much lower than the normal range.

**Table 3.2**

*differences in the 1<sup>st</sup> measurements of hemodynamic parameters between the interventional and conventional groups*

	Group	N	Mean	Std. D	t	df	Sig.
Heart rate/min	Interventional	32	90.8	16.1	1.421	63	.160
	Conventional	33	84.7	18.2			
Oxygen saturation	Interventional	32	81.5	9.5	.611	63	.544
	Conventional	33	80.2	8.7			
Respiratory rate/min	Interventional	32	26.8	6.2	.516	63	.608
	Conventional	33	25.9	6.5			
SBP (mmHg)	Interventional	32	132.4	22.9	.867	63	.389
	Conventional	33	127.8	20.3			
DBB (mmHg)	Interventional	32	77.8	10.3	-1.313	63	.194
	Conventional	33	80.8	8.1			
Temperature C <sup>0</sup>	Interventional	29	36.6	0.6	1.171	60	.246
	Conventional	33	36.4	0.5			

Table No3.3 reflects that the small differences in the measurements of hemodynamic parameters between the interventional and conventional groups still present during the period before administering treatment.

For example, the heart rate was slightly higher among the participants in the interventional group compared to the usual group (89.1 & 83.8 BPM), as well as in relation to the number of respirations and systolic pressure, where the readings were higher in the interventional group compared with the conventional (25.8 & 133.5 mmHg vs. 25.0 & 127.0 mmHg).

On the other hand, the diastolic pressure was higher in the conventional group compared to the interventional group (78.3 mmHg & 76.6 mmHg), but all those differences had no statistical significance and were within the normal range.

As for the oxygen saturation and temperature, the readings were higher in the conventional group compared with the interventional group (87.0 & 84.6), but it was much lower than the normal range.

**Table 3.3**

*pre medication measurements differences in the of hemodynamic parameters between the interventional and conventional groups*

<b>Pre</b>	<b>Group</b>	<b>N</b>	<b>Mean</b>	<b>Std. D</b>	<b>t</b>	<b>df</b>	<b>Sig.</b>
<b>HR</b>	Interventional	32	89.1	14.9	1.37	63	.174
	Conventional	33	83.8	16.0			
<b>O2SAT</b>	Interventional	32	84.6	10.3	-1.11	63	.268
	Conventional	33	87.0	6.4			
<b>RR</b>	Interventional	32	25.8	5.6	.556	63	.580
	Conventional	33	25.0	5.3			
<b>SBP</b>	Interventional	32	133.5	17.4	1.53	63	.129
	Conventional	33	127.0	16.4			
<b>DBP</b>	Interventional	32	76.6	8.7	-.841	63	.404
	Conventional	33	78.3	7.3			
<b>TEMP</b>	Interventional	29	36.6	0.6			
	Conventional	33	36.6	0.5			

Table No 3.4 reflects that despite the fact that the level of shortness of breath (dyspnea) was higher among the acute asthma patients in the interventional group compared with the conventional group, the level of shortness of breath (dyspnea) was clearly reduced and to a lower level among the patients in the interventional group who received a dose of magnesium compared with the patients of the conventional group.



