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IMPORTANCE AND EFFICACY OF LONG ACTING B2 AGONIST SALMETEROL, IN THE TREATMENT OF MILD TO MODERATE ASTHMA

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Abstract:
Aim: *To evaluate the role of salmeterol in adjuvant therapy with inhaled corticosteroids in patients with mild to moderate asthma.*
Study design: *A Randomized clinical trial*
Place and duration of studies: *The study was conducted at the Medicine Unit-II of Sir Gang ram Hospital Lahore for one-year duration from August 2019 to August 2020.*
Methodology: *Fifty patients with mild to moderate asthma aged 15-65 years were divided into two groups. Patients in the study group received a combination of salmeterol 50 µg and fluticasone propionate 250 µg twice daily, patients in the control group received beclomethasone dipropionate 500 µg twice daily. The endpoints were reduction in Symptom Score and improvement in maximum expiratory flow (PEFR) checked every two weeks. The paired student test was used to analyze the data.*
Results: *In patients in the study group, the mean total symptom score decreased significantly from 11.16 from baseline to 0.41 (p <0.001) at the end of the study, and the mean PEFR increased significantly from 189.4 L / min ± 0. 34 to 354.58 l / min, 0.15; P-value <0.001. While in the control group, the reduction in the mean total symptom score and the increase in mean PEFR was negligible, i.e. Total symptom score 11.04 from baseline to 5.29 and mean PEFR reduced from 182.60 L / min ± 17, 05 to 231.73L / min ± 13.84.*
Conclusion: *Salmeterol plays a significant role in the treatment of mild to moderate patients with asthma.*
Key words: *beclomethasone dipropionate, fluticasone, inhaled corticosteroids, peak expiratory flow, salmeterol, symptom score.*

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INTRODUCTION:

Almost 300 million people worldwide suffer from asthma and it is therefore a global health problem. In addition to geographical differences, there are differences in outcomes such as hospitalizations by gender and age, with the highest rates among young boys and adult women. Asthma is a chronic respiratory disease associated with inflammation of the airways, over-reactivity and mucus overproduction. Clinical diagnosis of asthma is based on a history of recurrent breathlessness, wheezing, chest tightness, with or without coughing, usually in the early morning or night. Inhaled β2-agonists are routinely used as bronchodilators to relieve asthma symptoms and play a key role in the treatment of asthma. The frequent use of short-acting β2 agonists alleviates symptoms in patients with asthma who are prescribed "as needed", but many patients use them more frequently or routinely. Currently, long-acting inhaled β2-agonists are available that provide sustained bronchodilation and are used as an adjuvant to inhaled corticosteroids in the treatment of asthma. Twice daily administration of salmeterol, a long-acting bronchodilator, has been observed to be better in achieving asthma control in terms of lung symptoms and lung function than albuterol monotherapy four times daily. This effect may be due to the fact that this treatment regimen inhibits airway inflammation and therefore improves asthma control by reducing asthma symptoms and improving lung function. The purpose of this clinical trial was to evaluate the effect of salmeterol as an add-on therapy to inhaled corticosteroids in patients with mild to moderate asthma.

MATERIALS AND METHODS:

This randomized, open-label, parallel group study was conducted at the Medicine Unit-II of Sir Gang ram Hospital Lahore for one-year duration from August 2019 to August 2020. A total of 60 male and female patients with mild to moderate asthma were registered in the study. Patients 15 to 70 years of age were receiving ICS therapy for asthma. Patients who have received systemic steroids or have been on systemic steroids in the last 6 months; you have had respiratory infections and have given antibiotics in the last 4 weeks; or suffering from diabetes, heart disease, high blood pressure, liver and kidney diseases. The study lasted 12 weeks and was preceded by a 2-week lead-in period. Patients were assessed for eligibility and randomization based on specific criteria, i.e. male or female patients diagnosed with mild to moderate persistent asthma who were already taking ICS. During the treatment period, patients were randomized to one treatment group to receive the Salmeterol 25 µg / Fluticasone 125 µg inhaler (Salmicort), two puffs twice daily; or Control Group, giving Beclomethasone Dipropionate inhaler, 250 µg, two puffs of B.D. for 12 weeks with a biweekly check-up. An asthma diary (Symptom Rating Score) was provided to each patient at baseline, and relevant information was recorded at the two-week visits. The diary included questions about daytime and nighttime wake symptoms, frequency of β2-agonist use, asthma exacerbations, number of days without asthma, and use of other measures when asthma worsened. The peak expiratory flow rate (PEFR) was measured with a Peak flow meter. The tolerability and safety of Salmeterol was checked by monitoring adverse events (asthma exacerbations), heart rate, and blood pressure at each clinic visit during the study. All readings were taken as mean ± SEM. Efficacy was measured by the mean change in symptom scores and PEFR every two weeks during the study from baseline to the end of the study. The student pair test was used to analyze the data.

