Evaluation of the improvement of the clinical symptoms and spirometric indices in asthmatic patients having different treatments

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Abstract: since most of the asthmatic patients do not use the proper medicine to control their persistent symptoms, we decided to accomplish a study to find out the relation between the treatment, clinical symptoms and spirometric indices in asthmatic patients. this study is a cross-sectional study on 150 patients suffering from persistent moderate asthma admitted to naghavi and beheshti hospital. They have less than three attacks weekly. After recording of their clinical symptoms (dyspenea, cough, wheezing and nocturnal) and spirometric indices (FEV1, FEV1/FVC, FVC) twice with intervals of 3-6 months, they were divided into three groups. The first group was treated with salbutamol inhaler, the second with salbutamol and floxitide and the third one withsalmeterol and floxitide. Then all the data was evaluated through SPSS program. the group treated with salmeterol and floxitide inhaler showed the greatest remission in coughing (%80.4), Dyspnea (%77.8), Wheezing (%77.8) and nocturnal symptoms (80%). In comparison to the other groups, the variance was statistically significant. In the study, most variances in FEV1and FEV1/FVC were observed in the receiver group of salbutamol, and most FVC variances were in receiver group of salbutamol-floxitid. Statistically there was no significant variance among the groups. This study showes the most clinical remission in the receiver group of salmeterol and floxitide, and spirometric indices are not sufficient to control the level of patients' treatment so that clinical symptoms are more valuable.
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1. Introduction

Asthmais a chronic, complex and heterogeneouslung disease in whichthe mucus of airway becomes abnormal and inflamed [1, 2]. Asthma incidence varies in different studies and societies. It seems tohaveincidenceequal to4%all around the world. However, GINAhas estimated the incidence of this diseasebetween5 to7percent in Iran [2]. In a study conductedbylotvallet al.in Sweden (2009) it was notedthatin thelast 50 years the incidence of asthmahas beenincreasedand abivalves in children can beexpected.Frequency of asthmain adults has been calculatedin therange of 7 to 10 percent[1]. Bunnaget al.conductedastudyin Thailand and measured epidemiology of allergic rhinitisand asthma in this country and finallyconcluded that the frequency of asthma increasedfrom12.2 to14.7percent [3]. There is nosingle testto diagnose asthma, therefore the asthma diagnosisis a clinical diagnosis and it is based on the questionsandclinicalsuspicion of doctors [4]. Seemingly, finding the relation between symptoms severity and treatments to improve patients and spirometric indicesneed further evaluation.While patients are receiving different treatments in different medical centersGINAhas a specific treatment protocol. Asthmatreatmentis divided into two parts: 1. Drugs to control attacks quickly: Inhaledshort-acting β2 agonist bronchodilator, Inhaledanticholinergic, Aminophyl line 2.Conservativeorcontroler treatments: Corticosteroids and anti-leukotrienes, chromone, anti-IgE, long-acting β2 agonists[5].The problem in our societyis thatmanyasthmatic patients referring to the doctors use bronchodilatorand it has been seen that patientseven useshort-acting bronchodilators to control persistent symptoms. Their drugs do not include Inhaled corticosteroids and long-acting bronchodilators. They even preferedoral corticosteroids in moderate andsevere asthma which has a lot of complications. Thus we decided to design a study on asthmatic patients admitted to Naghavi and Beheshti hospitalsin Kashan(2010-2011) to evaluate the relation between the recommended treatments and control level of clinical symptoms in

asthmatic patientsand to identify the efficacy ofthe treatments in the patients.

2. Material and methods

This is a cross-sectional study. It was done on asthmatic patients admitted in Naghavi and Beheshti hospitals in Kashan (2010-2011). Asthmatic patients with the symptoms including Daily clinical signs twice a week, nightly clinical signs twice a month, increase inFEV1at least 12%or inPEFat least20% after bronchodilator inhalation and taking at least one of the inhaled drugs including bronchodilator with long or short effector inhaled steroids Continuously orperiodically entered the study. The Patient with acutepneumoniaa finding in favor of the tumor in the CXR, Known history of heart failure, known interstitialdisease,smoker patients and those who takeatroventcontinuously excluded the study. The patients were 15 to60years old. They weigh45to 85kg. 150patients suffering from persistent moderate asthmawhohadless than threeattacks per week were selected and divided into three groups. Theirclinical information (Dyspnea, coughing, wheezing and nocturnal symptoms) and spirometric indices (FEV1,FEV1/FVC-FVC) were recorded twicewith intervals of three to sixmonths. The first group was treated with salbutamol and the second with salbutamol and flixotide and the third with salmeteroland flixotide.Related investigator teached the patients to use short and long actin bronchodilator and inhaled stroid.Data was put in the questionnaire and analyzedthrough Spss software. mac namar tests were used to evaluate the relations between quantitative variables.Questionnaire data was reflected in tables and figures according to the achieved results.

