The Professional Medical Journal
www.theprofesional.com

DOI: 10.17957/TPMJ/17.4443

ORIGINAL PROF-4443

ASTHMA;

COMPARISON OF SALMETEROL /FLUTICASONE PROPIONATE AND FORMOTEROL / BUDESONIDE IN PERSISTENT ASTHMA

Muhammad Abdullah[1], Zaheer Ahmed[2], Hassan Fareed[3]

1. MBBS
PGR, Medicine Department,
Allied Hospital, Faisalabad.
2. MBBS, FCPS (Medicine)
Senior Registrar, Medical Unit I,
Sir Ganga Ram Hospital,
Lahore
3. MBBS,
Medical Officer, BHU, Faisalabad

Correspondence Address:
Dr Zaheer Ahmad
Senior Registrar Medical Unit I,
Sir Ganga Ram Hospital, Lahore.
House No. 35-C PMC Colony,
Faisalabad.
trueman228@gmail.com

Article received on:
21/07/2017
Accepted for publication:
31/09/2017
Received after proof reading:
03/11/2017

ABSTRACT… The aim on the study was to compare the efficancy of salmeterol and formoterol in persistent asthama. **Study Design:** Randomized-Controlled-Trial(RCT). **Setting:** Department of Medicine, Allied Hospital, Faisalabad**. Period:** June 2014 to December 2014. **Methodology:** Patients of both genders with ages between 18 and 70 years having persistent bronchial asthma while Pregnant or lactating mothers, patients with upper or lower respiratory tract infections, acute asthma exacerbations within 4 weeks of first visit, Oral corticosteroids within 4 weeks or depot steroids within 12 weeks of first visit and Smoking history of more than 10 pack years were excluded from study. Patients were randomly divided into two groups (Group A & Group B) using computer generated random number table. Salmeterol/Fluticasone combination was given to group A with a dose of 50/250μg, 2 actuations with ABEL SPACER DEVICE twice a day for a period of 24 weeks. Formoterol/Budesonide combination was given to group B with a dose of 400/6μg with Rotahaler twice a day. Follow up was done by patient's outdoor visits at 6th,12th,18h and 24th week. **Results**: 180 patients were enrolled in the study. 79 (44%) were males and 101 (56%) were females. Mean age of study population was 45.25+13.382 years. Patients in Group B experienced lesser number of exacerbations than patients in Group B. Group B showed better response to treatment than Group A using chi square test. (P-Value 0.001). **Conclusion:** It has been concluded that budesonide/Formoterol is more effective in controlling asthma symptoms than fluticasone/Salmeterol.

Key words: Budesonide/Formoterol, Fluticasone/Salmeterol, Asthma

Article Citation: Abdullah M, Ahmed Z, Fareed H. Asthma; Comparison of salmeterol / fluticasone propionate and formoterol /budesonide in persistent asthma. Professional Med J 2017;24(11):1749-1754. **DOI:**10.17957/TPMJ/17.4443

INTRODUCTION

Asthma is a major contributor of morbidity, health care costs and adversely affected quality of life of its affected patients.it is a very common condition with a high prevalence rate among children and adolescents. It contributes to loss of work productivity and high health care resource utilization.[1] Asthma is a highly prevalent condition with up to 9.8% prevalence in UAE.[2] In Pakistan, it is even higher with up to 15.8% prevalence in a survey conducted in 2009 in Karachi.[3]

It is well established that long acting β_2 agonist (LABA) combined with inhaled-corticosteroid (ICS) has more efficacy than only inhaled-corticosteroid(ICS) in controlling asthma symptoms. The ICS and LABA combination is a mandatory part of asthma treatment guidelines.[4] ICS and LABA combinations are available in market for quite sometime now and these have increased the compliance and acceptance of asthma treatment. [5]

Studies have shown that Formoterol/Budesonide combination is effective than Salmeterol / Fluticasone as it provides maintenance and rescue therapy.[6] Formoterol /Budesonide is also cost effective than Salmeterol/Fluticasone combination.[7]

It has been observed in current clinical practice in our country that use of Salmeterol/fluticasone propionate combination is more popular than Formoterol/budesonide combination. This study will help to set a new direction to this trend and promote use of a more effective combination for control and prevention of asthma symptoms.

OBJECTIVE

We have compared the efficacy of Salmeterol / Fluticasone and Formoterol /Budesonide for control of exacerbation of asthma in adults with persistent asthma.

