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Comparative Study on the Efficacy of Symbicort vs. Brequal in Iraqi Asthmatic Patients

A thesis

submitted to the Al-Zahrawi University College and the Committee of Undergraduate studies of Al-Zahrawi College in Partial Fulfillment of the Requirements for the Degree of Bachelor of Science in Pharmacy

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Abstract

Background

Asthma regarded as chronic respiratory disorder that significantly affects the quality of life of millions of people globally. Between the most effective approaches for controlling asthma is the use of combination treatments including long-acting beta- agonists (LABA) and inhaled corticosteroids (ICS).

Objective

The key objective of this study is to contrast between efficacy of Symbicort and Brequal on decreasing asthma exacerbations, pneumonia development, visiting emergency unit (ED) and enhancing lung function.

Materials & Methods

Study Design: A randomized, double-blind, controlled trial.

Patients: 150 patients aged 35-75 years, with moderate to severe asthma.

Intervention:

*** Control group: 50 patients with asthma but without treatment.

*** Symbicort group: 50 patients with asthma receiving symbicort inhaler 160/4.5mcg/60 dose once daily for a period of 2 months.

*** Brequal group: 50 patients receive brequal inhaler 50/250mcg/60 dose once daily for a period of 2 months.

Results

Forced expiratory volume in second 1 (FEV1), number of asthma exacerbation, number of ED visits and pneumonia incidence were significantly higher in control group ($p < 0.05$), while symbicort and brequal showed significant ($p < 0.05$) higher FEV1 and lower levels of other factors. Study also showed that symbicort was better than brequal where it significantly increased FEV1 value and decreased the other factors ($p < 0.05$).

Conclusions

The findings from this study demonstrate that Symbicort is more effective than Brequal in reducing the number of asthma exacerbations and emergency department visits. Additionally, patients treated with Symbicort showed significant improvement in lung function, as measured by FEV1, over the two-month treatment period, but it may increase the risk of pneumonia in some patients. These results suggest that Symbicort may be a more favorable combination therapy for managing asthma in Iraqi patients, potentially leading to better clinical outcomes and improved quality of life.

1.Introduction and Literature Review

1.1Background

Asthma is considered as a chronic inflammatory compliant of the airways recognized by variable and frequent symptoms, airflow blockade, hyper-responsiveness of bronchi and underlying inflammation.

The complication of asthma is affected by many factors including genetic, environmental in addition to several triggers (1,2).

1.2 Signs and Symptoms

Asthma can be characterized by a wide range of signs and symptoms which are vary in occurrence and intensity among peoples.

Between the most common symptoms of asthma are coughing, which frequently become worse especially at night and in first morning hours. Wheezing also can occur which is a creaky sound when breathing out. In addition to that, dyspnea (difficulty breathing) is considered as a characteristic sign of asthma which often associated with physical activity or even at rest in case of severe conditions. Chest tightness (sensation of pressure in the chest) is also an additional asthmatic symptom (1).

Many factors lead to triggering of these symptoms like allergens (e.g. pollen, mold...), infection of respiratory system, exercise, cold air and emotional stress. The intensity of these symptoms can vary from minor, intermittent occurrences to severe, permanent symptoms that considerably affects daily actions and quality of life (3).

1.3 Causes

Asthma result from a complex interaction between genetic inclinations and environmental exposures. Family history with asthma and allergic disorders are more likely to progress the disease. Also, environmental elements also play a significant role in developing disease symptoms and exacerbations. Pollen, dust mites, mold and pet dander are an examples on these environmental conditions. Moreover, infections of respiratory system principally with viral infection, air pollution, physical activity, emotional stress and smoking all of them can aggravate symptoms of asthma as they result in shortness of breath (4). It is significant to know causes of asthma in order to provide effective management.

1.4 Pathophysiology

Chronic inflammation of the airways which is a characteristic of asthma may result in hyper reactivity and occasional airflow obstruction. Numerous immune cells are included in the processing of inflammation in asthma like T-lymphocyte, mast cells and eosinophils. However, these cells produce many inflammatory factors as cytokines and leukotrienes, which participate in bronchoconstriction, improved airway resistance and accumulation of fluids (edema) in airway walls. As a result, airways will be narrowed, resistance of airways increased and breathing become difficult. Frequent inflammation and bronchospasms episodes, with time, can result in structural changes in airways (airway remodeling). Airway remodeling characterized by stiffening of the airway walls, increased in the mass of smooth muscle in addition to fibrosis. These alterations may decrease the reversibility of airway blockade and lead to chronic asthma (1,2).

1.5 Diagnosis

Detailed medical history in addition to physical and specific diagnostic examinations should be applied in the diagnosis of asthma.

Medical history includes information about person's symptoms, frequency and severity of these symptoms and any probable factors that exacerbate them. On the other hand, physical examination concentrates on the respiratory system, such as attending for wheezing or any other unusual breath sounds.

An important diagnostic apparatus which is used in the measuring of lung functions in addition to diagnosis of asthma is the spirometry. Spirometry measure the forced expiratory volume in one second (FEV1) and forced vital capacity (FVC). A sign of substantial improvement in FEV1 after bronchodilator administration supports asthma diagnosis. Some allergy tests should be occurring in order to detect specific allergens which might be eliciting symptoms (5).