3. Results

In this study treatment efficacy on common symptoms of asthma in the patients was evaluated. In salbutamol group 50 patients(100%) had wheezingand after the treatment 7 patients (14%) became symptomless. In salbutamol and flixotide group 47 cases(94%) had wheezing before the treatment that 32(68%) cases improved after the treatment. In salmeteroland flixotide group 45(90%) patients had wheezing before treatment and 35 patients (77.8%) became symptomless. This variance among the groups wasstatisticallysignificant (P value <0.001). In comparison with others, the receiver patients of salmeterol and flixotidehad the most wheezingremission after the treatment. This was statistically significant (table 1).

50 patients(100%) in salbutamol group coughed at first that only 6 (12%) cases improved after the treatment. Before the treatment,46 patients (92%) in salbutamol and flixotidegroup coughed, but 31 cases (67.3%) improved at the end of the treatment. In salmerol and floxitide group,46 patients (92%) coughed before the treatment, but 37 cases (80.4%) improved after the treatment. These variances were statistically significant. The most improvement was in salmeterol and flixotidegroup(P value <0.001) (table 1).

49 cases (98%) in salbutamol group,48 cases (96%) in salbutamol and flixotide group and 45 cases (90%) in salmeteroland flixotide group had dyspnea, but after the treatment 2 (4%) ,30 (62.5%) and 35 cases (77.8%) improved respectively . The best result was in salmeterol and flixotidegroup. These results werestatistically significant.(P value <0.001) (table 1).

Improvement of nocturnal symptoms after the treatment, in all groups was significant and the highest improvement was in salmeterol and flixotide group (P value <0.001) (table 1).

Table 1. Comparison of symptoms in asthmatic patients after the treatment

Treatment groups		salbutamol	salbutamol&flixotide	salmetrole&flixotide	P value
wheezing	Have	43(86%)	15(31.9%)	10(22.2%)	<0.001
	Have not	7(14%)	32(68.1%)	35(77.8%)	
cough	Have	44(88%)	15(32.6%)	9(19.6%)	<0.001
	Have not	6(12%)	31(67.4%)	37(80.4%)	
dyspnea	Have	47(95.9%)	18(37.5%)	10(22.2%)	<0.001
	Have not	2(4.1%)	30(62.5%)	35(77.8%)	
Nocturnal symptoms	Have	46(95.9%)	15(32.6%)	9(20%)	<0.001
	Have not	2(4.1%)	30(67.4%)	36(80%)	

Most changes in FEV1 as a spirometric index after the treatment were firstly observed in salbutamol group (34%),then in salmeterol and flixotide group (24%) and Lastlyin salbutamol and flixotide group (20%), but the variances were not statistically significant (P value =0.09) (table 2).
Most changes inFEV1/FVCas the spirometric indicesafter the treatment were observed first in salbutamol group (28%),then in salbutamol and flixotide group (20%) and Lastlyin salmeterol and flixotide group (10%) but thevariances were not significant (P value= 0.130) (table 2).
Most changes of FVC as a spirometric index were seen in salbutamol and flixotide group (36%) and after it in salbutamol (26%), salmeterol and flixotide groups (26%) (P value =0.565) (table 2).

Table 2. Comparison spirometric parameters change among treatment groups

Treatment groups		salbutamol	Salbutamol & flixotide	Salmetrole & flixotide	P value
FEV1	5>	14(28%)	15(30%)	24(48%)	0.09
	5-10	19(38%)	25(50%)	15(28%)	
	10>	17(34%)	10(20%)	12(24%)	
FEV1/FVC	5>	13(26%)	17(34%)	23(46%)	0.13
	5-10	23(44%)	23(46%)	22(44%)	
	10>	14(28%)	10(20%)	5(10%)	
FVC	5>	9(18%)	8(16%)	13(26%)	0.565
	5-10	28(56%)	24(48%)	24(48%)	
	10>	13(26%)	18(36%)	13(26%)	

4. Discussion and conclusions

In this study most changes of FEV1 and FEV1/FVC were in salbutamol group and most changes of FVC were in salbutamol and flixotide group. However, no statistically significant variance has been reported among the groups. (P value= 0.09) (P value= 0.130) (Pvalue= 0.565). None of the three therapeutic groups has sustained beneficial effect on spirometric parameters in asthmatic patients (as mentioned it was not significant).

Asthmatic patients in salmeterol and flixotidegroup had further improvement of clinical symptoms after the treatment (cough, dyspenea, wheezing, nocturnal symptoms) than the other groups (Pvalue< 0.001) .Therefore, spirometry alone is not enough to evaluate control of the treatment level and clinical symptoms are more practical and important.