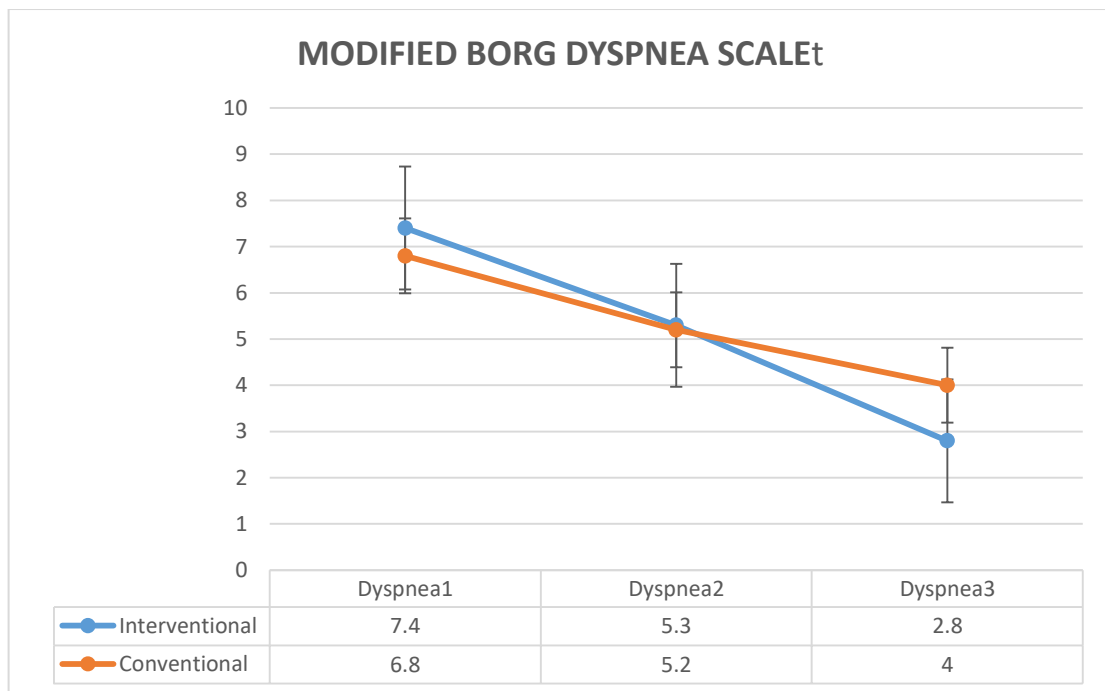
**Table 3.4**

*differences in the measurements of dyspnea between the interventional and conventional groups during study period*

MODIFIED BORG DYSPNEA SCALE	Group	N	Mean	Std. D	T	df	Sig.
Dyspnea1 ( at admission )	Interventional	32	7.4	1.9	1.184	62	.241
	Conventional	32	6.8	1.9			
Dyspnea2 (after inhalers and cortisone )	Interventional	32	5.3	2.2	.044	61	.965
	Conventional	31	5.2	2.2			
Dyspnea3 ( after mgso4)	Interventional	32	2.8	2.3	-2.175	58	.034
	Conventional	28	4.0	1.8			

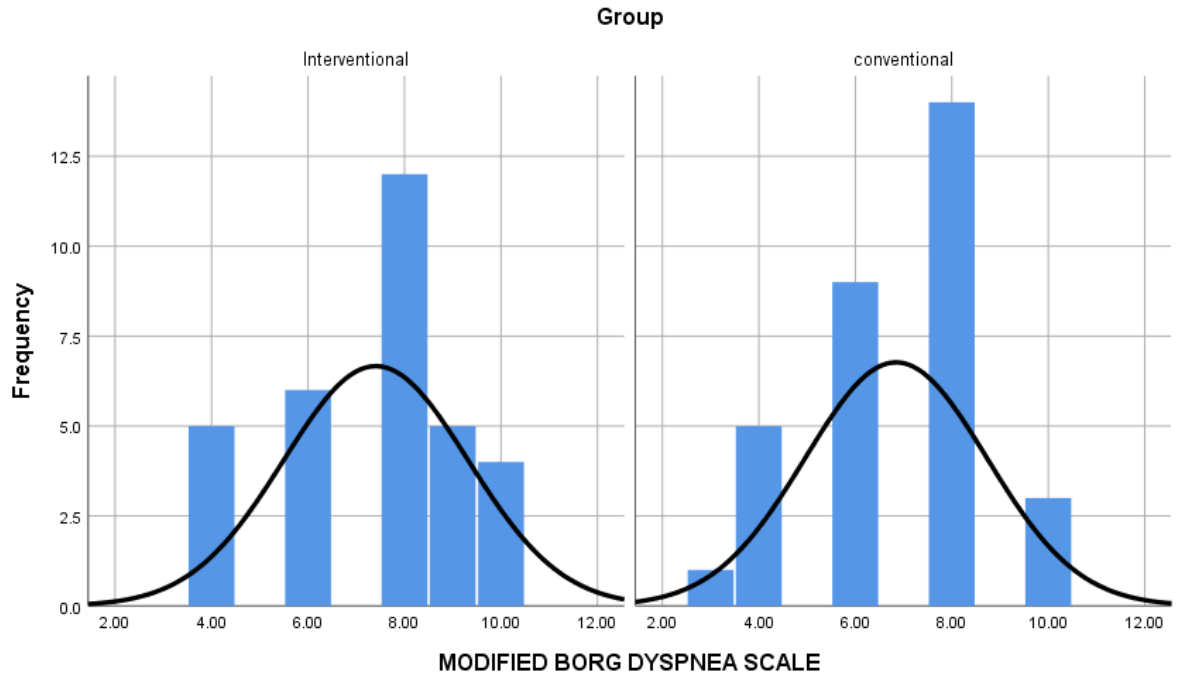
**Figure 3.1**

*dyspnea level among intervention and convention groups in the three points time measurements*



**Figure 3.2**

*dyspnea level among intervention and convention groups in the three points time measurements*



It is clear that magnesium not only affected the level of shortness of breath (dyspnea), but also had a clear effect on the hospital length of stay for patients with acute asthma in the hospital, as shown in Table No 3.5 that the rate of hospital stay for acute asthma patients who received magnesium dose treatment was clearly less than the acute asthma patients who received regular conventional treatment and this difference was statistically significant, where the value of the t test was 3.72 and the value of the  $p$  was  $< 0.001$

