Combined inhalers salbutamol and steroid versus isolated its uses in adults' asthmatic patients

Abstract:

Inhaled long acting B2-agonist combined with inhaled steroid being longed used in chronic persistent bronchial asthma as a therapy to reduce the needs for admission to hospital and to improve quality of life instead of isolated single uses.

Patients and Methods: Two hundred Seven patients with chronic persistent bronchial asthma on variety of inhalers, enrolled randomly in this study, One hundred Twenty (58.0%) were female and Eighty Seven (42.0%) were male, their ages range from sixteen to seventy five with mean ages (45.59±14.67) year's. type of inhalers used, dose, control with a question about admission to hospital, adherence to inhalers ,confidents and recording the parameter of pulmonary function test FEV1, FVC and PEFR while patients on own inhalers type used.

Results:

In this study there are statistically significant different between, single and combined inhalers in chronic persistent asthma (p value0.005)in FEV1LFVC but not between the types of combined inhalers (p.value 0.12), age in both types of comparisons indicate no statistically significant effects (p value 0.85,0.47) respectively.

Conclusions: combined inhalers therapy for patients with persistent asthma superior for either alone, preferred and confident by patients; ages of patients neither significantly alter the response nor the patients desire.

Key words: chronic persistent asthma, inhalers therapy, patient's confidents



Introduction:

Owing to the known fact, that bronchial asthma and in particular chronic persistent one is a common health problem and result in persistent threatening to patients in respect to their life, social and economic state of them and ultimately, their family and community.⁽¹⁾

By no mean the incidence of bronchial asthma was increasing and by the years 2025,400 million sufferers is expected word wide. (1, 2)The climates changes and the dietary habit, humidity, noxious substances and the indoor and outdoor risk factors, perhaps change the natural history of bronchial asthma in away or other regarding incidence, prevalence and of course the prognosis through morbidity and mortality effects.(3)

the remedy of bronchial asthma in revolutionized in parallel to the complexity of the incidence, prevalence and the outcomes of the problem, so a great deals regarding the treatment of bronchial asthma and a lot of modifications of strategy of treatments was adapted and guidelines annually modified and revise the managements approach the new single therapy. (3,4)

double combined and even triple therapy was a real revolutionized the treatments, several studies deals with combinations therapy in particular the inhalers types and drugs type and the developments of long acting medications, direct bronchodilators or indirect one in a form of verities of steroid medications used either alone or in combinations.

The patients role is encourage in choice the type of inhaler's, rout of its preferable use, resemble an anew methods to enhances the communication of patients toward treatments types and rout, this further increase the compliance of patients, quality of life and the prognosis.^(5,6,7)

Combined bronchodilators, long acting's salbutamol (LADA) and long acting steroids in varying doses; low or high doses, when recommended for patients with chronic persistence asthma, reduce the symptoms, increase quality of life, reduce admission to hospital through decreasing a chance of developing an acute asthmatic attack, reduce exacerbations and ultimately reduces the absence from jobs as well the unwanted side effects of short acting bronchodilators and short acting high potency steroids therap. (8,9,10)

The tendency to adapt this type of therapy by primary healthcare center and general practioners doctor by no means encourage therapy adherence and delate the unreal wrong believes that adapted by patients and their relatives about inhalers therapy. (11,12)

Still in the strategy of chronic asthma managements on community or in individual levels no clear-cuts ideations regarding the combinations long-acting therapy and even at least no data available on national levels especially in respect to short and long term prognosis and cost effectiveness of this approach. If a patient remains poorly controlled, despite regular use of ICS, a thorough review should be undertaken of adherence, inhaler technique and ongoing exposure to modifiable aggravating factors. (13,14,15) A further increase in the dose of ICS may benefit some patients but, in general, add-on therapy should be considered in adults taking 800 μ g/day BDP (or equivalent). (16,17)

remodeling phenomenon, though to be the sequel of chronic asthma, the use of modifying approach of treatments plus the age factors; as reflected in difficulties in handling inhaler devices, may alter the optimum response. (18,19,20)

This study aimed to approve whether this type of inhalers therapy for patients with chronic asthma, reduce complaints, hospital need for admission, improve quality of life and whether, a high dose combination is superior to low dose in patients managements.