In studies on beta-agonists it has been mentioned that after taking beta-agonists, alleviation of symptoms and PEF incrementwill occur without any improvement in airway inflammation and monotherapy with long-acting beta-agonists increases the risk of hiding the severity of the disease and inflammation in the airways continues [6].

Kraan et al. in their clinical trials have indicated that regular use of short-acting beta-agonists increases sensitivity of the airways in asthmatic patients,but this cannot be applied to the patients who are receiving corticosteroids[7].

Lundback and Lenneyaccomplished two clinical trials to compare the effect ofsalmeterol and salbutamol in remission of clinical symptoms in asthmatic patients. They concluded that salmeterol is more effective in improving asthmatic patients' symptoms, but in spite of the fact that clinical symptoms had been reduced, there was no significant alleviationin asthmatic attacks [8,9].

In a clinical trial on evaluation of the changes in spirometric parameters in asthmatic patients receiving corticosteroid, (budesonide) patients who started taking budesonide five years after the onset of asthma were compared to those who started taking it two years after the onset of asthma. In the first group FEV1 was less than in the second group, and FEV1 value was related to the interval between the onset of asthma clinical symptoms and taking corticosteroid [10].

The relationship between clinical symptoms and early corticosteroid consumption has also been observed in another clinical trial[11].According to the results of two clinical trials by Donahue and Suissa on the effects of corticosteroids on the death caused by asthma and hospitalization, they showed that hospitalization and mortality rate have been declined during the treatment with inhaled corticosteroids[12,13].

In our study, the number of patients who improved after taking drugs, in the salmeterol group and flixotide was more than in salbutamol and flixotide group, and it was not statistically significant. Regarding this fact, it seems that combination of salmeterol and flixotide is more preferred to control

asthma symptoms. This corresponded to the results obtained in Greening and Woolcock's clinical trials[14,15].

Greening et al.in their clinical trial concluded that combination of corticosteroid and salmeterol improves clinical symptoms [14].Woolcocket al. in their clinical trial evaluated the combination of corticosteroids andsalmeterol in controlling the symptoms of asthmatic patients and similar results were obtained [15].

Verberneet al. concluded that salmeterol as monotherapyis not efficient in controlling asthma symptoms and it should be used along with beclomethasone[16]. Agertoftet al. in their trial on comparison of the effects of Long-acting beta-agonist (salmeterol) and corticosteroid (budesonide) noted that FEV1 was the same in the two groups, but both treatments improved symptoms [17].Barnes et al. reported that long continuous treatment with bronchodilators without corticosteroids can hide decrement of ventilatory function; therefore it hides the patient's need to receive Corticosteroids [18].

Lack of warning about decrement in lung function confuses physicians in choosing the most appropriate therapy for asthmatic patients. Perhaps it was the main reason that many patients who need an anti-inflammatory drug only receive bronchodilator [6-19]. PALMER et al. in their clinical trials stated that spirometric parameters including FVC, FEV1and FEV1% significantly increased only after the consumption of salbutamol[20].

Douma et al. in their clinical trialaiming at comparing the efficacy of long-acting beta-agonist (salmeterol) and corticosteroid (fluticasone) came to the conclusion that they has no effect on FEV1 and even combination of these two drugs also has no effect on FEV1[21].

JEFFREY et al. did a clinical trial aiming at comparing the effect of two methods of administration of beta-agonists (periodically and only as needed) on spirometric parameters and clinical symptoms in asthmatic patients. They concluded that although one group has received beta-agonists four times more than the other but there was no significant variance between the two groups. The results of this study showed that beta-agonists use is reasonable only when it is needed not periodically[22].

CHEUNG et al. stated that in comparison with the long use of long-acting beta-agonists, placebo does not make any difference in spirometric parameters (FEV1) and treatment only with long-acting beta-agonists is not effective in controlling asthma [23].

BRIAN et al. stated that beta-agonists had no changes on spirometric parameters (FEV1) of asthmatic patients after seven days and their effect on spirometric parameters is limited to the early hours of indication [24]. Finally the study showed that spirometry alone is not enough to evaluatethe control of treatment level and clinical symptoms are more valuable and practical. Also short-acting beta-agonists are not efficientincontrolling theclinical symptoms of asthma and the best treatment is combination of salmeterol and flixotide.

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References

[1] Lötvall J, Ekerljung L, Rönmark EP, Wennergren G, Lindén A, Rönmark E, Torén K, Lundbäck B. West Sweden Asthma Study: prevalence trends over the last 18 years argues no recent increase in asthma. Respir Res. 2009 Oct 12;10:94

[2]. http//:www. Asthma.org.2006

[3] Bunnag C, Jareoncharsri P, Tantilipikorn P, Vichyanond P, Pawankar R. Epidemiology and current status of allergic rhinitis and asthma in Thailand -- ARIA Asia-Pacific Workshop report. *Asian Pac J Allergy Immunol*. 2009 Mar; 27(1):79-86.