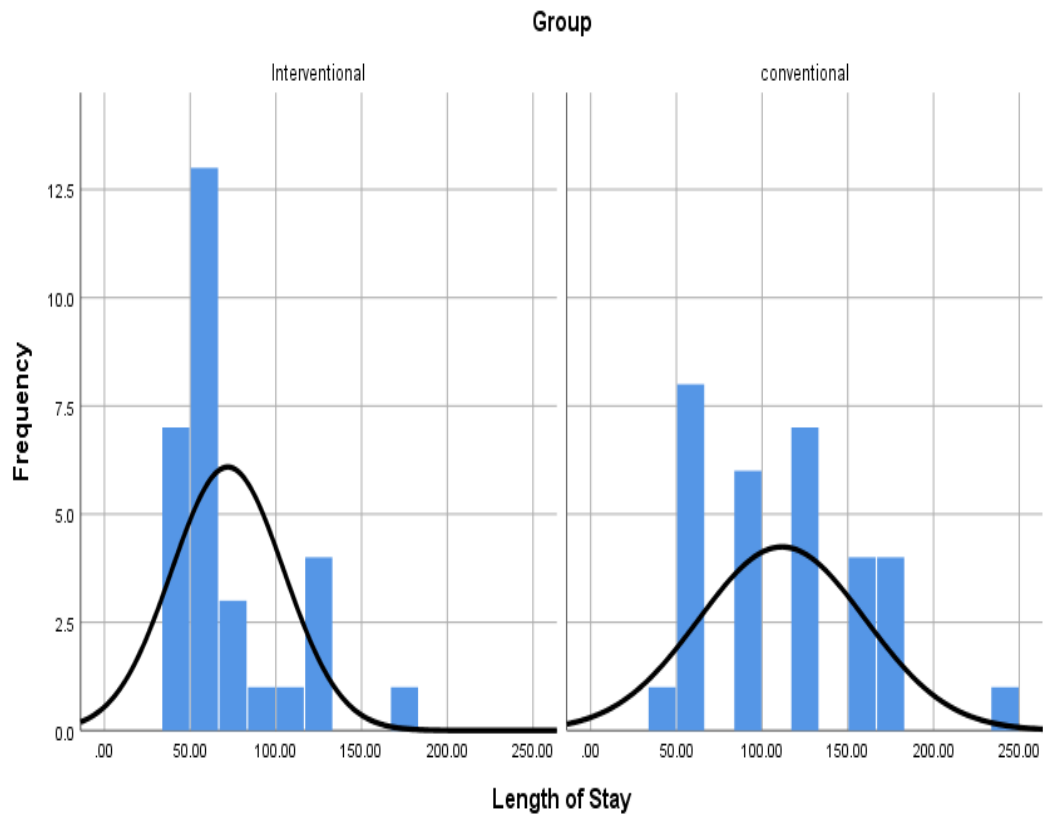
**Table 3.5**

*differences in the measurements of hospital length of stay between the interventional and conventional groups during study period*

	Group	N	Mean	Std. D	t	Df	Sig.
Length of Stay (min)	Interventional	30	71.9	32.7	-3.72	59	<.001
	Conventional	31	111.6	48.5			

**Figure 3.3**

*Differences in the measurements of hospital length of stay between the interventional and conventional groups during study period*



When the effect of magnesium was analyzed for the two groups (interventional & conventional) with controlling the effect of the personal characteristics of the acute asthma patients participating in the study and using the ANCOVA statistical test, it was found that there is a statistically significant difference (P value <0.001) with a high effect size ( $\eta^2 = .27$ ) between the two groups.

While the rest of the personal characteristics of the study participants did not have a statistically significant effect (p value > 0.05). see table 3.6.

**Table 3.6**

*hospital length of stay comparison between groups and controlling effect of participants' characteristics*

Source	Df	MS	F	Sig.	$\eta^2$
Intercept	1.00	2525.25	1.26	0.28	0.08
	13.71	2002.31			
Gender	1.00	1445.11	0.94	0.34	0.02
	49.00	1533.66			
Age	1.00	3179.97	2.07	0.16	0.04
	49.00	1533.66			
Occupation	1.00	271.53	0.18	0.68	0.00
	49.00	1533.66			
Educational	1.00	5178.02	3.38	0.07	0.06
	49.00	1533.66			
Social	1.00	0.89	0.00	0.98	0.00
	49.00	1533.66			
Economic	1.00	87.17	0.06	0.81	0.00
	49.00	1533.66			
Group	1.00	27616.10	18.01	0.00	0.27
	49.00	1533.66			

Computed using alpha = .05 **MS**: Mean Square;  **$\eta^2$** : Partial Eta Squared

When the effect of magnesium was analyzed for the two groups with controlling the effect of the personal characteristics of the acute asthma patients participating in the study and using the ANCOVA statistical test, it was found that there is a statistically significant difference (P value <0.001) with a high effect size ( $\eta^2$ = .334) between the two groups with respect to the hospital length of stay.