Material and methods:

A cross-section prospective descriptive study of 207 patients, 120 (58.0%) were female and 87(42.0%) were male, their ages range from 16 to 75 with mean ages (45.59±14.67) years, during the 2021-2022 after approving by scientific research committee in basrha college of medicine. All participants with chronic persistent asthmatic, patients in acute asthmatic attack or acute life threatening asthma was excluded from study, complain from shortness of breath, cough, night shortens of breath and cough, scatter wheeze reduce quality of life. enrolled in this descriptive study, demographic character of the studied sample were collected from each separately through an sheets distributed to participants, Involve data about, age, gender, duration of asthma, diagnosis, treatment types, inhaler use and types of it, after take an oral consent, sample then subdivided to two main groups, first is that one short acting inhalers and second, whom on long acting combined

inhalers, the second group further subdivided to two main groups: high dose combinations inhalers and low dose combination inhalers; High dose (salmeterol / fluticasone) 25/250, Low dose (salmeterol / fluticasone 25/125), pulmonary function test particularly, FEVI/FVC and PEFR are used to compare between the studied groups, the results of these objective parameters, their means and standard deviations , percentage of FEV1/FVC consider the cut point for the beneficial effects gained by inhaler type and dose. Data collected, feed to IMB statistic package for social sciences (SPSS), version 22, and variables according to design calculated by independent sample test , Levene's Test for equality of Variances and t. test for equality of means and 95%CI of differences were p value of less than 0.05considerd significant.

Results:

Table1: general characterstic of studied groups; demographic criteria and confidence of patients with the treatments; regarding inhalers types and doses types.

| | o, regaraning initiators ey pes i | arra acces cypec. | | |
|----------------|-----------------------------------|--------------------|-------------|---------|
| Variable | | | Total | P value |
| Age | 16 to 75years | 45.59±14.67years | | |
| Gender | 120(58.0%) female | 87(42.0%) male | 207 (100%) | |
| FEV1 | 3.15± | 0.79 | | |
| FVC | 2.65± | 0.67 | | |
| FEV1/FVC | 80.54± | 3.46 | | |
| PEF | 7.07± | 1.40 | | |
| Inhaler types | 85(41.1%) short | 122(48.9%) long | 207 (100%) | |
| Combined types | 64(52.5%)low dose | 58(47.5%)high dose | 122 (48.9%) | |

Confidence of patients regarding single or combined, high dose or low dose inhaler's

| Туре | Not confidence no & % | Confidence no&% | Total no& % | P value |
|--------------------------|-----------------------|------------------|-------------|---------|
| Confident with- Short | No: 51(24.6 %) | Yes: 34(16.4%) | 85(41.1%) | 0.001 |
| Confident with - Long | No: 34 (16.4%) | Yes: 88 (42.5 %) | 122(58.9%) | |
| | | | | |
| Confidence-High | N: 19(15.6%) | Yes: 39(23.00%) | 58 (47.5%) | |
| Confidence Low | N: 13 (10.7%) | Yes: 51 (41.8%) | 64(52.5%) | 0.17 |

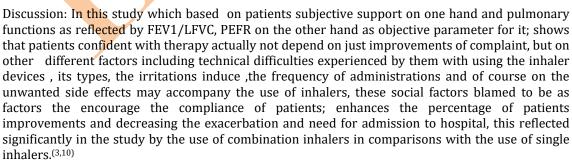
Table2: shows the confidence of patients with both types of inhaler; short acting and long acting, reflecting by the measurements of FEV1/FVC, PEFR and the age of patients as non-modifiable factor in both groups (single or combined inhalers.

| | | | | | | 95% Confidence Interval of the Difference | | Sig. |
|----------------|------|-----|-------|-----------|-------|---|--------|------|
| confidence Sir | ngle | | | Std. | Std. | | | |
| inhalers | | N | Mean | Deviation | Error | Lower | Upper | |
| | No | 85 | 78.14 | 2.94 | .319 | -4.85 - | 3.28 - | |
| FEV1/FVC | Yes | 122 | 82.21 | 2.75 | .249 | -4.86 - | 3.27 - | 0.05 |
| | | | | | | | | |
| | No | 85 | 7.01 | 1.25 | .136 | 498 - | .28 | |
| PEF | Yes | 122 | 7.12 | 1.50 | .136 | 48 - | .27 | 0.58 |

| Ī | | No | 85 | 45.82 | 13.55 | 1.47 | -3.71 - | 4.47 | |
|---|-----|-----|-----|-------|-------|------|---------|------|------|
| | Age | Yes | 122 | 45.44 | 15.45 | 1.39 | -3.62 - | 4.38 | 0.85 |

Table 3: shows the confident of patients with both; high dose and low dose combined inhalers by leavens test for equality of means reflected by FEV1/FVC, PEFR and age factors as non-modifiable factor, were no significant difference between both types.

