Ali Vefagh Nematollahi, Hassan Motamed, Kambiz Masoumi, Arash Forouzan, Elnaz Nobakht

Emergency Medicine Department, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Efficacy evaluation of budesonide nebulizer as an adjunctive medication in post-rain asthma acute phase attack

Abstract

Introduction: Bronchospasm attacks occur following syndromic rainfall and are increasing due to air pollution and need effective treatments. In this study, the effect of salbutamol nebulizer in comparison with salbutamol plus budesonide nebulizer in patients referred to the emergency department with dyspnea was investigated.

Material and methods: The trial study was conducted on 228 patients with dyspnea after the first rainfall in Ahvaz. Two groups of 114 patients have been randomly allocated. On the course of treatment, the first group received salbutamol plus budesonide nebulizer and the second group received salbutamol alone. In the experimental group, budesonide 0.5 mg with salbutamol was nebulized three times for 20 minutes. In all patients, 20, 40, and 60 minutes after the start of the intervention, forced expiratory volume in 1 second (FEV1) and peak expiratory flow rate (PEFR) and vital signs of size were recorded and analyzed by SPSS and t-test.

Results: Data revealed that there were significant differences between PEFR parameters of studied. Groups in minute 40 and 60 after intervention ($p = 0.000001$). There was better improvement.in PEFR values in minute 40 and 60 in budesonide plus salbutamol study group. There were no significant differences for FEV1 in minute 0, 20, 40, 60 between to studied group. Also there were no significant differences for borg dyspnea scale for minute 0 and 60 between two experimented group. Respiratory rates have significant differences in minutes 20, 40 after intervention and there was better improvement for salbutamol plus budesonide group rather than sulbutamol intervention group alone.($p = 0.001142$).

Conclusion: Experiment data revealed. that due to the significant difference between PEFR and increased FEV1 in the combination of the two drugs and due to the corticosteroid effects of budesonide in reducing and preventing inflammation and swelling of the lungs, nebulizer salbutamol + budesonide has better effects on moderate breath than in nebulizer salbutamol.

Key words: budesonide, dyspnea, post-rain asthma, recovery, salbutamol

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Introduction

Post-rainy asthma and dyspnea in patients with allergies to plant pollens and airborne allergens have always been a health challenge in the early fall in many countries around the world. There is ample evidence that storms, thunderstorms, and rainfall can cause an allergic asthma epidemic in patients with a pollen allergy [1]. Asthma and dyspnea are the most common chronic respiratory diseases that have been steadily increasing over the past decade and currently affect 300 million people (about 5% of the population) worldwide [2]. Asthma defines as small airway obstruction that changes spontaneously and greatly with treatment. People with asthma develop a certain type of inflammation of the small airways and, as a result, they become sensitive to a wide range of stimuli [3]. This inflammation causes the airways to become too narrow, resulting in decreased airflow, wheezing, and symptomatic shortness of breath. Airway stenosis is usually reversible, but in some cases and chronic conditions, a degree of irreversibility may be seen [4]. Specific chronic inflammation involves the respiratory mucosa of the trachea to the terminal bronchioles, and one of the main goals of treatment is to reduce this inflammation. None

Address for correspondence: Hassan Motamed, Emergency Medicine Department, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran, e-mail: hasan_motamed@yahoo.com

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of the major inflammatory cells involved in severe asthma-induced dyspnea (eosinophils, dendritic cells, macrophages, mast cells and neutrophils) is superior to the others [5]. By releasing histamine, leukotrienes, cytokines, and growth factors, and neurotrophins, mast cells are essential in inducting Broncho constrictor's acute inflammatory response to smoke, allergens, and hyperventilation [6]. Cytokines released from TH2 lymphocytes (IL3, IL4, IL5) mediate allergic inflammation [7]. Cocaine also absorbs inflammatory cells into the airways [8]. Inflammatory mediators alter the threshold of excitability of airway smooth muscle cells by altering their resting potential. Hypertrophy and hyperplasia of smooth muscle cells are also seen [9]. In the case of thunderstorms, along with rain and thunderstorm, acute asthmatic attacks increase, which is called "thunderstorm asthma". Symptoms of this disease occur very quickly as short breathing, dyspnea, coughing, and wheezing. The epidemic of this disease occurs in some regions of the world, usually in spring and summer. Large amounts of pollen in plants, spores of fungi, warm climate, and various other factors can be conducive factors for this phenomenon. Asthma with thunderstorms has been reported in several countries around the world; for the first time, the relationship between a thunderstorm and a large number of patients with asthma attacks has been reported in Birmingham, England, followed by many cases of the epidemic in different parts of the world, including the UK, Australia, Canada, the US, etc. [10]. The onset of bronchospasm may be sudden or maybe a progressive start and last more than a few minutes. The main medications for asthma dyspnea are bronchodilators (rapid relief of symptoms by relaxing smooth muscles) and controllers (inhibition of the underlying inflammatory process) [11]. The head of the group of bronchodilators are agonists that have no effect on underlying inflammation [9]. The most effective treatment for acute exacerbation of dyspnea is the short-effect inhaler agonist (salbutamol) given by nebulizer, spray, and spacer [8]. In the absence of a satisfactory response, an inhaled anticholinergic is also added [11]. Since many patients do not respond to inhalation treatments and need injectable drugs and invasive treatments such as intubation and ventilators, the discovery of new inhaled drugs with different mechanisms of action seems necessary [12]. One of the controversial inhalation drugs in dyspnea and asthma is Pulmicort. Corticosteroids are dominant with glucocorticoid activity and have inhibitory effects on mast cells, eosinophils, neutrophils, and macrophages and inhibit cytokines [12]. This study focused on compare of influences of salbutamol nebulize alone compared to salbutamol and budesonide in the treatment of dyspnea exacerbation in the first rainfall of 2020 in referral patients of a university hospital in Ahvaz, Iran. Post-rainy asthma and dyspnea in patients with allergies to plant pollens and airborne allergens have always been a health challenge in the early fall in many countries around the world. There is ample evidence that storms, thunderstorms, and rainfall can cause an allergic asthma epidemic in patients with a pollen allergy [1]. Asthma and dyspnea are the most common chronic respiratory diseases that have been steadily increasing over the past decade and currently affect 300 million people (about 5% of the population) worldwide [2]. Asthma defines by small airway obstruction that changes spontaneously and greatly with treatment. People with asthma develop a certain type of inflammation of the small airways and, as a result, they become sensitive to a wide range of stimuli [3]. This inflammation causes the airways to become too narrow, resulting in decreased airflow, wheezing, and symptomatic shortness of breath. Airway stenosis is usually reversible, but in some cases and chronic conditions, a degree of irreversibility may be seen [4]. Specific chronic inflammation involves the respiratory mucosa of the trachea to the terminal bronchioles, and one of the main goals of treatment is to reduce this inflammation. None of the major inflammatory cells involved in severe asthma-induced dyspnea (neutrophils, macrophages, eosinophils, dendritic cells and mast cells)is better than the other cells [5]. By releasing histamine, leukotrienes, cytokines, and growth factors, and neurotrophins, mast cells are central in inducting the Broncho constrictor's acute inflammatory response to allergens, smoke, and hyperventilation [6]. Cytokines released from TH2 lymphocytes (IL3, IL4, IL5) mediate allergic inflammation [7]. Cocaine also absorbs inflammatory cells into the airways [8]. Inflammatory mediators alter the threshold of excitability of airway smooth muscle cells by altering their resting potential. Hypertrophy and hyperplasia of smooth muscle cells are also seen [9]. In the case of thunderstorms, along with rain and thunderstorm, acute asthmatic attacks increase, which is called "thunderstorm asthma". Symptoms of this disease occur very quickly as short breathing, dyspnea, coughing, and wheezing. The epidemic of this disease occurs in some regions of the world, usually in

