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What to use for bronchial asthma; nebulized or intravenous magnesium sulfate?

Ibrahim Salah-Eldin Ibrahim *, Reham Mohamed Elkolaly

Chest Department, Faculty of Medicine, Tanta University, Tanta, Egypt

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ABSTRACT

Background: Asthma is characterized by airways narrowing and airflow limitation. The conventional therapy for asthma exacerbation is usually efficient but sometimes patients not respond to it, consequently; other additive drugs may be used as magnesium sulfate($MgSO_4$) either intravenously or by nebulization.
Objective: To compare the bronchodilator effect of $MgSO_4$ via intravenous injection and nebulization in controlling asthma exacerbation.
Methods: 40 patients with asthma exacerbation were equally and randomly enrolled in two groups. One group received nebulized $MgSO_4$ (A), and the other group received intravenous $MgSO_4$ (B).
Results: Improvement was higher in group B than in group A but without significant change in PEFR also there was no high significant difference in the two group parameters after $MgSO_4$ treatment. Complications were few and manageable in both groups.
Conclusion: Intravenous $MgSO_4$ is effective affordable and cheap drug for asthma exacerbation management with good response while nebulized $MgSO_4$ didn't give the aimed response in these patients.

Introduction

Asthma is one of the common chronic airway diseases that leads to decrease of airflow and characterized by bronchial and bronchioles inflammation with airways smooth muscle contraction and increase mucous synthesis and secretion. Leading to recurrent wheeze, breathing difficulties and coughing either at night or/and early morning [1]. This airways narrowing is often reversible with or without treatment [2].

Asthma morbidity and mortality rates are high and are mostly related to acute exacerbations [3]. So severe asthma attacks must be treated rapidly and effectively to avoid its fatal consequences, to decrease triggering for further future exacerbation [4] and to prevent more decline in lung functions after these attacks [5].

Patients having asthma exacerbations usually need rapid treatment to relieve their suffering, so they use inhaled bronchodilators in form of β2 agonists (±anticholinergic) in addition to parental corticosteroids if they are admitted to hospitals [6].

And in spite of that; corticosteroids used in emergency department need a relatively longer time (6–8 h) to produce their anti-inflammatory effect and control the acute attack [7], while inhaled β2 agonists give their adequate bronchodilator effect in only two thirds of treated patients and the rest of patients still suffer from the attack effect [6].

For that reason; physicians tried to use other additive drugs to give rapid bronchodilator effect to manage asthma early before patients deterioration.

Magnesium sulfate ($MgSO_4$) is the drug that was previously used as an additive line of treatment in many cases with acute severe asthma [8].

Magnesium sulfate was studied and supposed to reduce intracellular calcium influx via closure of calcium channels and inhibits calcium release from endoblasmic reticulum [9], it also inhibits inflammatory mediator release from mast cells and inhibits acetyl choline release from nerve endings, that leads finally to muscle relaxation [10].

Some physicians used magnesium via nebulization-especially in children-during severe asthma attacks to achieve bronchodilatation and to avoid the systemic side effects of the intravenous drug

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* Corresponding author at: Chest Department, Tanta University Hospitals, Elgharbyia, Tanta, Egypt.
E-mail addresses: isalahi72@yahoo.com (I.S.-E. Ibrahim), R.elkolaly@gmail.com (R.M. Elkolaly).

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[11]. While others used it parentrally to give rapid action and relieve of the bronchoconstriction, but this may lead to some side effects like arrhythmia flushing, hypotension and renal intoxication in high doses [2]

Aim of the study

To compare the bronchodilator effect of magnesium sulfate via intravenous route versus nebulization in patients with asthma exacerbation.

Patients and methods

The study was conducted from March 2016 through July 2011 at Tanta University Hospital, Tanta, Egypt.

This study was conducted on 40 patients with acute bronchial asthma exacerbation with the following inclusion criteria:

- Patient with acute exacerbation of asthma according clinical assessment of asthma using GINA guidelines [12].
- Patient not controlled on conventional therapy for acute exacerbation.

Exclusion criteria were as follow

Patients with stable asthma, COPD, pneumonia, heart failure or renal insufficiency, in need for endotracheal intubation, inability to do peak flow meter, pregnant or breastfeeding mothers or had received oral, inhaled or parenteral bronchodilators in the past 6 h, or steroids in the past 12 h.

All patients were subjected to history taking, clinical examination and PEF% (wright peak flow meter) and scoring was done according guidelines [13].