| Variable | | | | | Sig. | 95% CI of the Difference | ġ |
|----------|---------------|-----------|---------------|------------|------|-----------------------------|---------|
| | | | Mean Std. | Std. Error | | | |
| | low/high/dose | No&% | Deviation | Mean | | Lower | Upper |
| FEV1/FVC | low dose | 64(52.5%) | 82.96± | .23720 | 0.12 | 16445- | 1.30248 |
| | | | 1.89 | | | | |
| | high dose | 58(47.5%) | 82.40± | .28800 | | 17015- | 1.30817 |
| | | | 2.19 | | | | |
| PEF | low dose | 64(52.5%) | 7.13± | .1548 | 0.32 | 2456- | .7427 |
| | | | 1.23 | | | | |
| | high dose | 58(47.5%) | 6.88± | .1989 | | 2510- | .7481 |
| | | | 1.51 | | | | |
| Age | low dose | 64(52.5%) | 45.32± | 1.88220 | 0.47 | -7.32916- | 3.39921 |
| | | | 15.05 | | | | |
| | high dose | 58(47.5%) | 47.29± | 1.94573 | 1 | -7.32528- | 3.39532 |
| | | _ | 14.8 1 | | | | |



In study conducted as outpatient in Bangladesh, reflecting the patient's role in selecting or leading physicians to select best inhalers types, this study showed parallel results. The improvements which reflected the objective, negative or positive reactions response of the inhalers, were adding, LABA components to ICS, showing significant improvement of the parameters of FEV1/FVC, but not PEFR in both types. (17)

Age, though matched, imply no effects in both type neither on pulmonary functions nor on the desire and confidents of the users, which not consistent with many different studies as older age group may have a difficulties in handling and inhaling properly. (21,22)

combined or single inhalers in this study both parameter; reflecting the improvement in lung function, when used in chronic persistent asthmatic patients using combined inhaled steroid and LABD, and less significantly in patients using single based therapy as steroid or LADA, this was consistent with multiple studies. (12)

Combinations steroids and LADA inhalers; on other hand was studied regarding its two main types, high dose and low dose type, subjectively and objectively, bearing the wish and choice of patient secondary to the objective improvement demonstrated by pulmonary function test, shows no significates different in both types, dis regarding patient's wishes as this may subjected to bias if we consider the patients idea about the exact dose of components of inhalers. But the pulmonary functions test which is more solid parameter to differentiate in between types, this may similar to a study in. ^(1, 8) even if not consistent with a studies regarded as foreign to it; in this area; this study, the peculiarity of environmental factors including wet weather, industrial, like vapors delivered from oil companies present in and surrounding this area affects the patients factors including the confide dance of inhalers.

In contrary to other studies; age factors, whether young age group or older; it appears in this study not affect the course of response to inhalers, in both single use inhales or combined inhaler uses. (3,21,22) though theoretically advancing age and longer duration of disease may lead to remodeling phenomena, in which there is decrease response to bronchodilators therapy, patients desire and confidences. (23,24,25) through questioners answered, may subjected to bias, which not gave an ideal response to differentiate between types, in this study, they are confident with combined than single drug inhalers and response with no differences between high dose and low dose combined one. (13) this is consistence with many met analysis study (Patel 2013, Papi 2013, Cates 2013, and Kew 2013). (3)

In conclusions; combined inhalers therapy for patients with chronic persistent asthma are superior to single drugs inhalers either as B-agonist drugs or steroids, this actually occurs for a variety of reasons including the improvements of quality of life, decrease the side effects, from the common simple side effects to more serious one, like deaths associated with LADA alone, as well the use of minimum doses inhalers in combined types rather than high doses to decrease side effects and the prices for economic reasons as the disease has chronic sequel.

References:

- 1. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald M, et al. Global strategy for asthma management and prevention: GINA executive summary; Eur Resp J. 2008; 31:143-78.
- 2. Global Initiative for Asthma (GINA).Global Burden of Asthma Report 2009.Available from: HTTP://www, gin asthma. org. Accessed December 2011.
- 3. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2016. Available from: www.ginasthma.org: report pp: 50-63
- **4.** Stefanie C. Nigro, Diana M. Sobieraj. (2022) Budesonide/Glycopyrrolate/Formoterol Fumarate Co-suspension Metered Dose Inhaler: A Triple Therapy for the Treatment of Chronic Obstructive Pulmonary Disease. Annals of Pharmacotherapy **56**:5, 582-591.
- 5. Kelly HW, Sternberg AL, Lescher R, et al; CAMP Research Group. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med.* 2012 Sep 6;367(10):904-912.
- 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. doi: 10.1002/14651858.CD009019.pub2.
- 7. Melani AS. Inhalation therapy training. apriority challenge for the physian Acta Biomed.2007;(78):233-245.
- 8. Nair SJ, Daigle KL, DeCuir P, Lapin CD, Schramm CM. The influence of pulmonary function testing on the management of asthma in children. *J Pediatr.* 2005 Dec;147(6):797-801.
- 9. SestiniP, CappielloV, AlianiM, MartucciP, SenaA, VaghiA, CanessaPA, et al. Prescription bias and factors associated with improper use of inhalers. JAerosal Med. 2006; (19):127-136.