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Material and methods

Type of Study

In the experiment, dyspnea referral patients to a university Hospital emergency department were included in the study after the first rainfall in 2020.

Sampling

The sample size was selected by simple random sampling and the patients were allocated to two groups.

Randomization

Eligible patients were randomly divided into 40 groups of 6 patients. Twenty groups were given envelopes number one and the other 20 groups were given envelopes number two and we do not know which type is in each envelope and were randomly determined by software and finally, the number of patients in each group was completely the same and no other variables such as the researcher's opinion were effective in assigning people to groups.

Blinding

The patient and the doctor do not know which treatment they have received.

Method

At first, the patients were visited by an Emergency Medicine Specialist and subjected to clinical evaluation and physical examination. 228 patients were included in the study there patients allocated to two groups randomly each consist of 114 patients. One group received salbutamol l5 mg × 3 in 20 minute + budesonide 0.5 mg × 3 in 20 minute nebulize (Kromker IP32SN1304947) at minute 0, 20 and 40 after arrival. Another group received salbutamol l5 mg × 3 in 20 minute nebulize (Kromker IP-32SN1304947) alone at minute 0 and 20 and after arrival. All experiments were approved by the Research and Ethics Committee of ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran, (IR-AJUMS.REC.1398.684). The code for Iranian clinical registry was granted (IRCT20200109046061N1).

Before the intervention, according to history, physical examination was assessed considering speaking ability of patients in form of communication as sentence or phrase or word, state of consciousness, use of respiratory accessory muscles, wheezing and parameters of respiratory rate (RR), blood pressure (BP), and %Sato2 of the clinical condition and according to revised borg dyspnea scale [28], were evaluated for all patients at minute 0 and 60 after arrival PEFR (Vitalogragh company W4515 (England)) FEV1 (Vitalogragh company W4515 (England)), RR, PR, O_2Sat, BP, were recorded at minutes 0, 20, 40 and60 after arrival and drug administratian.at minutes 0,20,40 and 60 at the end of the study clinical parameters consist of Modified borg dyspnea scale, RR, PR, use of accessory respiratory muscles and paraclinical values such as PEFR, FEV1, O_2sat were Measured, the data have been analyzed using t test. Study Flowchart are showed in Figure 1.

In case of need to any further treatment more than our intervention the patient was excluded from the study.