[4] Bruce R, Gordon MA.MD. Asthma history and presentation inotolaryngolgic clinics of north America, Vol 41,Issue 2,Apr 2008.

[5] Mullolj, Valero.A, Alobid.I, Bartraj, Navarro Am, Chivato. T, Khaltaev.N, Bousauty, Allergic Rhinitis and its Impact on Asthma update Caria 2008. The perspective from spain, *J Investig Allergolclin Immuno*l.2008,18(5):327-34.

[6] Barnes PJ. Effect ofcorticosteroids on airway hyperresponsiveness. *Am Rev RespirDis* 1990;141:S70-6.

[7] Kraan J, Koe¨ter GH, van der Mark ThW, Sluiter HJ, de Vries K. Changes in bronchial hyperreactivity induced by 4 weeks of treatment with antiasthmatic drugs in patients with allergic asthma: a comparison between budesonide and terbutaline. *J Allergy ClinImmunol* 1985;76:628–36.

[8] Lundback, B., D. W. Rawlinson, and J. B. D. Palmer. 1993. Twelve month comparison of salmeterol and salbutamol as dry powder formulations in asthmatic patients. Thorax 48:148–153.

[9] Lenney, W., S. Pedersen, A. L. Boner, A. Ebbutt, and M. M. Jenkins. Efficacy and safety of salmeterol in childhood asthma.*Eur. J. Pediatr.* 154:983–990.

[10] Agertoft L, Pedersen S. Effects of long-term treatment with an inhaled corticosteroid on growth and pulmonary function in asthmatic children. *Respir Med*. 1994 May;88(5):373-81.[11] Haahtela T, Jarvinen M, Kava T et al. First line treatment of newly detected asthma: an inhaled steroid? one year's follow up after two years treatment. *Eur Respir J* 1992; 5 (suppl. 15): 13s.

[12] Donahue JG, Weiss ST, Livingston JM. Inhaled steroids and the risk of hospitalization for asthma. JAMA 1997;277:887-91.

[13]Suissa S, Ernest P, Benayoun S. Low dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med* 2000;343:332-6.

[14] Greening AP, Ind PW, Northfield M, Shaw G. Added salmeterol versus higher-dose corticosteroid in asthma patients with symptoms on existing inhaled corticosteroid. *Lancet* 1994;344:219-24.

[15] Woolcock A, Lundback B, Ringdal N, Jacques LA. Comparison of addition of salmeterol to inhaled steroids with doubling of the dose of inhaled steroid. *Am J RespirCrit Care Med* 1996;153:1481-8.

[16] Verberne AAPH, Frost C, Roorda RJ, van der Laag H, Kerrebijn KF and the Dutch Paediatric Asthma Study Group. One year treatment with salmeterol compared with beclomethasone in children with asthma. 1997;156:688–695

[17] Fuglsang, G., L. Agertoft, J. Vikre-Jorgensen, and S. Pedersen. 1995. Influence of budesonide on the response to inhaled terbutaline in children with mild asthma. *Pediatr.AllergyImmunol*. 6:103–108.

[18] Weir DC, Sherwood Burge P. Use of corticosteroids in patients with chronic airflow obstruction by physicians in the west Midlands. Thorax 1990;45:791.

[19] Van Schayck CP, van Weel C, Folgering H, Verbeek ALM, van Herwaarden CLA. Treatment of patients with chronic airflow obstruction by general practitioners and chest physicians. Scand7Prim Health Care 1989;7:137 -42.

[20] Palmer KN, Diament ML. Effect of salbutamol on spirometry and blood-gas tensions in bronchial asthma. Br Med J. 1969 Jan 4;1(5635):31-2.

[21] Weersink, E. J. M., W. R. Douma, G. Koëter, and D. S. Postma. 1995. Is there a synergistic effect between salmeterol and fluticasone in asthmatics with nocturnal airway obstruction? (abstract). Am. J. Respir. Crit. Care Med. 151:A268.

[22] Drazen JM, Israel E, Boushey HA, Chinchilli VM, Fahy JV, Fish JE, et al. Comparison of regularly scheduled with as-needed use of albuterol in mild asthma. Asthma Clinical Research Network. N Engl J Med. 1996 Sep 19;335(12):841-7.

[23] David Cheung, M.D., Mieke C. Timmers, Aeilko H. Zwinderman et al. Long-Term Effects of a Long-Acting β2-Adrenoceptor Agonist, Salmeterol, on Airway Hyperresponsiveness in Patients with Mild Asthma. N Engl J Med 1992; 327:1198-1203.

[24] Brian J. O'Connor, Sarah L. Aikman, Peter J. Barnes. Tolerance to the Nonbronchodilator Effects of Inhaled β2-Agonists in Asthma. N Engl J Med 1992; 327:1204-1208.

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