- 10.Adams R J . Smith B J, Ruffin R E. Patient preference for autonomy in decision making in asthma management Thorax, (2001) 65: 126 132.
- 11. PapiA, HaughneryJ, Virchow JC, Roche N, palko nen S, priceD. Inhaler devices for asthma :A call for action in a neglected field, Eur RespirJ.2011;(37):982-5.
- 12. Christy H, Price D. Not all asthma inhalers are the same. Factors to consider when prescribing an inhaler. Primary Care Respiratory Journal. 2009; 18 (4):243-9.
- 13. Haughney J, Price D, Barnes NC, Virchow C, Roche N, Chrysin H. Choosing inhaler devices for people with asthma: Current knowledge and research needs. Respiratory Medicine.2010;(104):1237-4.
- 14. Haughney J, Price D, Kaplan A, Chrystyn H, Horne R, May N, et al. Achieving asthma control in practice: Understanding the reasons for poor control. Respiratory Medicine. 2008;102.
- 15.Takemura M,Kobayashi M, Kimura K, 15-Melani AS, ZanchettaD, BarbatoN, SestiniP, CintiC, CanessaPA, Aiolfi S, et al. Inhalation technique and variables associated with misuse of conventional metered dose inhaler and newer dry powder inhaler inexperienced adults. Ann Allergy Asthma Immunol, 2003;(93):439-446.
- 16. Davidsons principle and practice of medicine 22 : respiratory : pp 669-672.
- 17. Md. Abdur Rafi, Chowdhury Ibtida Tahmin , Symom Tashrik , Atia Sharmin Bonna , Ferdousy Jannat ,Sabrina Jahan Mily , Abhigan Babu Shrestha , etal. Adherence to inhalers and associated factors among adult asthma patients: an outpatient based study in a tertiary hospital of Rajshahi, Bangladesh: Asthma Research and Practice (2022) 8:1 https://doi.org/10.1186/s40733-022-00083-7
- 18. Bond K, Coyle D, O'Gorman K, Coyle K, Spooner C, Lemière C, Vandermeer B, Tjosvold L, Rowe BH. Long-Acting Beta2-Agonist and Inhaled Corticosteroid Combination Therapy for Adult Persistent Asthma: Systematic Review of Clinical Outcomes and Economic Evaluation. (Technology report no. 122). Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009.
- 19. Piersanti S, Vita C, Maria A, Paula M, Angelo S, Adriano V et al. Prescription Bias and Factors Associated with Improper Use of Inhalers. Journal of Aerosol Medicine 2006;(19):127-136.
- 20. MelaniAS, Bonuvia M, CilentiC, LodiM, MartucciP, Serra M, et al. Inhaler mishandling remain common in real life and is associated with reduced disease control. Respir Med.2011;(105):930-938
- 21. SestiniP, CappielloV, AlianiM, MartucciP, SenaA, VaghiA, CanessaPA, et al. Prescription bias and factors associated with improper use of inhalers. JAerosal Med. 2006; (19):127-136.
- 22. Ho SF, OMahony M, Steward JA Bray P, Burr ML. Inhaler technique in the older people in the community. Age And Aging. 200;33(2):185-8.
- 23.BashetIA ,Armour CL, Bosnic AnticevichSz, Reddel Hk. Evaluation of a novel educational strategy including inhaler based reminder labels, to improve asthma inhaler technique. Patient education and counseling 2008;(72):26-33.
- 24. Piersanti S, Vita C, Maria A, Paula M, Angelo S, Adriano V et al. Prescription Bias and Factors Associated with Improper Use of Inhalers. Journal of Aerosol Medicine 2006;(19):127-136.
- 25. John Haughney a, *, David Price , Neil C. Barnes , J. Christian Virchow , Nicolas Roche , Henry Chrystyn : Choosing inhaler devices for people with asthma: Current knowledge and outstanding research needs: a review: Respiratory Medicine (2010) 104, 1237e1245