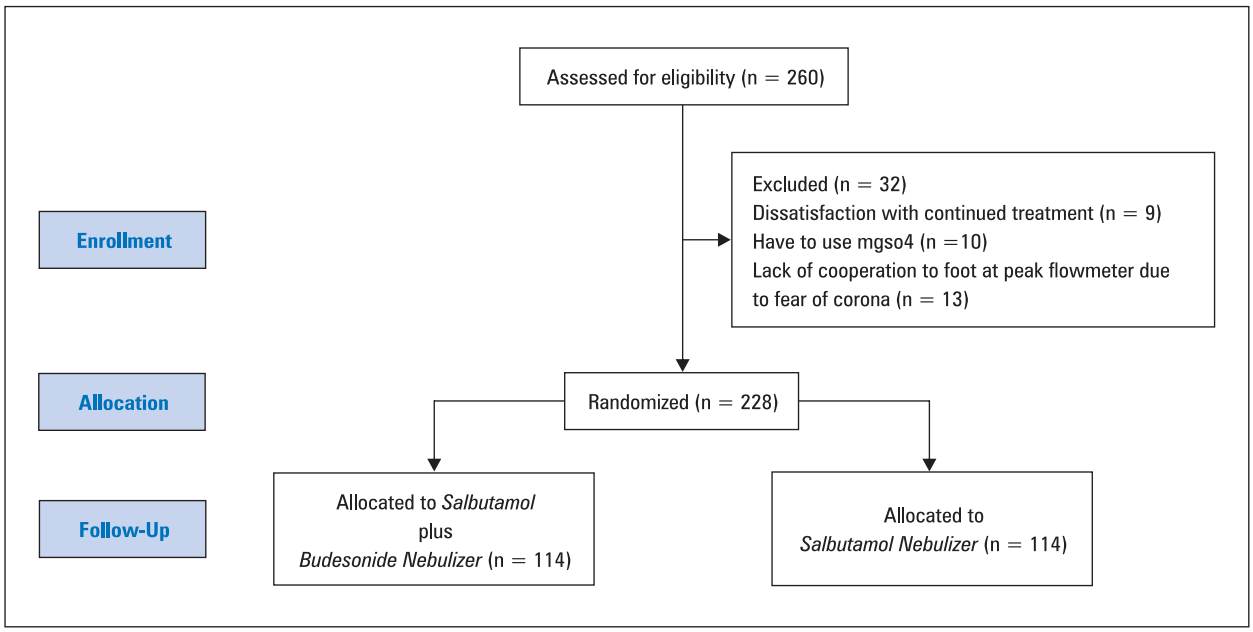

Figure 1. Flowchart diagram of the study

Inclusion criteria

- Minimum age 18 and a maximum of 55 years
- Patients who have referred to the hospital with bronchospasm and dyspnea following rainfall

Exclusion criteria

Lack of response to treatment and worsening of the patient's clinical condition so that for complementary treatment, there is a need for further asthma Medication. whenever the patient refuses to cooperate in the treatment process, as well as an underlying pulmonary disease with asthma-like manifestations such as interstitial lung disease (ILD), History of smoking more than 10 packs per year, a previous background for acute medical problems, coronary heart disease, chronic bronchitis, cardiac arrhythmia, pregnancy, and recent treatment of beta-agonist nebulizer over the past six hours all were exclusion criteria. People who did not announce their consent in writing were not studied.

Sample Size

Based on the information in this article [13] and considering the percentage of changes for PEFR variable compared to the beginning of the study in the two groups, at the confidence level of 95% and the power of 80% of the sample size in each group, 114 people were obtained.

Power	N^1	N^2	Ratio	Alpha	Beta	$Mean^1$	$Mean^2$	S1	S2
0.80011	114	114	1.000	0.05000	0.19989	36.3	19.7	50.8	37.2

$$n = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2 \times (\sigma_1^2 + \sigma_1^2)}{d^2}$$

Statistical Methods

To describe the data, we used statistical indicators such as mean, standard deviation, frequency, percentage, and so on. For comparing the mean variables in these groups, the independent t-test was used, and for studying the trend of improvement changes in these groups, a repeated measurements test was used. Data analysis was preformed using SPSS version 22.

Results

The participants 'mean age was 0.727 ± 36.79. None of the women were pregnant, and in general, none of the patients smoked cigarettes.

According to Table 1, the results did not show any significant statistical difference between the disease duration, the previous hospitalization history due to asthma, history of drug allergy, anti-asthmatic drug, and gender in both groups ($p > 0.05$).

As Table 2 shows, according to the t-test's results, a significant statistical difference was seen in the group receiving budesonide plus salbutamol and the salbutamol group alone in heart rate at zero, 20 minutes later and one hour later, maximum inspiratory flow after 40 minutes and one hour later, breathing rate at 40 minutes later,

Table 1. Comparison of past medical history data of patients of budesonide plus salbutamol receiving group versus salbutamol group alone

			The frequency of past medical history for thunderstorm asthema			P-value
			Last one year	Previous 1 to 5 year	Previous 5 to 10 years	
Groups	Salbutamol	Frequency	31	71	12	0.110
		Frequency percentage	27.2%	62.3%	10.5%	
	Budesonide + salbutamol	Frequency	31	71	12	
		Frequency percentage	27.2%	62.3%	10.5%	
Have you ever been hospitalized because of asthma?						
				yes	no	P-value
Groups	Salbutamol	Frequency		6	108	0.616
		Frequency percentage		5.3%	94.7%	
	Budesonide + salbutamol	Frequency		6	108	
		Frequency percentage		5.3%	94.7%	
Do you have a history of drug allergies?						
				yes	no	P-value
Groups	Salbutamol	Frequency		6	108	0.616
		Frequency percentage		5.3%	94.7%	
	Budesonide + salbutamol	Frequency		6	108	
		Frequency percentage		5.3%	94.7%	
Drug Allergy						
				No	Yes	P-value
Groups	Salbutamol	Frequency		107	7	0.608
		Frequency percentage		93.9%	6.1%	
	Budesonide + salbutamol	Frequency		107	7	
		Frequency percentage		93.9%	6.1%	
Anti-asthma medication						
			No use	Salbutamol	Salbutamol spray	P-value
Groups	Salbutamol	Frequency	107	1	6	0.110
		Frequency percentage	93.9%	0.9%	5.3%	
	Budesonide + salbutamol	Frequency	107	1	6	
		Frequency percentage	93.9%	0.9%	5.3%	
Gender						
			Man	Woman		P-value
Groups	Salbutamol	Frequency	57	57		0.553
		Frequency percentage	50.0%	50.0%		
	Budesonide + salbutamol	Frequency	57	57		
		Frequency percentage	50.0%	50.0%		

oxygen saturation at 40 minutes later and blood pressure level at 40 minutes later ($p < 0.05$).