While the rest of the personal characteristics of the study participants did not have a statistically significant effect (p value > 0.05), with the exception of gender and social, where it was found that there is a small effect size ( $\eta^2$ = .10 & .095) and statistically significant (p value = 0.027 & 0.031) relationship between gender and the time for first rescue analgesia post operatively.

**Table 3.7***dyspnea comparison between groups and controlling effect of participants' characteristics.*

Source	Type III Sum of Squares	df	MS	F	Sig.	$\eta^2$
Intercept	44.517	1	44.517	5.225	.027	.100
Gender	44.477	1	44.477	5.220	.027	.100
Age	4.614	1	4.614	.542	.465	.011
Occupation	31.634	1	31.634	3.713	.060	.073
Educational	3.287	1	3.287	.386	.537	.008
Social	42.095	1	42.095	4.941	.031	.095
Economic	2.569	1	2.569	.302	.585	.006
Group	15.831	1	15.831	1.858	.179	.038
Error	400.448	47	8.520			

**MS:** Mean Square;  **$\eta^2$** : Partial Eta Squared

## **Chapter Four**

### **Discussion and Conclusions**

This chapter discusses the main findings in the light of the main aims and objectives of the study, appraises the methodology used, discusses the main strengths and limitations of the study, and provides the principal implications of the findings of this study on future research and practice.

#### **Summary of the main findings**

Several guidelines have recommended adding a single bolus intravenous dose of magnesium sulfate to standard therapy of inhalational salbutamol and ipratropium and intravenous corticosteroids in the managements of episodes of acute asthma exacerbations in emergency settings, especially, when these episodes of acute asthma exacerbations do not respond to standard therapy. However, the effectiveness of this addition remained elusive, notably in less severe cases (Griffiths & Kew, 2016; Gross Júnior et al., 2021; Jose E. Irazuzta, Fatima Paredes, Viviana Pavlicich, & Sara L. Domínguez, 2016; Javor & Grle, 2019; Kew, Kirtchuk, & Michell, 2014; Mathew, 2015; Stojak, Halajian, Guthmann, & Nashelsky, 2019).

This prospective controlled cohort study was sought to evaluate the effectiveness of magnesium sulfate administered intravenously in combination with standard treatment to patients with acute asthma admitted to emergency room settings in a major governmental hospital in Palestine. To the best of our knowledge, this is the first prospective controlled cohort study on the effectiveness of intravenous magnesium sulfate among patients with acute asthma admitted to emergency room settings in Palestine. Findings of this study demonstrated that adding intravenous magnesium sulfate to standard treatment significantly reduced level of shortness of breath (dyspnea) compared to patients in the control group who received standard treatment.

Additionally, findings of this study demonstrated that patients in the intervention group who received intravenous magnesium sulfate in addition to standard treatment stayed significantly shorter period of stay in the emergency room compared to patients who received standard treatment alone. Findings of this study could be informative to intensivists, emergency medicine specialists, pulmonologists, and other healthcare providers caring for patients with acute asthma and/or patients whose asthma conditions exhibit episodes of acute exacerbations.

## **Appraisals of the methodology**

### **Appraisal of the study design**

This study was conducted in a prospective quasi-experimental design. This study design is considered more robust and evidence generated from these studies is considered superior to those generated from expert opinions/ideas, in vitro laboratory studies, laboratory animal studies, case reports, case report series, and case control studies (Milano, 2016; Mulimani, 2017; Murad, Asi, Alsawas, & Alahdab, 2016b).

Because of placement of this study design on the top of the pyramid of hierarchy of evidence, quality findings generated from such study designs often influence recommendations/guidelines used in the management of different health conditions (Norton, Pusic, Taha, Heathcote, & Carleton, 2007; Peters et al., 2011; Rogliani, Beasley, Cazzola, & Calzetta, 2021; Rowe & Camargo, 2006; Smyth & O'Byrne, 2002).

### **Appraisal of the recruitment method, sample size and comparability of the patients in the two groups**

The patients included in this study were recruited from the emergency department of the National Governmental Hospital, Nablus. The National Hospital is the oldest governmental hospital in the West Bank. This hospital is the main referral hospital for internal medicine cases in the north of the West Bank. Recruitment of patients from this hospital should have ensured representation of the population of patients admitted/referred for episodes of acute asthma exacerbations from the north of the West Bank. Because this study was a single study, recruitment of patients from a major referral hospital where patients from all over the north of the West Bank receive healthcare for episodes of acute asthma exacerbations should have reduced the risk of recruitment bias and should have ensured representation of patients with diverse demographic characteristics (Albers et al., 2018; Costa et al., 2011; Emerman et al., 1999; Postma et al., 2019).

