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Effect of nebulized furosemide in patients with acute asthma in Iraq

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ABSTRACT

Objective: Identify whether nebulized frusemide has any therapeutic benefit in patients with acute attack of asthma. *Methods:* A total of 24 patients were diagnosed with acute asthma; 12 of them were given nebulized frusemide 40mg and the other 12 patients were given nebulized saline as control. Every patient in the two groups has FEV1 measured before and after the test and received IV aminophylline over 60 minutes on admission and before the test. *Results:* a mean increase in the FEV1 of 27.6 ± 9.1 in the furosemide group while there is a mean in the FEV1 of 4.8 ± 4.4 in the other group. These changes are regarded as statistically significant (P value <0.005). *Conclusions*: When it comes to patients with severe asthma, receiving IV aminophylline, the use of nebulized frusemide produced significant improvement in the FEV1.

Keywords: frusemide, inhalation, nebulizer, pulmonary function test

1. INTRODUCTION

Asthma is a condition characterized by chronic inflammation of the airways and increased airway hyper responsiveness resulting in symptoms of cough, chest tightness and wheeze (Hargreave and Parameswaran, 2006). A variety of environmental factors can provoke an attack of asthma such as pollutants like nitrogen dioxide, sulfur dioxide and house dust mites (Flavahan et al., 1985). Furosemide (frusemide) is a strong diuretic that prevents Na and K from being reabsorbed in the renal tubules (Myers et al., 1997). In asthmatic patients, the medication prevents or reduces bronchospasm produced by a variety of causes including hyperpnea, medicines, physical agents, and allergen challenge (Grubbe et al., 1990).

Furosemide also has an effect on the mucosa of the upper airway, where it reduces nasal resistance in patients with non-allergic rhinitis and protects nasal mucosa responsiveness to a specific allergen in atopic subjects (Levasseur-Acker et al., 1994). Furosemide's mechanism of action on the airways is still unknown; however it is thought to interfere with electrolyte epithelial transport, prostaglandins, inflammatory cell activity, vascular and neuronal control (Bianco et al., 1988). Changes in water concentration and surface osmolarity of the airway epithelium have been well-accepted as contributing factors to exercise-induced bronchospasm and have prompted the first use of inhaled frusemide as a potential treatment for asthma (Welsh,

1983). The mechanism of action does not appear to be related to the diuretic effects of the drug. Furosemide is not effective against asthma when administered orally at the usual diuretic doses and must be inhaled at relatively high doses (20-40mg) for significant antiasthma effects (Barnes, 1993).

In vitro data have suggested that furosemide may attenuate bronchoconstriction by reducing apical chloride channel activity and by decreasing the potential difference and short-circuit current in airway epithelial cells (Alton et al., 1996). The drug's inhibition of chloride transport also appears to inhibit the release of eosinophil mediators (Lucci and Warnock, 1979) and could be linked to the modulatory effects observed on presynaptic nuropeptide release from noncholinergic, nonadrenergic sensory nerves and cholinergic responses in animal models (Elwood et al., 1991).

A short report (Anderson et al., 1991) has described furosemide inhibiting the release of histamine and leukotrienes from passively sensitized human lung. Furosemide is well-known to enhance renal synthesis of prostaglandin E2 (Miyanoshita et al., 1989). Bronchoconstrictors that work directly on the smooth muscle of the airway like histamine, methacholine, and prostaglandin F2 have not been demonstrated to be affected by frusemide (Pavord et al., 1992).The similarities between the protective spectrum of frusemide and cromolyn have led to speculation about acommon mechanism of action, although cromolyn has been shown to have a statistically greater protective effect on airway reactivity when equal doses of the two inhaled drugs were compared (Siffredi et al., 1997). In healthy participants, inhaled frusemide inhibited the cough reflex elicited by inhalation of low chloride-content solutions (Ventresca et al., 1990), but not in asthmatic patients (Stone et al., 1993).

In recent years, there has been an increase in interest in using breathed furosemide in therapeutic settings. Some researchers looked at whether the medicine is beneficial in treating acute asthma attacks. One of the medications now used to prevent exercise-induced asthma is furosemide (Niven and Argyros, 2003).