According to Figure 2, Data reveled no significant differences for patients age between the studied groups of salbutamol alone versus budesonide+ salbutamol.

According to Figure 3, there was not significant differencebetween the groups in the mean FEV1 of patients receiving salbutamol alone and budesonide + salbutamol before receiving the drug minute 0, 20, 40, and 60 minutes after drug administration.

Table 2. Comparison of FEV between the group receiving budesonide + salbutamol and group receiving salbutamol alone

Variable	Groups	N	Mean	Std. Deviation	Std. Error Mean	P-value
FEV_1 0 min	Salbutamol	114	104.00	14.857	1.391	0.712
	Budesonide + salbutamol	114	102.40	14.087	1.319	
FEV_1 20 min	Salbutamol	114	119.89	21.109	1.977	0.765
	Budesonide + salbutamol	114	138.69	21.050	1.971	
FEV_1 40 min	Salbutamol	114	136.89	28.523	2.671	0.754
	Budesonide + salbutamol	114	176.40	27.772	2.601	
FEV_1 60 min	Salbutamol	114	151.13	31.717	2.971	0.603
	Budesonide + salbutamol	114	206.45	34.623	3.243	

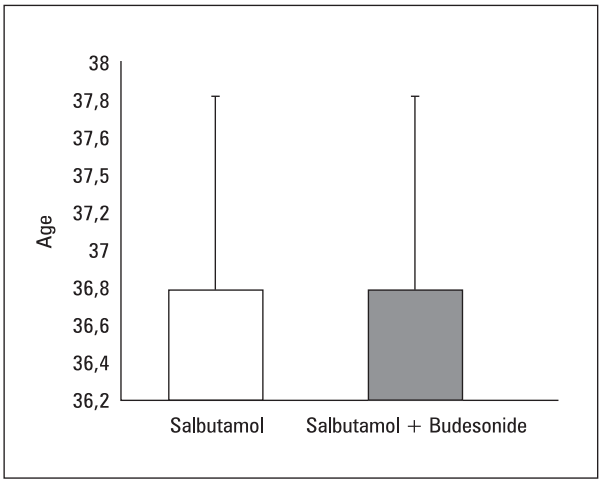

Figure 2. The patients'mean age in two intervention groups

According to Figure 4, there was not any significant statistical differences for PEFR Mean values between patients receiving salbutamol alone versus patient receiving budesonide + salbutamol at minutes 0, 20 after intervention ($p > 0.05$) but there was a significant statistical differences in the mean PEFR mean values in minute 40, 60 after drug administration and there were better improvement for PEFR values of minutes 40 and 60 after intervention for salbutamol + budesonide intervention group ($p = 0.000001$) (Table 3).

According to Figure 5, There was, no significant statistical differences were found in the mean Respiratory Rate (RR) values of between patients receiving salbutamol alone and the combination of budesonide + salbutamol group at minutes 0 and 60 after intervention. But a significant difference was seen in RR at minute 20 between two studied groups and there were More decrease in RR in Minutes 20 and 40 for patient of salbutamol + budesonide intervention group ($p = 0.01142$) (Table 4).

According to Figure 6, there was, no significant statistical differences were seen in the mean $SatO_2$% values of patients of groups receiving salbutamol alone versus patients receiving budesonide + salbutamol at minutes 0, 20 and 60 minutes after drug administration, but a significant differences was found in the mean $SatO_2$% at minute 40 drug administration after receiving drug between two studied groups and there was a higher O_2 sat% in minute 40 in salbutamol + budesonide group in contrast to salbutamol alone receiving group ($p = 0.000027$).

According to Figure 7, there was no significant statistical differences were seen in the mean values of Borg dyspnea scale for patients receiving salbutamol alone versus patients receiving budesonide + salbutamol at minutes 0 and 60 after drug intervention (Table 5).

Discussion

The results showed that no significant difference was found between the duration of the disease, a previous hospitalization history due to asthma, history of drug allergy, an anti-asthma drug, and gender in both groups ($p > 0.05$). A significant difference was seen between groups receiving salbutamol alone and budesonide + salbutamol and at heartbeat rate at 0 per minute, 20 minutes later and 60 minutes later, maximum inspiratory flow at 40 and 60 minutes later, respiration rate 40 minutes later, oxygen saturation 40 minutes later and blood pressure level 40 minutes later between the two groups receiving salbutamol alone and budesonide + salbutamol ($p < 0.05$) (Table 6).

In a study in Birmingham, England, a significant relationship was found between hospitalization due to respiratory, vascular, cerebral, bronchitis and PM10 diseases per day of hospitalization. Pneumonia, respiratory disease, and