The sample size needed for this study was calculated using a commonly used and powerful software (Kang, 2021; Verma & Verma, 2020). The sample size was calculated to detect effect size at an adequate power (Kendrick et al., 2000). The patients recruited for this study were assigned either to the intervention or control group

This method of allocation of patients to the groups should have reduced bias (Altman & Bland, 1999; Schulz & Grimes, 2002).

When the demographic characteristics of the patients in both control and intervention groups were compared using Chi-squared test, there was no significant differences in terms of distribution in both genders, age groups, professional occupations, educational levels, social, and economic classes. These similarities and absence of differences between the patients in both groups should have promoted the possibility of assessing the effects of the intervention (Egelund, Wassil, Edwards, Linden, & Irazuzta, 2013; Jones & Goodacre, 2009; Mathew, 2015; Mukerji et al., 2015).

Additionally, these similarities should have reduced the potential confounding effects brought by differences in demographic characteristics of the patients in both groups. Similarly, there was no statistically significant differences in the relevant clinical variables of the patients in both groups in terms of HR, SaO<sub>2</sub>, RR, SBP, DBP, and body temperature. Additionally, these similarities and absence of differences in the relevant clinical variables between the patients in both groups should have promoted the possibility of assessing the effects of the intervention and should have reduced the potential confounding effects brought by differences in these variables among patients in both groups.

### **Appraisal of the study period**

The patients in this study were recruited in the period between August and December 2020 which covered autumn and early winter. In autumn, leaves fall off trees and respiratory viruses spread in early winter and cold season. Therefore, patients were more likely to be exposed to air-borne particles and experience episodes of acute asthma exacerbations during the study period (Abe et al., 2009; Altzibar et al., 2015; Eggo, Scott, Galvani, & Meyers, 2016; Zuo et al., 2019).

### **Appraisal of the assessment tool**

The assessment tool used in this study collected the demographic characteristics of the patients and their relevant clinical variables like heart rate, respiratory rate, and SaO<sub>2</sub>. Dyspnea was measured using the modified Borg dyspnea scale. Opinions of three experts who were academicians, researchers, and healthcare professionals were obtained to ensure the face validity of the study assessment tool used in this study. The modified



Borg dyspnea scale was previously assessed for validity and reliability in measuring dyspnea (Banerjee et al., 2017; Kendrick et al., 2000).

## **Discussion of the main findings**

### **Effect of intravenous magnesium sulfate on dyspnea**

Findings of this study demonstrated that the level of dyspnea was significantly lower ( $p$ -value = 0.034) among patients in the intervention group who received magnesium sulfate compared to the patients in the control group as measured using the modified Borg dyspnea scale. The effectiveness of intravenous magnesium sulfate for episodes of acute asthma exacerbations has been a subject for long debate (Griffiths & Kew, 2016; Gross Júnior et al., 2021; Jose E. Irazuzta et al., 2016; Javor & Grle, 2019; Kew et al., 2014; Mathew, 2015; Stojak et al., 2019). While some studies have demonstrated that magnesium sulfate was effective in reducing dyspnea among patients with episodes of acute asthma exacerbations (Gross Júnior et al., 2021; Rowe, Bretzlaff, Bourdon, Bota, & Camargo, 2000; Stojak et al., 2019).

Other studies suggested that intravenous magnesium sulfate does not provide any significant benefits over standard therapy in episodes of acute asthma exacerbations (Aniapravan, Pullattayil, Al Ansari, & Powell, 2020; Bradshaw, Matusiewicz, Crompton, Alastair Innes, & Greening, 2008; Javor & Grle, 2019).

Findings of this study were not surprising because intravenous magnesium sulfate was recommended in many practice guidelines for episodes of acute asthma exacerbations that are refractory to standard therapy (Indinnimeo et al., 2018; Ohn & Jacobe, 2014). However, the evidence was elusive and limited by the sample size included in the clinical trials (Javor & Grle, 2019). Patients suffering from episodes of acute asthma exacerbations often receive first-line therapy which includes delivery of O<sub>2</sub> in case the patient had signs of hypoxia, inhalational short-acting  $\beta$ 2-agonists, corticosteroids, and in severe cases, patients may also receive inhalational ipratropium (James & Lyttle, 2016a, 2016b; C. V. Powell & Cranswick, 2015).

When the episodes of acute asthma are severe and prove refractory to first-line therapy, patients might receive intravenous short-acting  $\beta$ 2-agonists or other agent like magnesium sulfate or aminophylline (NHLBI, 2007).