2. PATIENTS AND METHODS

A total of 24 individuals with acute asthma exacerbations were chosen, 11 of them were female and 13 of whom were male. They are between the ages of 26 and 61. The cases were sent to the hospital's emergency room of Al-Kadhimya Teaching Hospital during the period from December 2019 to March 2020. All of them received an IV infusion of aminophylline 250mg over 1hour on admission. 12 of our patients (50%) were given nebulized furosemide 40mg before and after which we measure their FEV1 (furosemide Group). The other 12 patients (50%) received nebulized isotonic saline as a placebo (control group).

3. RESULTS

The furosemide group has a mean age of 43.33 ± 10.7 (year) with a minimum age of 29 and maximum age of 61 (year). The control group has a mean age of 45.0 ± 10.21 (year) with a minimum age of 24 and maximum of 63. The study shows an increase in the FEV1% of 27.6± 9.14 which is regarded as highly significant (P value 0.005) in the group receiving nebulized furosemide compared to an increase in the FEV1 of 4.8± 4.4 in the control group. Table (1) shows the FEV1 before and after nebulized furosemide. There is an increase in the FEV1% of 27.6 ± 9.1. Figure 1 shows diagrammatic representation of FEV1 before and after furosemide while Figure 2 shows diagrammatic representation of FEV1 before and after control. There is a marked increase of FEV1 in the first group as compared to the second group.

Table 1 assessment of change in FEV1 before and after administration of furosemide

Variable	Furosemide group	Control group
Baseline	39.2 ± 5.8	38.2 ± 9.5
After 1 hour	66.9 ± 11.6	43.1 3± 13.1
p-value	0.005	0.753