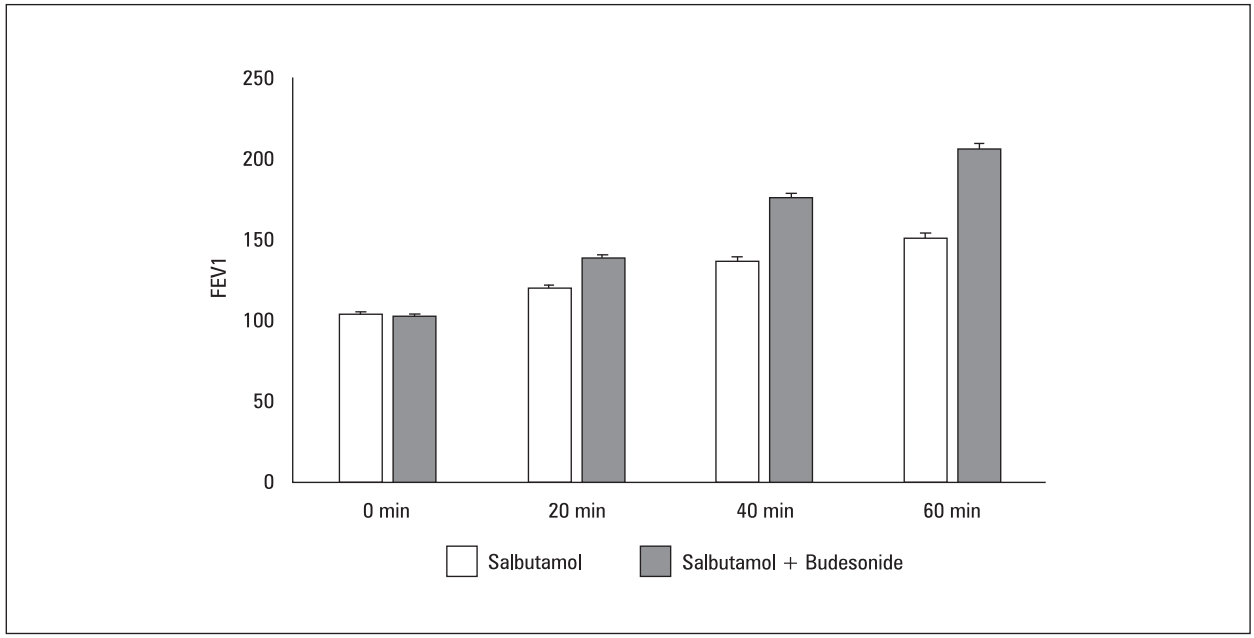

Figure 3. Mean FEV1 in the two intervention groups

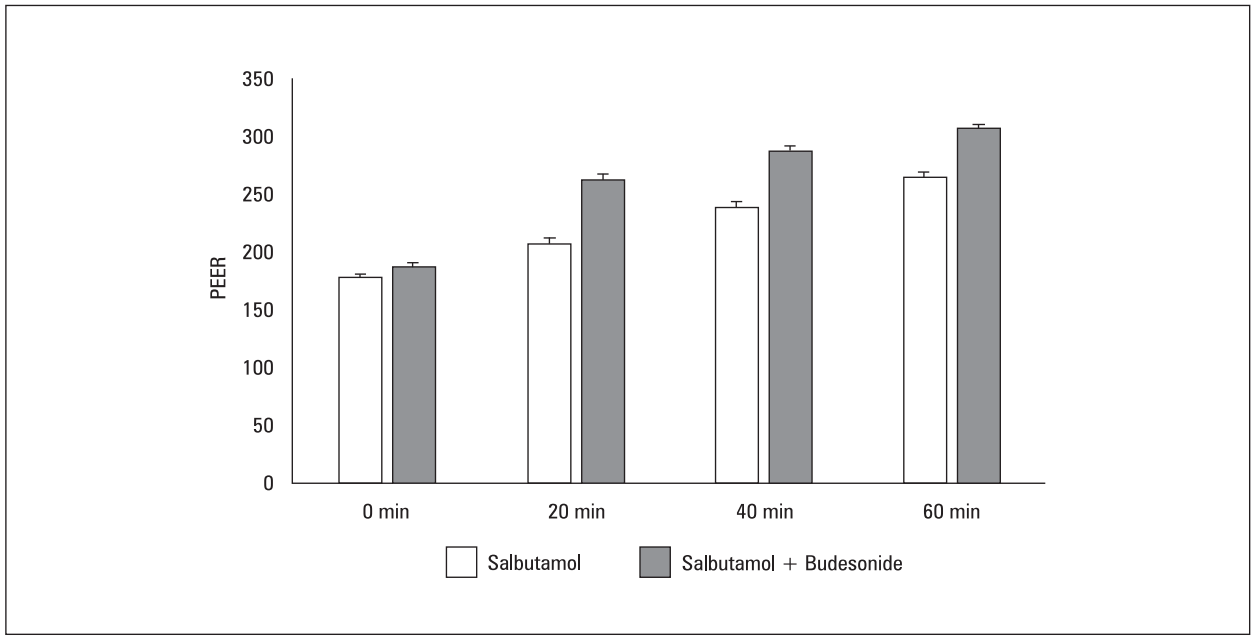

Figure 4. Mean PEFR in the two intervention groups

asthma were significantly associated with mean PM10 over the past three days. Deaths from chronic obstructive pulmonary disease (COPD) and overall death were significantly correlated with levels of PM10 in the past 24 hours, and COPD deaths were significantly correlated with levels of PM10 on an identical day. Each 310/g/m^3 growth in PM10 was correlated with a 2.4% increase in hospitalization due to respiratory distress and a 1.1% increase in overall death [14].

Researchers have shown that there is a significant relationship between occurrence of Asian dust storms with death due to the respiratory diseases. The researchers compared the mortality rate a few days before the dust storm with the period of the storm and concluded that one day following the storm, the respiratory disease rate