RESULTS:

A total of 60 patients enrolled in the study, 50 were randomized to treatment groups, 25 per group. Five patients withdrew from the study during the treatment period. One patient withdrew from the study group Salmeterol and two patients from the ICS control group due to non-adherence. Demographics and baseline PEFR are shown in Table 1.

Table I: Demographic and baseline characteristics of patients

Groups	**Total Patients**		**Age (Mean) Range (15-65)**	**Gender**		**Type of Asthma**		**PEFR L/min**(±SEM)
	Remained	**Left**		**Male**	**Female**	**Mild**	**Moderate**	
Study	24 (96%)	1(4%)	34	6(25%)	18(75%)	13(54.16%)	11(45.83%)	189.4(±16.4)
Control	23 (92%)	2(8%)	35	6(26%)	17(73.91%)	12 (52.1%)	11 (47.8%)	189.8(±17.0)

Patients in both groups were matched for age, gender, and the type of asthma they had. The ratio of men to women was similar to that in the international studies, 25:75.

Symptom Rating Scale: There was a significant reduction in the patient-rated mean total symptom score of wheezing, chest tightness, and dyspnea in the study group, compared to the control group after each two-week treatment. In the study group, the mean total symptom score decreased significantly from the baseline value of 11.16 to 0.41 ($p < 0.001$) on day 90. At the end of the study, rescue medication use was reduced from daily to once a week. Symptomatic days increased from a mean of 2 to 12.16 ($p < 0.01$) and the mean of a symptom-free night increased from 4 to 13 ($p < 0.002$) in these patients at the end of the study. Compared to the control group, the mean overall symptom score reduction was not significant, i.e. from a baseline value of 11.04 to 5.29 at day 90. By the end of the study, the daily use of rescue medication had decreased to 4-5 weeks. The increase in the number of asymptomatic days ranged from a mean of 2.2 to 5 (p value not significant) and the increase in the mean number of asymptomatic nights was from 3.78 to 6 (p value not significant) at the end of the study (Table II).

Table II: Reduction in Individual Symptom Rating Score among Both Groups from Day 0-90

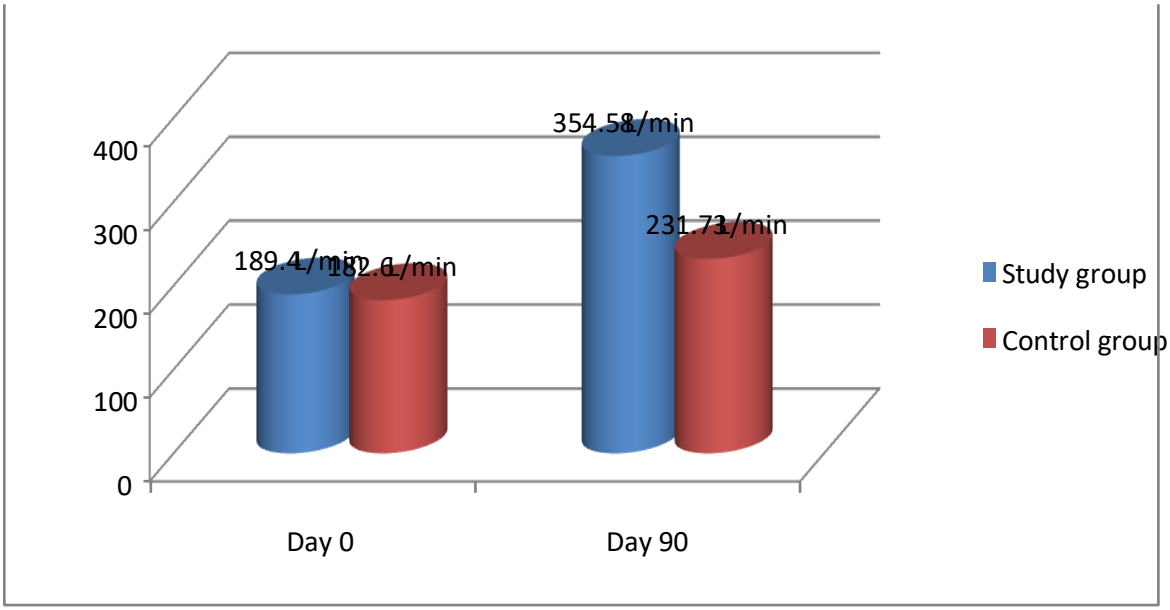
Groups	Symptom Rating Score	Day 0	Day 90	P-value
Study Group	Day time symptoms. Mean (SEM)	6.6(±0.21)	0.41 (±0.15)	<0.01
	Night time symptoms. Mean (SEM)	4.4 (±0.15)	0.5 (±0.12)	<0.001
	Use of rescue medicine.	Daily	0nce/ week	
	No. of symptom-free days/fortnight.	2 (±0.14)	12.16(±0.15)	<0.01
	No. Of symptom-free nights/fortnight	4 (±0.12)	13 (±0.18)	<0.002
Control Group	Day time symptoms. Mean (SEM)	7.34(±0.16)	5(±0.2)	N.S
	Night time symptoms. Mean (SEM)	4.65(±0.14)	3.26(±0.12)	N.S
	Use of rescue medicine.	Daily	4-5/week	
	No. of symptom-free days/fortnight.	2.2 (±0.15)	5 (±0.14)	N.S
	No. Of symptom-free nights/fortnight	3.78(±0.12)	6 (±0.16)	N.S