MATERIALS & METHODS

It was a Randomized-Controlled-Trial(RCT) conducted at Department of Medicine, Allied Hospital, Faisalabad from June 2014 to December 2014. Approval from hospital ethical review committee was taken. Patients fulfilling the inclusion criteria were enrolled in the study. Total 172 patients were enrolled in study. WHO sample size calculator for two proportions (2-sided) was used and sample size was calculated using following values: P1 = 57%[8], P2 = 77%[8], Power of study = 80%, Level of Significance = 5%, Sample size = 86 in each group (total 172). Non-probability consecutive sampling technique was used. Both male and female patients between 18 and 70 years of ages having persistent bronchial asthma while Pregnant or lactating mothers, patients with upper or lower respiratory tract infections, acute asthma exacerbations within 4 weeks of first visit, Oral corticosteroids within 4 weeks or depot steroids within 12 weeks of first visit and Smoking history of more than 10 pack years were excluded from study. Patients were randomly divided into two groups (Group A & Group B) using computer generated random number table. Salmeterol/ Fluticasone combination was given to group A with a dose of 50/250μg, 2 actuations with ABEL SPACER DEVICE twice a day for a period of 24 weeks. Formoterol/Budesonide combination was given to group B with a dose of 400/6μg with Rotahaler twice a day. Follow up was done by patient's outdoor visits at 6th,12th,18h and 24th week.

Bronchial asthma was defined as Patients who were having recurrent shortness of breath and more than 20% increase in peak expiratory flow rate(PEFR) after 2 actuations (90microgram/ actuation) of salbutamol. Persistent Bronchial Asthma was defined as Patients who have been diagnosed bronchial asthma for more than 6 months and having symptoms for more than 2 times/week or nocturnal awakenings 4 times/month or need of rescue therapy for more than 2 times/week despite of high dose inhaled corticosteroid treatment (Budesonide > 1200microgram or equivalent).

Asthma Exacerbation Scale was used as under: Mild- >3 rescue therapy of reliving medication per day as compared to baseline for 2 consecutive days, or Night time awakening because of asthma symptoms over 2 consecutive nights.

Moderate - Asthma symptoms worsening requiring steroids (Prednison 40 – 60 mg for 7 to 10 days as assessed by the investigating physician.

Severe- Asthma symptoms worsening requiring hospital admission.

Rate of exacerbations was defined as number of all asthma exacerbations experienced by the patient was expressed as a rate over the 24-week treatment period. Efficacy was measured in terms of decrease in number of exacerbations per 24 weeks period (less than 2 exacerbation/24weeks period).

Information was collected by trainee researcher and comprised of age, sex, address, and contact number and number of exacerbations in 24 weeks study period. All the collected information was transferred to SPSS version 16 and analyzed accordingly. Mean and standard deviation was calculated for all quantitative variables like age and number of exacerbations. Frequency and percentage were calculated for all qualitative variables like gender. Chi square test was applied to compare efficacy of both drugs at 24 weeks period. P value of <0.05 was considered as significant.

RESULTS

180 patients were enrolled in the study. 79 (44%) were males and 101 (56%) were females Figure 1. Mean age of study population was 45.25+13.382 years. Table I. Patients in Group B experienced lesser number of exacerbations than patients in Group B as described in Table II. Group B

showed better response to treatment than Group A using chi square test. (P-Value 0.001) Table III. Stratification was done for with respect to efficacy Gender and Age as described in table IV & V respectively.

DISCUSSION

Asthma, a common respiratory condition that results from inflammation in both large and small airways, and directly impacts an estimated 24.6 million people in the United States.[9]

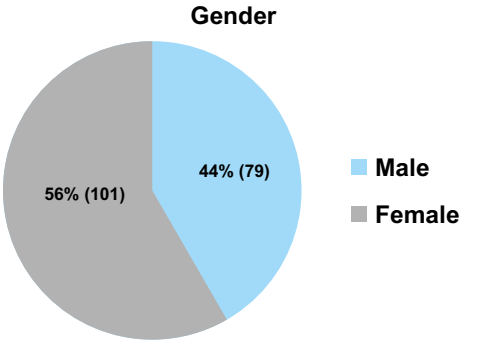


Figure-1. Gender Distribution of Study Population

Age	Whole Study Population	Group A	Group B
Mean	45.25	46.03	44.47
Std. Deviation	13.382	12.829	13.941
Minimum	19		
Maximum	69		