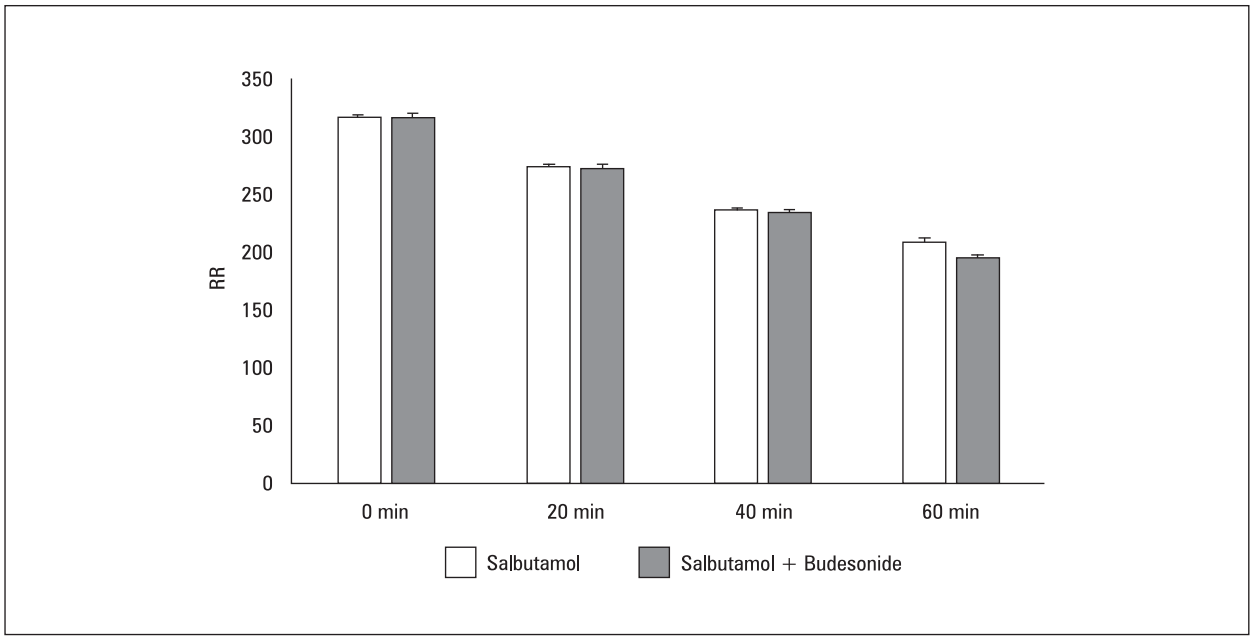

Figure 5. Mean RR in the two intervention groups

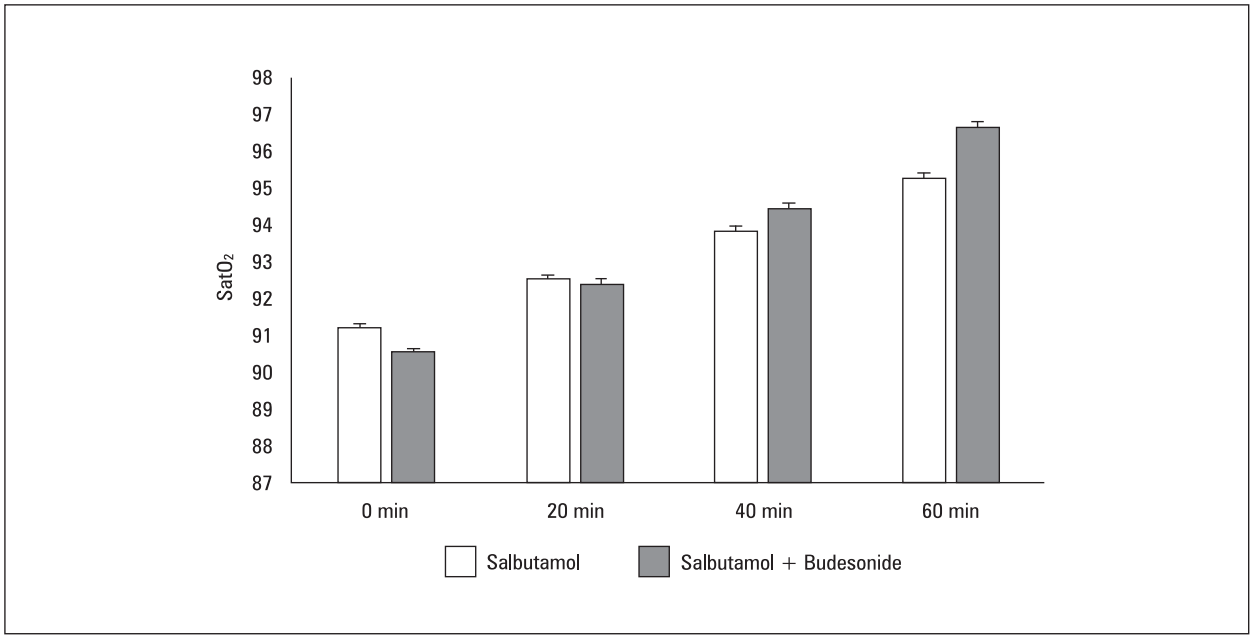

Figure 6. Mean $SatO_2$ in the two intervention groups

was 7.6%, and 48 hours following the storm, the total death rate raised by 4.2% [15].

In 2016, in a 26-week study of severe asthma and pulmicort combined with formoterol versus budesonide alone, Peters et al. examined the $12–12^{+}$ year-old patients tolerating four severe asthma attacks during the last twelve months and receiving pulmicort drugs along with formoterol or budesonide alone. The risk of asthma exacerbation (16.5%) with pulmicort and formoterol was lower than pulmicort alone [16], which was in line with the current study's results. In this study, salbutamol + budesonide nebulizer has better effects in the treatment of dyspnea compared to salbutamol nebulizer.

In a clinical trial study by Memon et al. (2016), at the Institute of Child Health Karachi between October 2012 and March 2013, response

of children suffering from acute severe asthma to nebulized salbutamol contrasted withthe ipratropium bromide compound was evaluated. In group B (salbutamol + ipratropium bromide nebulizer), 93 children (93%) improved their clinical score (< 10 points) while in group A, 84 children (84%) improved their clinical score [17], which is in line with the findings of the current research (Table 7).