Magnesium sulfate is a potent bronchodilator that can cause relaxation of bronchial cells through a number of mechanisms including decreasing intracellular calcium within bronchial smooth muscle cells through activation of the sodium-calcium pump and blocking entry and release of calcium from the sarcoplasmic reticulum, mitigating inflammatory responses through stabilization of T cells, attenuation of neutrophil activation, and prevention of degranulation of mast cells, and reducing acute asthma exacerbations through releasing nitric oxide and promoting synthesis of prostacyclin (Cairns & Krafi, 1996; Gourgoulisanis, Chatziparasidis, Chatziefthimiou, & Molyvdas, 2001; Turner, Ford, Kidd, Broadley, & Powell, 2017). Findings of this study might reinforce these theories and might add to the literature supporting the use of magnesium sulfate in the management of patients admitted to the emergency room with episodes of acute asthma exacerbations.

#### **Effect of intravenous magnesium sulfate on length of stay in the emergency room**

Findings of this study showed that the length of hospital stay was significantly shorter ( $p$ -value  $< 0.001$ ) for patients in the intervention group who received magnesium sulfate compared to the patients in the control group. When the potential effects of personal characteristics of the patients were controlled using ANCOVA, differences between the two groups were still statistically significant ( $p$ -value  $< 0.001$ ) with large effect size ( $\eta^2 = 0.334$ ). ANCOVA showed that personal characteristics of the patients had no effects ( $p$ -value  $> 0.05$ ).

Findings of this study were consisted with those reported in the literature. Devi et al showed that patients suffering episodes of acute asthma exacerbations who received intravenous magnesium sulfate stayed significantly shorter period of time in emergency room compared to patients who received standard therapy (Devi, Kumar, Singhi, Prasad, & Singh, 1997). In a systematic review, Griffiths & Kew included and appraised the quality of Devi et al's study as well as other studies (Griffiths & Kew, 2016). The evidence on the effects of magnesium sulfate on reducing the length of stay in the emergency room was graded as low because of the small sample size included in the study, absence of sufficient data on the length of hospital stay in some studies, and publication bias in other studies (Griffiths & Kew, 2016). Together, findings of this study may add to the benefits of intravenous magnesium sulfate for patients suffering episodes of acute asthma exacerbations who are admitted to the emergency room.

## **Discussion of the strengths and limitations of the study**

The study has a number of strengths and limitations.

- First, this study was the first to evaluate the effectiveness of magnesium sulfate administered intravenously in combination with standard treatment to patients with acute asthma admitted to emergency room settings in Palestine.
- Second, a prospective quasi-experimental design was used in this study. Prospective designs are more robust and can produce superior findings compared to retrospective study designs.
- Third, the patients included in this study were recruited from the main referral hospital in the north of the West Bank.
- Fourth, both control and intervention groups were comparable in terms demographic variables before the intervention.
- Fifth, the study participants were recruited in the high season for asthma exacerbations. Finally, Valid assessment tools were used to collect and measure the data used in this study.

### **Limitations**

This study was not without limitations. Many of these limitations were inherent in the prospective cohort studies (Ramirez-Santana, 2018).

- First, although the demographic variables of the patients in the control and intervention groups were compared, selection bias cannot be completely excluded. This might have affected associations between the exposures and outcomes in this study.
- Second, information bias could have originated among the included patients in both control and intervention groups, in the scale used to measure dyspnea and other outcome data, and between the different time the data were measured (observation times).
- Third, confusion and interaction biases cannot be excluded. Although the variables in this study were controlled when the protocol was designed, other confounders could also be associated with the exposure and might have interacted with the

outcomes. This might have constituted spurious association and might have led to making inaccurate causal inference.

- Fourth, one scale was used to measure dyspnea in this study. Although the modified Borg scale was valid and reliable, the baseline (BDI) and transition (TDI) dyspnea indexes, and the UCSD Shortness of Breath Questionnaire showed higher reliability and validity levels compared to the Borg scale (Ambrosino & Scano, 2004; Eakin, Sassi-Dambron, Ries, & Kaplan, 1995). Using more than one scale or using another scale with higher level of validity and reliability should have yielded more reliable results. Finally, dyspnea was measured on 2 time points after the intervention. More frequent measurements might have provided more reliable results.

### **Principal implications for future practice**

Findings of this study might support those reported in previous studies on the use of intravenous magnesium sulfate in combination with standard treatment for patients with acute asthma admitted to emergency room settings. Intensivists and emergency healthcare providers might need to consider the benefits and risks of administering intravenous magnesium sulfate in combination with standard treatment for patients with acute asthma admitted to emergency room settings.