All patients received the conventional treatment of acute exacerbation as follow:

- Supplemental oxygen to have O_2 sat. greater than 90%.
- Nebulization of 1 ml Farcolin respirator solution® mixed with 9 ml saline for two sessions with interval of 15 min [Farcolin respirator solution®: each 20 ml of Farcolin contains Salbutamol sulfate 0.121 gm. Made in Egypt, by: Pharco Pharmaceuticals – Alexandria].
- Intravenous Solu-Cortef® 100 mg once [Solu-Cortef®: vial contains powder of 100 mg Sodium hydrocortisone hemisuccinate dissolved with 2 ml solvent of sterile bacteriostatic water for IV injection. Manufactured by: Egyptian Int. Pharmaceutical Industries co. (e.i.p.i.co.) – Egypt. Under license of: Pfizer].

Patients were assisted clinically every 15 min. If the patient didn't improve after one hour; he was randomly enrolled in one of the two groups that contained 20 patients in each group.

Each patient was evaluated clinically for blood pressure (BP) and Fischl index that consists of seven items (pulse, respiratory rate (RR), pulsus paradoxicus (PP), PEF%, dyspnea, wheeze and accessory muscle use) and scored 0–1 for each [6].

These pre-treatment parameters were labeled (level zero) before $MgSO_4$ treatment.

Group A (nebulization group): four doses of nebulization solution with 15 min apart, each dose contained 1 ml $MgSO_4$ mixed with 9 ml saline, to have isotonic mixture to avoid hyperosmolar broncho-constriction [14].

Group B (injection group): 2 g of $MgSO_4$ diluted in 30 ml saline to have a 50 ml solution for slow intravenous injection along 20–30 min [15].

Magnesium Sulfate USP2® 1 g/10 ml [Magnesium Sulfate®: Sterile ampoule 10 ml. 100 mg/ml = 0.41 mMol/ml. Manufactured by: Egyptian int. Pharmaceutical industries co. (e.i.p.i.co.) – Egypt].

Patients were assisted after 30 min (level 1) then after 1 h (level 2)

N.B.; Patients who deteriorated were re-evaluated for other management procedures.

Statistical analysis

All data were statistically analysed by the SPSS software for Windows (IBM SPSS Statistics 21.0). *P* value <0.05 was significant.

Results

Forty patients with acute asthma were enrolled in this study; they were divided into two groups. **Group A** consisted of 20 patients (12 female and 8 male) that received nebulized $MgSO_4$ and **group B** that consisted of 20 patients (11 female and 9 male) who received intravenous $MgSO_4$.

There was no statistically significant difference between the two groups as regard age, pre-treatment pulse, BP, RR and PEFR, Fischl's index) (Table 1).

After 30 min of treatment; patients were re-evaluated (Table 2).

These parameters improvement showed no significance difference between the two groups, but the improvement in group B was more than that in group A.

Another re-evaluation was done after one hour as follow (Table 3)

Which revealed improvement in group B than that in group A; but also without significant difference.

The significance of changes in group A as regard pre-treatment, after 30 min and after one hour were as follow (Table 4).

The significance of changes in group B as regard pre-treatment, after 30 min and after one hour were as follow (Table 5).

As regard results in Tables 4 and 5; the clinical parameter in group A showed mild improvement after I hour as regard BP and pulse with less improvement in other parameters. But in group B; there was significant improvement in BP and RR after 30 min while the improvement was more significant in all parameters after I hour.

There were minor complications that reported in 3 patients in group A including headache, flushing, hypotension and nausea.

The adverse effects in group B were recorded in 5 patients; including nausea, vomiting, arrhythmia and hypotension (Table 6).

Discussion

Asthma is one of the chronic respiratory disorders that has repeated episodes of exacerbations that may be mild, moderate and even severe attack which may lead to hospital or ICU admission, intubation or even death [8].

Intravenous magnesium sulfate was used as a possible additive drug for asthma exacerbation management especially in severe attacks [16].

Magnesium is an important ion in cellular and tissue homeostasis including airways musculature via its role for different enzymes action [16]. $MgSO_4$ helps smooth muscle relaxation via facilitating calcium ions influx to sarcoplasmic reticulum [17]. It also inhibits both acetyl choline and histamine release from nerve ending and mast cells respectively. Some authors suggest that it has a central sedative effect [17].

In that study; $MgSO_4$ injection had marvelous response in most patients in intravenous group while patients in group A not revealed the desired effect that most physicians aim to in asthma attack management.

In consistent with those results; Mohammed and his colleague [18] found in their systemic review that intravenous $MgSO_4$ had

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