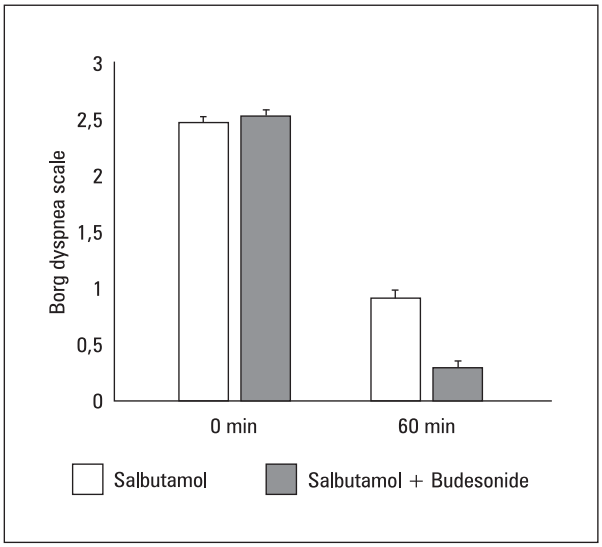

Figure 7. Mean Borg dyspnea scale in two intervention groups

In a 2014 study of "the role of nebulized salbutamol + magnesium sulfate versus nebulized salbutamol + normal saline in acute asthmatic attack in children, Mohammadzadeh et al. studied 80 moderate to severe asthma patients, the Global Initiative for Asthma (*GINA*) *guidelines*. They divided the patients into two groups (40 people with an age range of 5-14 years per each group), including the intervention group (salbutamol nebulizer + magnesium sulfate) and the controls (salbutamol + normal saline). At the end, the study concluded that salbutamol and magnesium sulfate nebulizers versus salbutamol and normal saline nebulizers is more effective in treating acute asthma attack [13].

In 2012 in a study by Arun et al. the bronchodilator effects of inhaled pulmicort/inhaled formoterol (200 μg and 12 μg, respectively), budesonide/salbutamol (200 μg and 200 μg, respectively) were compared in 5–15-year children. Their results showed that salbutamol or formoterol combined with pulmicort inhaled cortico-

Table 3. Comparison of PEFR between the group receiving budesonide + salbutamol and group receiving salbutamol alone

Variable	Groups	N	Mean	Std. Deviation	Std. Error Mean	P-value
PEFR 0 min	Salbutamol	114	177.54	35.888	3.361	0.261
	Budesonide + salbutamol	114	187.89	33.603	3.147	
PEFR 20 min	Salbutamol	114	264.81	48.247	4.519	0.237
	Budesonide + salbutamol	114	307.30	33.111	3.101	
PEFR 40 min	Salbutamol	114	238.60	46.463	4.352	0.000****
	Budesonide + salbutamol	114	287.90	32.620	3.055	
PEFR 60 min	Salbutamol	114	264.81	48.247	4.519	0.000****
	Budesonide + salbutamol	114	307.30	33.101	3.101	

Table 4. Comparison of RR between the group receiving budesonide + salbutamol and group receiving salbutamol alone

Variable	Groups	N	Mean	Std. Deviation	Std. Error Mean	P-value
RR 0 min	Salbutamol	114	27.04	2.043	0.191	0.253
	Budesonide + salbutamol	114	27.21	1.836	0.172	
RR 20 min	Salbutamol	114	23.47	2.049	0.192	0.043*
	Budesonide + salbutamol	114	23.40	1.692	0.158	
RR 40 min	Salbutamol	114	20.25	1.899	0.178	0.011*
	Budesonide + salbutamol	114	20.08	1.524	0.143	
RR 60 min	Salbutamol	114	17.93	1.813	0.170	0.469
	Budesonide + salbutamol	114	16.70	1.959	0.184	

Table 5. Comparison of BorgDyspnea scale between the group receiving budesonide + salbutamol and group receiving salbutamol alone

Variable	Groups	N	Mean	Std. Deviation	Std. Error Mean	P-value
Borg Dyspnea scale 0 min	Salbutamol	114	2.48	0.536	0.050	0.858
	Budesonide + salbutamol	114	2.54	0.534	0.050	
Borg Dyspneascale 60 min	Salbutamol	114	0.92	0.730	0.068	0.080
	Budesonide + salbutamol	114	0.31	0.597	0.056	

Table 6. Comparison of STATO_2 between the group receiving budesonide + salbutamol and group receiving salbutamol alone

Variable	Groups	N	Mean	Std. Deviation	Std. Error Mean	P-value
SatO_2% 0 min	Salbutamol	114	91.21	1.193	0.112	0.549
	Budesonide + salbutamol	114	90.55	1.082	0.101	
SatO_2% 20 min	Salbutamol	114	92.54	1.213	0.114	0.902
	Budesonide + salbutamol	114	92.43	1.269	0.119	
SatO_2% 40 min	Salbutamol	114	93.84	1.231	0.115	0.030*
	Budesonide + salbutamol	114	94.47	.980	0.092	
SatO_2% 60 min	Salbutamol	114	95.27	1.221	0.114	0.661
	Budesonide + salbutamol	114	96.65	1.262	0.118	

steroids with a dose measured at regular intervals in 5–15 year children with a diagnosis of mild to acute asthma is very effective and has similar bronchodilator effects [18], which is consistent with the present study's results. In this study, salbutamol + budesonide nebulizer has better effects in the treatment of dyspnea compared to salbutamol nebulizer.