Table-I. Age Demographics of Study Population

		No of Exacerbation in 24 weeks treatment period					Total
		0	1	2	3	4	
Groups	Group A	20	25	20	15	10	90
	Group B	41	25	10	7	7	90
Total		61	50	30	22	17	180

Table-II. Comparison of No. of Exacerbations in Group A & Group B

		Efficacy		Total
		Yes	No	
Groups	Group A	45	45	90
	Group B	66	24	90
Total		111	69	180
Chi Square Value		10.313		
P Value		0.001		

Table-III. Comparison of Efficacy in Group A and B using Chi Square Test

Gender			Efficacy		Total	
			yes	no		
Male	Groups	Group A	21	21	42	.002
		Group B	31	6	37	
	Total		52	27	79	
Female	Groups	Group A	24	24	48	.111
		Group B	35	18	53	
	Total		59	42	101	
Total	Groups	Group A	45	45	90	.002
		Group B	66	24	90	
	Total		111	69	180	

Table-IV. Stratification Of Efficacy With Respect To Gender In Both Groups

Age Stratification			Efficacy		Total	P-Value
			yes	no		
18-40	Groups	Group A	19	9	28	.603
		Group B	21	14	35	
	Total		40	23	63	
41-60	Groups	Group A	24	31	55	0.0001
		Group B	39	8	47	
	Total		63	39	102	
61 or more	Groups	Group A	2	5	7	0.132
		Group B	6	2	8	
	Total		8	7	15	
Total	Groups	Group A	45	45	90	0.002
		Group B	66	24	90	
	Total		111	69	180	

Table-V. Stratification of Efficacy With Respect To Age In Both Groups

Total health care costs directly attributable to asthma care in the United States were estimated at $37.2 billion (in 2007).[10] Medical Expenditure Panel Survey data for 2002 to 2007 showed that asthma imposed an incremental society-wide cost of $56 billion (adjusted to 2009 US$).[11] Treatment goals include achieving adequate control and reducing the risk of exacerbations and serious impairment. Long-term controller medications, such as inhaled corticosteroids (ICS), are recommended by the current Expert Panel Report-3 for patients with persistent asthma. For patients ages ≥12 years, the guidelines for the diagnosis and management of asthma indicate that the addition of a long-acting β_2-adrenergic agonist (LABA) be given equal weight to the option of increasing the ICS alone for patients inadequately controlled on ICS alone and for those patients with high levels of impairment and elevated risks of asthma exacerbation.[7]Currently, 3 ICS-LABA combination therapies are approved for use: budesonide–formoterol fumarate dihydrate (BFC), fluticasone propionate–salmeterol combinations (FSC) therapy.

Clinical trials that assess BFC and FSC showed mixed results.[12]

Lasserson et al[11] reviewed 5 randomized studies (5537 adults) in the Cochrane Airways Group register that compared fixed-dose fluticasone / salmeterol)FSC) and budesonide /formeterol(BFC) combination of adults and children diagnosed with asthma. Treatment durations were a minimum of 12 weeks; most of the studies assessed treatment for a 6-month period. Study populations had prior treatment with inhaled steroids (fluticasone/salmeterol or budesonide/formoterol) and had moderate or mild airway obstruction.

One study conducted by Blais L et al in Canada, concluded that subjects started on ICS and LABA treatment with budesonide /formoterol had fare better than those started on treatment with fluticasone /salmeterol. He demonstrated that patients who received BFC were significantly less likely to require asthma related emergency room visits or hospitalizations and oral corticosteroid fills, and required less short-acting β_2-adrenergic-agonists (SABA) per week. These results support the findings in my study which also concludes that budesonide/formoterol is better than fluticasone/salmeterol in controlling asthma symptoms.[13]

One study by Shoening SK et al in Germany demonstrated that patients with chronic asthma who initiated BFC therapy had a greater probability of treatment success with fewer severe asthma exacerbations and fewer OCS prescription fills. Because of better access, patients demonstrated a better treatment response with budesonide/formoterol. These are also in support of findings in my study which demonstrates a better response in asthma.[14]

One study by Halpin GL et al, demonstrated that budesonide /formoterol is associated with

fewer cases of lobar pneumonia than salmeterol /fluticasone. These also support my study which rates budesonide/formoterol better than fluticasone/salmeterol.[15]

It was a small study with no randomization and double blinding. Large randomized controlled trials are needed to further validate these results.