### **Recommendations for further investigations and future research directions**

Probably, more studies are needed to be conducted using blinded randomized controlled trials with large sample sizes to robustly evaluate the effectiveness of magnesium sulfate administered intravenously in combination with standard treatment to patients with acute asthma admitted to emergency room settings in Palestine. In future studies, more attention and planning should take place to control selection, information, and confusion bias (Ramirez-Santana, 2018).

Probably, more valid and reliable multidimensional tools could be used to measure dyspnea in future studies. The baseline (BDI) and transition (TDI) dyspnea indexes and the UCSD Shortness of Breath Questionnaire might be considered in future studies. Additionally, dyspnea might be followed up over a longer period of time after the intervention with more frequent measurements.

## **Conclusion**

Magnesium sulfate administered intravenously in combination with standard treatment to patients with acute asthma admitted to emergency room settings in Palestine might have improved signs and symptoms of dyspnea compared to standard treatment alone. Future blinded randomized controlled trials with larger sample sizes are currently needed to arrive at a more solid conclusion on the effectiveness of intravenous magnesium sulfate in combination with standard treatment to patients with acute asthma admitted to emergency room settings.

## List of Abbreviations

Abbreviations	Meaning
MgSO <sub>4</sub>	magnesium sulfate
GINA	Global Initiative for Asthma
ED	emergency department
MBDS	modified borg dyspnea scale
G	Gram
Iv	Intravenous
SaO <sub>2</sub>	respiratory rate and oxygen saturation
SPSS	Statistical Package for the Social Sciences
SABA	Inhaled short-acting beta <sub>2</sub> -agonists
L/min	Litter per minute
LOC	Level of consciousness
Hr	Heart rate
Spo <sub>2</sub>	Non- Invasive Oxygen saturation
BPM	Beat per minute
mmHg	Millimeter mercury
ANCOVA	Analysis of covariance
RR	Respiratory rate
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
BDI	Baseline dyspnea indexes
TDI	transition dyspnea indexes
UCSD	University of California San Diego

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## **Appendices**

### **Appendix (A)**

#### **Questionnaire**



**An-Najah National University**

**Faculty of Graduate Studies**

**Master of Intensive Care Nursing**

**Questionnaire about:**

**Effect of Intravenous Magnesium Sulfate in Acute Asthma**

**Proposed by:**

Abeer Mahameed

**Supervised by :**

Dr. Jamal Qaddumi

**Patient signature: .....**

## **Section one**

### **Assessment sheet**

#### **Demographic data**

- 1 . Gender :                male ☐                female ☐
- 2 . Age:    less than 20 ☐    from 20 to less than 35 ☐  
From 35 to less than 50 ☐    more than 50
- 3 . occupation : Governmental sector ☐ private sector ☐ other ☐
- 4 . city :.....
- 5 . Educational level : Not educated ☐ basic level ☐ high level ☐  
Diploma ☐ Bachelor's degree ☐ Postgraduate ☐
6. social status : single ☐ married ☐ widow ☐ divorced ☐
7. Economic status :
- ☐ Less than 1500
- ☐ 1500 \_ 2499
- ☐ 2500 \_ 3499
- ☐ more than 3500

## Section two








**Checklist for recording the value of heart rate, respiratory rate and oxygen saturation.**

The value	patient admission	Before intervention	After intervention
Heart rate			
Oxygen saturation			
Respiratory rate			
Blood pressure			
Temperature			

**Length of stay in emergency room .....**

## Section three

### ***Modified Borg Dyspnea Scale***

<b>0</b>	Nothing at all	
<b>0.5</b>	Very, Very Slight (Just Noticable)	
<b>1</b>	Very Slight	
<b>2</b>	Slight	
<b>3</b>	Moderate	
<b>4</b>	Somewhat Severe	
<b>5</b>	Severe	
<b>6</b>		
<b>7</b>	Very Severe	
<b>8</b>		
<b>9</b>	Very, Very Severe (Almost Maximal)	
<b>10</b>	Maximal	

## Appendix (B)

### IRB Approval Letter

An-Najah  
National University  
Health Faculty of medicine &  
Sciences  
IRB

جامعة النجاح الوطنية  
كلية الطب وعلوم الصحة  
لجنة أخلاقيات البحث العلمي

Ref: Mas /2020/23

IRB Approval Letter

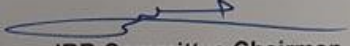
**Study Title:**  
Effect of Intravenous Magnesium Sulfate in Acute Asthma

**Submitted by:**  
Abeer Jameel Mahameed

**Supervisor:**  
Jamal A. Qaddumi, Alaa Shamlawia

**Date Approved:**  
29<sup>th</sup> Sep 2020

Your Study Title "Effect of Intravenous Magnesium Sulfate in Acute Asthma"  
reviewed by An-Najah National University IRB committee and was approved on 29<sup>th</sup> Sept.2020.