Peak Expiratory Flow: Salmeterol as add-on therapy significantly improved PEFR after each two-week treatment, while in ICS patients the improvement in PEFR was not significant. By week 12, in the study group (salmeterol plus ICS), the improvement in PEFR was 46.58% from baseline, while in the control group (ICS), the PEFR improved to just 21.2% from baseline (Table III, Fig. JA).

Table III: Improvement in peak expiratory flow rate in both groups from day 0-90

Groups	Day 0	Day 90	P-value
Study Group	189.4 L/min (±16.12)	354.58 L/min (±7.61)	<0.001 HS
Control Group	182.60 L/min (±17.05)	231.73 L/min (±13.84)	N.S

Fig. I: Improvement in Peak Expiratory Flow Rate in both Groups from Day 0-90



DISCUSSION:

Patients with symptomatic asthma who are already treated with corticosteroids require additional treatment. Inhaled corticosteroids and long-acting β2 agonists play a complementary role in the treatment of asthma. International guidelines suggest that long-acting beta 2-agonists should be added to inhaled corticosteroids for mild to moderate asthma. This study shows that adding salmeterol provided more benefits than ICS alone, as evidenced by improvements in symptom score and PEFR. These results are in line with the results of the Cochrane review, with significant improvements in lung function, symptom control and quality of life. The decline in symptom scores in our study corresponds to a study by Green et al. In 2006, pointing to a complex relationship between airway responsiveness and the clinical presentation of asthma. Patients who received salmeterol as an add-on show an improvement in all patient-assessed symptom scores (P <0.001), a reduction in the use of rescue albuterol inhaler (P <0.001), and a significant increase in symptom-free days (P <0.001) <0.001) 16. Similar results for symptom-free days and nights are seen in another study by Jeffery et al. A study by Bjermer et al. And Wilson et al. Produced similar results to our study on improving peak expiratory flow rate. The meta-analysis summarized the results of a number of randomized clinical trials, including symptomatic asthma patients taking inhaled steroids who were given salmeterol as an add-on to or an increased dose of inhaled corticosteroids. A marked improvement in lung function was seen in the salmeterol group, with a 28 L / min increase in morning peak expiratory flow after six months of using salmeterol with inhaled steroid therapy than after increasing the dose of inhaled steroid. The comparison of salmeterol and the combination of ICS with ICS alone in this study is supported by studies by Bergmann et al. And Zetterstrum et al, in which it is clear that combination treatment with salmeterol fluticasone (SFC) significantly increased PEFR and symptoms of control rather than doubling the dose fluticasone propionate (FP). At the end of week 12, the morning PEFR was increased by 52 L / min from baseline in patients receiving SFC and by 36 L / min in patients with FP. Studies by Murray et al., Chan et al. And Condemi et al. Show significant improvements in both symptom scores, PEFR, and lung function when comparing salmeterol and ICS combination therapy with double the dose of ICS alone.

CONCLUSION:

The use of salmeterol (LABA) as an add-on to inhaled corticosteroid was more effective in controlling asthma symptoms and improving lung function than using ICS alone.

REFERENCES:

1. Cheng, Shih-Lung, Ming-Lin Ho, Yun-Fa Lai, Hao-Chien Wang, Jeng-Yuan Hsu, Shih-Feng Liu, Ming-Shyang Huang et al. "Budesonide/Formoterol Anti-Inflammatory Reliever and Maintenance or Fluticasone Propionate/Salmeterol Plus As-Needed, Short-Acting β2 Agonist: Real-World Effectiveness in pAtients without Optimally Controlled asThma (REACT) Study." *Drug Design, Development and Therapy* 14 (2020): 5441.
2. Adams, Bryan S., and Hoang Nguyen. "Salmeterol." In *StatPearls [Internet]*. StatPearls Publishing, 2020.
3. Vogelberg, Christian, Stanley Goldstein, LeRoy Graham, Alan Kaplan, Alberto de la Hoz, and Eckard Hamelmann. "A comparison of tiotropium, long-acting β 2-agonists and leukotriene receptor antagonists on lung function and exacerbations in paediatric patients with asthma." *Respiratory Research* 21, no. 1 (2020): 19.
4. Papi, A., M. Humbert, K. Kostikas, C. Domingo, J. F. Maspero, M. Hosoe, A-M. Tanase, A. Pethe, X. Shu, and P. D'Andrea. "Medium-Dose Indacaterol/Glycopyrronium/Mometasone Furoate Fixed-Dose Combination Improves Lung Function Compared with High-Dose Indacaterol/Mometasone Furoate and Salmeterol/Fluticasone and Reduces Exacerbation Rates Versus High-Dose Salmeterol/Fluticasone in Moderate-to-Severe Asthma: The IRIDIUM Study." In *B31. ASTHMA CLINICAL TRIALS*, pp. A3008-A3008. American Thoracic Society, 2020.
5. Kerstjens, Huib AM, Jorge Maspero, Kenneth R. Chapman, Richard N. van Zyl-Smit, Motoi Hosoe, Ana-Maria Tanase, Catherine Lavecchia et al. "Once-daily, single-inhaler mometasone–indacaterol–glycopyrronium versus mometasone–indacaterol or twice-daily fluticasone–salmeterol in patients with inadequately controlled asthma (IRIDIUM): a randomised, double-blind, controlled phase 3 study." *The Lancet Respiratory Medicine* 8, no. 10 (2020): 1000-1012.
6. Gessner, Christian, Oliver Kornmann, Jorge Maspero, Richard van Zyl-Smit, Matthias Krüll, Anna Salina, Pritam Gupta et al. "Fixed-dose combination of indacaterol/glycopyrronium/mometasone furoate once-daily versus salmeterol/fluticasone twice-

daily plus tiotropium once-daily in patients with uncontrolled asthma: A randomised, Phase IIIb, non-inferiority study (ARGON)." *Respiratory Medicine* (2020): 106021.

7. van Zyl-Smit, Richard N., Matthias Krüll, Christian Gessner, Yasuhiro Gon, Oliver Noga, Alexia Richard, Amy de Los Reyes et al. "Once-daily mometasone plus indacaterol versus mometasone or twice-daily fluticasone plus salmeterol in patients with inadequately controlled asthma (PALLADIUM): a randomised, double-blind, triple-dummy, controlled phase 3 study." *The Lancet Respiratory Medicine* 8, no. 10 (2020): 987-999.
8. Kaplan, Alan, J. Mark FitzGerald, Roland Buhl, Christian Vogelberg, and Eckard Hamelmann. "Comparing LAMA with LABA and LTRA as add-on therapies in primary care asthma management." *NPJ Primary Care Respiratory Medicine* 30, no. 1 (2020): 1-11.
9. Virchow, Johann Christian, Piotr Kuna, Pierluigi Paggiaro, Alberto Papi, Dave Singh, Sandrine Corre, Florence Zuccaro et al. "Single inhaler extrafine triple therapy in uncontrolled asthma (TRIMARAN and TRIGGER): two double-blind, parallel-group, randomised, controlled phase 3 trials." *The Lancet* 394, no. 10210 (2019): 1737-1749.
10. Luz, Maria Inês, Rita Aguiar, and Mário Morais-Almeida. "The reality of LAMAs for adult asthmatic patients." *Expert Review of Respiratory Medicine* 14, no. 11 (2020): 1087-1094.
11. Kupczyk, Maciej, Paweł Majak, Piotr Kuna, Beata Asankowicz-Bargiel, Eliza Barańska, Rafał Dobek, Sławomir Garbicz et al. "A new formulation of fluticasone propionate/salmeterol in a metered-dose inhaler (MDI HFA) allows for the reduction of a daily dose of corticosteroid and provides optimal asthma control-A randomized, multi-center, non-inferiority, phase IV clinical study." *Respiratory Medicine* (2020): 106274.
12. Beauchesne, Marie-France, and Catherine Lemiere. "Global Initiative for Asthma report: How will new recommendations affect practice in Canada?." *CMAJ* 192, no. 17 (2020): E456-E458.
13. O'Byrne, Paul M., Helen K. Reddel, and Richard Beasley. "The Management of Mild Asthma." *European Respiratory Journal* (2020).
14. Tashkin, Donald P. "Formoterol for the Treatment of Chronic Obstructive Pulmonary Disease." *International Journal of Chronic Obstructive Pulmonary Disease* 15 (2020): 3105.
15. Matera, Maria Gabriella, Carmela Belardo, Michele Rinaldi, Barbara Rinaldi, and Mario Cazzola. "New perspectives on the role of muscarinic antagonists in asthma therapy." *Expert Review of Respiratory Medicine* (2020): 1-8.