CONCLUSIONS AND RECOMMENDATIONS

It has been concluded that budesonide/formoterol is more effective in controlling asthma symptoms than fluticasone/salmeterol. This can be attributed to easy access to budesonide/formoterol and its ease of use.

Hence, it is recommended that budesonide/formoterol should be first line drug in treatment of asthma.

REFERENCES

1. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA et al. **Global asthma prevalence in adults: findings from the cross-sectional world health survey.** BMC Public Health.2012;12:204.

2. Mahboub BH, Al-Hammadi S, Rafique M, Sulaiman N, Pawankar R, Al-Redha AI, Mehta AC. **Population prevalence of asthma and its determinants based on European Community Respiratory Health Survey in the United Arab Emirates.** *BMC Pulmonary Medicine.* 2012:**12**:4.

3. Hasnain SM, Khan M, Saleem A, Waqar MA. **Prevalence of asthma and allergic rhinitis among school children of Karachi, Pakistan, 2007.** J Asthma. 2009;46:86-90.

4. Ozkaya S, Dirican A, Tuna T. **The effects of long-acting β2-agonists plus inhaled corticosteroids for early reversibility in patients with airway obstruction.** J Thorac Dis. 2013;5:461-5.

5. Hirst C, Calingaert B, Stanford R, Castellsague J. **Use of long-acting beta-agonists and inhaled steroids in asthma: meta-analysis of observational studies.** J Asthma. 2010;47:439-46.

6. Kew KM, Karner C, Mindus SM, Ferrara G. **Combination formoterol and budesonide as maintenance and reliever therapy versus combination inhaler maintenance for chronic asthma in adults and children.** Cochrane Database Syst Rev. 2013 Dec 16;12:CD009019.

7. Paggiaro P, Patel S, Nicolini G, Pradelli L, Zaniolo O, Papi A. **Stepping down from high dose fluticasone/salmeterol to extrafine BDP/F in asthma is cost-effective.** Respir Med. 2013;107:1531-7.

8. Frew AJ, Holgate ST. **Respiratory disease.** In: Kumar P, Clarke M, editors. Clinical Medicine. 7 th ed. Spain: Saunders Elsevier 2009.Limited; 2009.

9. Akinbami LJ, Moorman JE, Liu X. **Asthma prevalence, health care use, and mortality: United States, 2005-2009.** Natl Health Stat Report. 2011:1–14.

10. Kamble S, Bharmal M. **Incremental direct expenditure of treating asthma in the United States.** J Asthma. 2009;73–80.

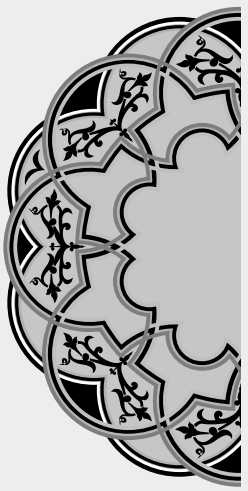
11. Barnett SB, Nurmagambetov TA. **Costs of asthma in the United States: 2002-2007.** J Allergy Clin Immunol. 2011;145–152.

12. Lasserson TJ, Ferrara G, Casali L. **Combination fluticasone and salmeterol versus fixed dose combination budesonide and formoterol for chronic asthma in adults and children.** Cochrane Database Syst Rev. 2011;3:p. CD004106.

13. Blais L, Beauchesne MF. **Acute care among asthma patients using budesonide/formoterol or fluticasone propionate/salmeterol.** Respir Med. 2009;103: 237–243.

14. Schoening SK. **Issues and challenges for managed care in the treatment of asthma and chronic obstructive pulmonary disease.** Am J Manag Care. 2004;10: S158–S163.

15. Halpin DM, Gray J, Edwards SJ, Morais J, Singh D. **Budesonide/formoterol vs. salmeterol/fluticasone in COPD: a systematic review and adjusted indirect comparison of pneumonia in randomised controlled trials.** Int J Clin Pract. 2011;65:764-74.



“Don't think outside the box.
Think like there is no box.”

Unknown

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Muhammad Abdullah	Article Writing	
2	Zaheer Ahmed	Statistical Analysis, Proof Read	
3	Hassan Fareed	Final Proof	