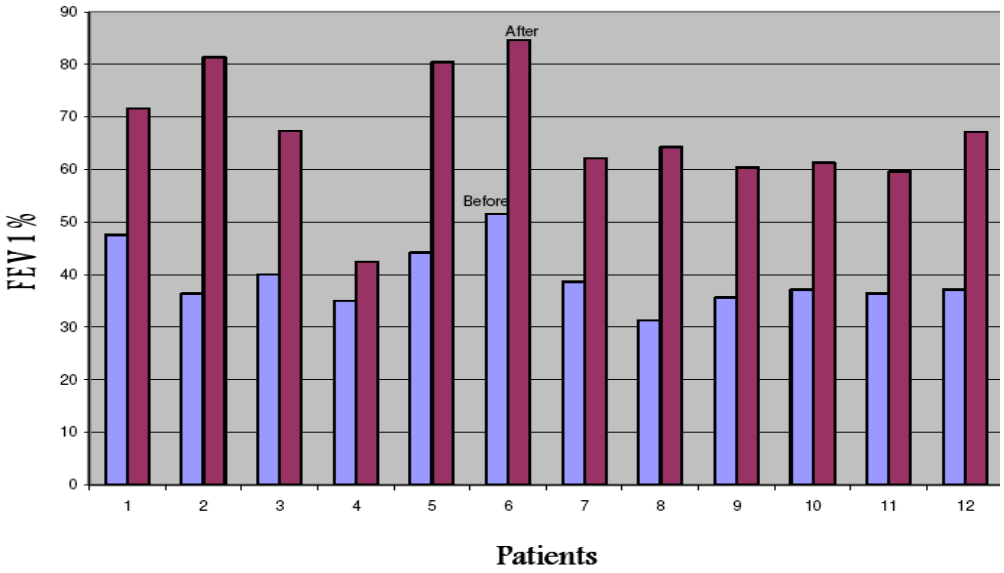

Figure 1 FEV1% before and after frusemide nebulizer

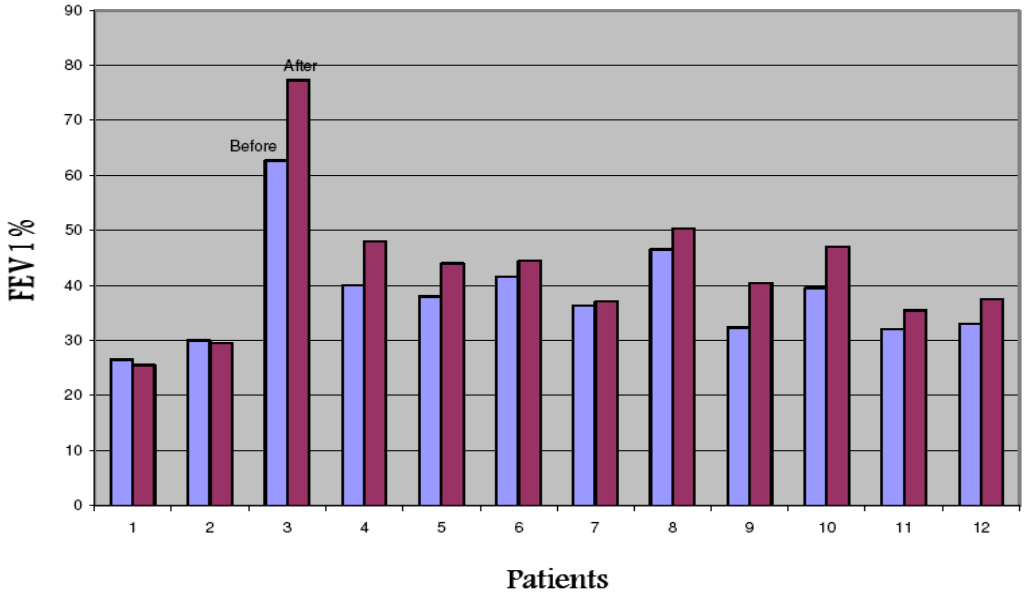

Figure 2 FEV1% before and after placebo nebulizer

4. DISCUSSION

This randomized, double-blind, placebo-controlled trial demonstrates that nebulized furosemide is useful in the therapy of adult patients with acute asthma exacerbations, particularly those who received an aminophylline IV infusion. The management of acute asthma attacks was studied in a RCT placebo-controlled trial, inhaled furosemide alleviated mild to moderate exacerbations of acute asthma (Ono et al., 1997). This study is consistent with their results , in which they utilized 40 patients with acute asthma who received iv hydrocortisone and aminophylline and then half of them received nebulized frusemide and the other received nebulized saline and the result of this study shows an increase in the FEV1% of 28.2 ± 5.9% in the frusemide group which is significantly higher than the result in control group and suggest that inhaled frusemide has a bronchodilator effect in patient with acute exacerbation of asthma who received IV aminophylline.

Three previous trials were conducted to determine whether adding nebulized furosemide to standard ß agonist therapy improves outcome in acute asthma, the first of which was published in 2010 (Yen and Chen, 2005), in this trial, 20 patients with acute asthma assigned to inhaled salbutamol/frusemide or inhaled salbutamol/saline, with the former seeing an increase in PEFR of 83% versus 35% in the latter. The second study (Karpel et al., 1994), there is no significant change in PEFR between the two groups

of 24 individuals with acute asthma who were randomized to nebulized metaproterenol or nebulized metaproterenol/frusemide. The third study (Pendino et al., 1998), the addition of nebulized fru to standard ß agonist therapy in 24 patients with acute asthma who were randomized to nebulized salbutamol/frusemide or salbutamol/saline did not have a significant effect. According to the findings of these studies, there is currently adequate evidence to warrant the routine inclusion of nebulized frusemide to standard ß agonist therapy in acute asthma (Yen and Chen, 2005).

5. CONCLUSION

Nebulized furosemide when given in asthmatic patients with severe symptoms who received IV aminophylline produced significant increase in FEV1 suggesting that nebulized furosemide has therapeutic benefit in asthmatic patients experiencing a severe exacerbation.

Informed consent

Written informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval for human

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards (Code: 2019/0341).

Author contribution

Abdullah Arnus Abdul-Hassan: Conception and design of the work, the acquisition, analysis, and interpretation of data for the work, and Drafting the work.

Hashim M.Hashim: Conception and design of the work, interpretation of data for the work, and revising it critically for important intellectual content

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Conflict of interest

The authors declare that they have no conflict of interest.

Data and materials availability

All data associated with this study are presented in the paper.

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