In a 2008 study of the effects of pulmicort suspension with salbutamol and ipratropium bromide in the handling of asthma exacerbations in children, Chin et al. included 113 children with asthma in three random groups. In group A, 53 patients were improved with pulmicort nebulizer with salbutamol and ipratropium bromide two times per day for five days. In group B, 41 patients were administered with pulmicort along with salbutamol and ipratropium aerosol. In group C, 29 patients were treated with dexamethasone and aminophylline once daily for 5 days. There were significant differences in therapeutic effects in both groups A and C, and children had much better control of the asthma attack. Conversely, merely a small number of children in group B improved, indicating treatment uselessness, and ultimately, they stated that the nebulizer was one of the best ways to control the acute asthma exacerbation in children and also that the pulmicort nebulizer combined with salbutamol and ipratropium bromide is able to dismiss asthma indications in them by observing the dose and easy administration [19].This study, in line with our study, showed that salbutamol works better in the treatment of respiratory problems with another adjuvant drug.

In a 2006 randomized study conducted by Aggarwal et al., one hundred patients tolerating acute bronchial asthma attack, directed to the emergency department, were divided into two groups: group A that was receiving nebulizer compounded with salbutamol and magnesium sulfate and group B that was receiving salbutamol nebulizer alone. In the end, it was concluded that no medical advantages found by addition of magnesium sulfate to the salbutamol nebulizer in treating patients suffering from severe or fatal acute asthma [9], which was inconsistent with the present study but in this study, the budesonide drug was used to increase the salbutamol therapeutic properties.

In 2004, in a prospective study, Mahajan et al. compared nebulized magnesium sulfate plus albuterol to nebulized albuterol plus saline in treating children with acute exacerbations of mild to moderate asthma, and used a magnesium sulfate nebulizer at 3 doses + salbutamol at 10 and

Table 7. Comparison of age between the group receiving budesonide + salbutamol and group receiving salbutamol alone

Variable	Groups	N	Mean	Std. Deviation	Std. Error Mean	P-value
Age	Salbutamol	114	36.79	11.072	1.037	0.816
	Budesonide + salbutamol	114	36.80	10.936	1.024	

20 minutes, with better bronchodilator effects compared with 3 different doses of salbutamol alone [20].

The results of a study aimed to evaluate the effect of inhaled salbutamol before general anesthesia in patients with heavy smoking and the incidence of bronchospasm and hypoxia during induction of anesthesia and surgery and the occurrence of recurrent and annoying postoperative cough in these patients showed that prophylactic use of salbutamol spray is useful in reducing the incidence of bronchospasm, hypoxia, and cough after anesthesia in patients with heavy smoking [21]. But our study looked at the effect of salbutamol and budesonide together, which showed that those who took both drugs had a greater improvement than those who received salbutamol alone.

In a study by Nannini et al., after measuring PEFR, patients treated with salbutamol and normal saline or magnesium sulfate and salbutamol were nebulized, and at 10 and 20 minutes after the start of the study, the average increase percentage in PEFR in the magnesium-salbutamol sulfate group was significantly higher than normal saline-salbutamol group [22].

In a study by Hughes et al., 52 patients suffering from severe asthma attacks, who referred to the emergency department of two hospitals in New Zealand, underwent salbutamol and magnesium sulfate (group 1) or salbutamol and normal saline nebulizers (group 2). During ninety minutes, the mean FEV1 in the first group was 1.96 liters and in the second group, it was 1.55 and a significant difference was observed between these groups [6]. In line with the present study, these studies suggest that a combination drug better than salbutamol only works to improve respiratory problems.

A study was conducted to investigate ability of nebulized lidocaine as an adjunctive therapy for improving clinical parameters, FEV1, and PEFR in the course of an acute asthma attack. According to the results obtained from this study, no advantage was found in addition of nebulized lidocaine with a standard therapy method for asthma attacks. The minimal benefits of using nebulized lidocaine, at least for short-term use in the acute phase of an asthma attack are denied by the results of obtained from this study [23].

A study was conducted to evaluate the role of excess magnesium sulfate nebulizer as adjunctive treatment in the management of acute asthma attacks. As this study's results show, it can be said that as an adjunct to standard treatment, nebulized magnesium sulfate administration is effective in handling attacks of moderate to severe acute asthma and significantly causes a better control of acute attack in a short time [24]. In fact, it has been in line with the present study that drug supplements have a greater effect on improvement.

In line with the present study, the following studies can be mentioned that complementary therapy helps in the process of recovery of dyspnea; one study compared the rate of clinical improvement with the findings of pulmonary role in asthma patients before and after two weeks of treatment with the drug combination of formoterol plus budesonide. According to that study's results, the utilization of a drug combination of formoterol plus budesonide is useful for treating patients tolerating moderate and severe asthma and more use of the drug combination in the clinic is effective and satisfactory results are obtained [25].

In a 2003 study by Rosenhall, a combination of formoterol plus budesonide spray was used for people with asthma, 321 patients were given a 6-month spray containing formoterol and budesonide at a dose of 4.5 μg and then, 160 μg and compared with those who used the drugs separately. According to the results, there was a significant dissimilarity between both groups and that the use of this combined medication compared to the separate use of each medication has been most effective for people with asthma in the long run [26].

In a 2011 study of patients tolerating moderate asthma (n = 25), Cheng used and examined a combined spray of salmeterol plus fluticasone in the amount of 25 μg, 50 μg, and a spray of formoterol plus budesonide in the amount of 4.5 μg, 160 μg to improve their treatment.

The results showed a significant difference between FEV1 and forced vital capacity (FVC) and clinical signs after treatment in people who took salmeterol plus fluticasone compared to people who took formoterol plus budesonide ($p < 0.05$) [27].

Conclusion

As this study's results show, it can be concluded that administration of budesonide along with standard salbutamol treatment possibly has a positive effect on the recovery process of patients with asthma attacks.

Conflict of interest

None declared.

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