Hasan Fitian, MD  
  
IRB Committee Chairman  
An-Najah National University

IRB

REDMI NOTE 8  
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Ref.: .....  
Date:.....

الرقم: ١١٣٢١/٢٠٢٠  
التاريخ: ٢٠٢٠/١١/٢٥

الأخ مدير عام الإدارة العامة للمستشفيات المحترم ،،  
تعية واحترام،،،

الموضوع: تسهيل مهمة بحث

لاحقاً لموافقة معالي وزيرة الصحة، يرجى تسهيل مهمة الطالبة: عبير جميل محاميد،

ماجستير ترميز الغاية، جامعة النجاح، لاجراء بحث الماجستير بعنوان:

**" Effect of Intravenous Magnesium Sulfate in Acute Asthma"**

حيث ستقوم الطالبة بجمع المعلومات عن عن طريق المشاهدة فقط، ولا يسمح لها بالتدخل

العلاجي،، مع العلم ان مشرف الدراسة: د. جمال قدومي، وذلك في:

- مستشفى الوطني

حيث سيتم الالتزام باساليب وأخلاقيات البحث العلمي.

على ان يتم الالتزام بجميع تعليمات واجراءات الوقاية والسلامة الصادرة عن وزارة الصحة

بخصوص جائحة كورونا، وتحت طائلة المسؤولية.

مع الاحترام،،،

د. عبد الله القواسمي

مدير وحدة التعليم الصحي

والبحث العلمي





جامعة النجاح الوطنية  
كلية الدراسات العليا

## دراسة تأثير دواء المغنيسيوم وريديا على تقليل حدة

### مرض الأزمة

إعداد

عبير جميل نايف محاميد

إشراف

د. جمال القدومي

قدمت هذه الرسالة استكمالاً لمتطلبات الحصول علي درجة الماجستير في برنامج العناية المكثفة، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس - فلسطين.

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# دراسة تأثير دواء المغنيسيوم وريديا على تقليل حدة مرض الأزمة

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## الملخص

**خلفية:** يمكن أن تؤدي نوبات الأزمة (الربو) الحادة إلى دخول غرفة الطوارئ. عندما لا تستجيب هذه التفاعلات للعلاج التقليدي، توصي الدلائل الإرشادية بإعطاء جرعة واحدة من كبريتات المغنيسيوم في الوريد بالإضافة إلى العلاج التقليدي لعلاج المرضى المدخلين في غرفة الطوارئ.

**الهدف:** أجريت هذه الدراسة لتقييم فعالية إعطاء كبريتات المغنيسيوم عن طريق الوريد مع العلاج التقليدي لمرضى الربو الحاد الذين تم إدخالهم إلى غرف الطوارئ في مستشفى حكومي رئيسي في فلسطين.

**الطريقة:** أجريت هذه الدراسة بتصميم شبه اختباري. تم اختيار المرضى في كلا المجموعتين الضابطة والتدخل من مستشفى الوطني. تم اختيار المرضى خلال موسم الذروة من تفاقم الربو الحاد. تلقى المرضى في المجموعة الضابطة العلاج التقليدي . تلقى المرضى في مجموعة التدخل جرعة واحدة عن طريق الوريد من كبريتات المغنيسيوم بالإضافة إلى العلاج التقليدي. تم جمع المتغيرات الديموغرافية والسريية للمرضى في ورقة جمع البيانات. تم قياس ضيق التنفس باستخدام مقياس بورج ضيق التنفس المعدل.



**النتائج:** تم تعيين ما مجموعه 65 مريضاً التحكم (ن = 32) والتدخل (ن = 33) مجموعات. كان المرضى في كل من مجموعات التحكم والتدخل متشابهين من حيث المتغيرات الديموغرافية والسريية قبل التدخل. لم تكن هناك فروق ذات دلالة إحصائية في ضيق التنفس قبل العلاج. تبين أن إعطاء جرعة واحدة في الوريد من كبريتات المغنيسيوم بالإضافة إلى العلاج التقليدي يقلل بشكل كبير من علامات ضيق التنفس حيث تم قياسه في مقياس بوج لضييق التنفس المعدل.

**الخلاصة:** إن إعطاء كبريتات المغنيسيوم عن طريق الوريد مع العلاج القياسي للمرضى الذين يعانون من الربو الحاد الذين تم إدخالهم إلى غرف الطوارئ في فلسطين (بالمشفى الوطني) قد يكون لديهم علامات وأعراض ضيق التنفس أقل حدة مقارنة بالعلاج القياسي لوحده.

**الكلمات المفتاحية:** الربو، التفاقم، كبريتات المغنيسيوم، الطوارئ.