1.6 Prevention

Strategies for preventing asthma should focus on diminishing contact with triggers to decrease exacerbations risk. Firstly, for effective prevention, the patient should recognize and avoid any allergens and irritants like pollen, mold, tobacco smoke…etc. Another strategy include regular vaccination with

flu and pneumonia vaccines will effectively reduce respiratory infections and as a result asthma exacerbation. Also individuals with asthma should be adhere with their prescribed treatment and follow asthma action strategy with their healthcare providers. Plan should explain the regular management strategies and steps that should be taken throughout asthma attack. Furthermore, changes in lifestyle such as weight reduction, regular exercise and handling stress play an important role to overcome asthma attack (6,7).

1.7 Epidemiology

Asthma prevalence differs depending on geographic area, environment and socioeconomic status. Prevalence of asthma increased in several advanced countries, may be due to suburbanization and increment exposure to many pollutions and allergens. Between the most affected age group with asthma is the children. Also in adulthood women, incidence of asthma is highly common. Rates of asthma are increased also depending on socioeconomic status where become high in regions with lower socioeconomic state as this category is more exposed to environmental elicits in addition to poor healthcare services. (8).

1.8 Management

Management of asthma include two parts the first is the lifestyle modification and the second is the drug treatment.

1.8.1 Lifestyle Modification

Lifestyle modification should involve avoidance of asthma stimulants which include allergens and specific irritants. Additionally, regular practice, weight reduction and stress controlling play very important role in healthy lifestyle. Moreover, patient education about asthma management, identifying initial exacerbations signs and obeying to medicinal treatment participate in avoiding asthma attack (9).

1.8.2 Drug treatment

- Short-acting beta agonists (SABAs): this class of drugs is used for quick relief of asthma symptoms.
- Long- acting beta agonists (LABAs): can be used with inhaled corticosteroids to control long term asthma.
- Inhaled corticosteroids (ICS): ICS play key role in decreasing inflammation and asthma symptoms.

- Leukotriene antagonists (LTA): LTA are used to decrease inflammation and bronchospasm.
- Biologics: used in case of acute asthma where they target specific paths (e.g. omalizumab) (9).

1.9 Hypothesis

Symbicort is hypothesized to be more effective than Brequal in reducing the number of asthma exacerbations, emergency department visits, and pneumonia incidence, as well as improving lung function (FEV1) in Iraqi asthmatic patients.

1.10 Aims of the Study

The aims of this study summarized in:

The key objective of this study is to contrast between efficacy of Symbicort and Brequal on decreasing asthma exacerbations, pneumonia development, visiting emergency unit (ED) and enhancing lung function.

2.Materials and Methods

2.1 Materials

The following table (2-1) comprise the instruments and drugs that are included in this study.

Table (2-1): Instruments and Drugs with their suppliers

Instruments and Drugs	Suppliers
Symbicort® Inhaler	AstraZeneca Company, Switzerland
Brequal® Inhaler	ABDI IBRAHIM Company, Turkey
Spirometry	Elite International Medical & Lab Equipment
Face mask	China
Gloves	China

2.2 Time and site of research

The study was completed over a period of two months, from 1/10/2024 to 1/12/2024 involving patients from hospitals in the Karbala and Babylon provinces.

2.3 Study design

Study Design: A randomized, double-blind, controlled trial.

Patients: 150 patients aged 40-75 years, with moderate to severe asthma.

Intervention:

*** Control group: 50 patients with asthma but without treatment.

*** Symbicort group: 50 patients with asthma receiving symbicort inhaler 160/4.5mcg/60 dose once daily for a period of 2 months.

*** Brequal group: 50 patients receive brequal inhaler 50/250mcg/60 dose once daily for a period of 2 months.

2.4 Collection and Preparation of Samples

2.4.1 Baseline Data Collection:

Timeline: Data collected at the start of the study (baseline) and at the end of the 2-month period.

Patient Selection: Randomly selected 150 patients aged 40-75 years diagnosed with moderate to severe asthma from hospitals in Karbala and Babylon.

2.4.2 Grouping:

Control group: 50 patients with asthma but without treatment.

Symbicort group: 50 patients administered with 160/4.5 mcg Formoterol/Budesonide (Symbicort) once daily for 2 months.

Brequal group: 50 patients administered with 50/250mcg Salmeterol/Fluticasone (Brequal) once daily for 2 months.

2.4.3 Sample Collection:

Exacerbations: Document the number of asthma exacerbations requiring oral corticosteroids.

Pneumonia: Note incidences of pneumonia

ED Visits: Track the number of emergency department visits for asthma.

Lung Function: Measure lung function using spirometry (FEV1/L) at each data collection point.

Inclusion Criteria

- Patients aged between 40-75 years.
- Patients diagnosed with moderate to severe asthma.
- Patients treated in hospitals located in Karbala and Babylon provinces.
- Patients who consented to participate in the study for a two-month period.

Exclusion Criteria

- Patients suffering from other chronic diseases that might affect the study results (e.g., severe heart disease or uncontrolled diabetes).
- Patients who did not complete the two-month study period.

- Patients with a history of severe allergies to any components of the study medications (Symbicort or Brequal).

- Patients who refused to sign the written informed consent for study participation.

2.5 Statistical Analysis

The Kulmogorov-smirnov and shapiro tests were used to assess the normal distribution of data in SPSS program. For normal distributed data (Parametric), t test and ANOVA were applied while for exacerbations

Pneumonia incidence and ED Visits (non-parametric), the Kruskal wallis test for more than three means was used for comparison of results at level of significance $\alpha = 0.05$.

3.Results

3.1 The effects of Control, Symbicort and Brequal on FEV1

FEV1 expression showed significantly lower level in control group ($p < 0.05$) while this level was significantly higher in treated groups ($p < 0.05$) with Symbicort and Brequal.

Differences in FEV1 values are summarized in figure (3-1).

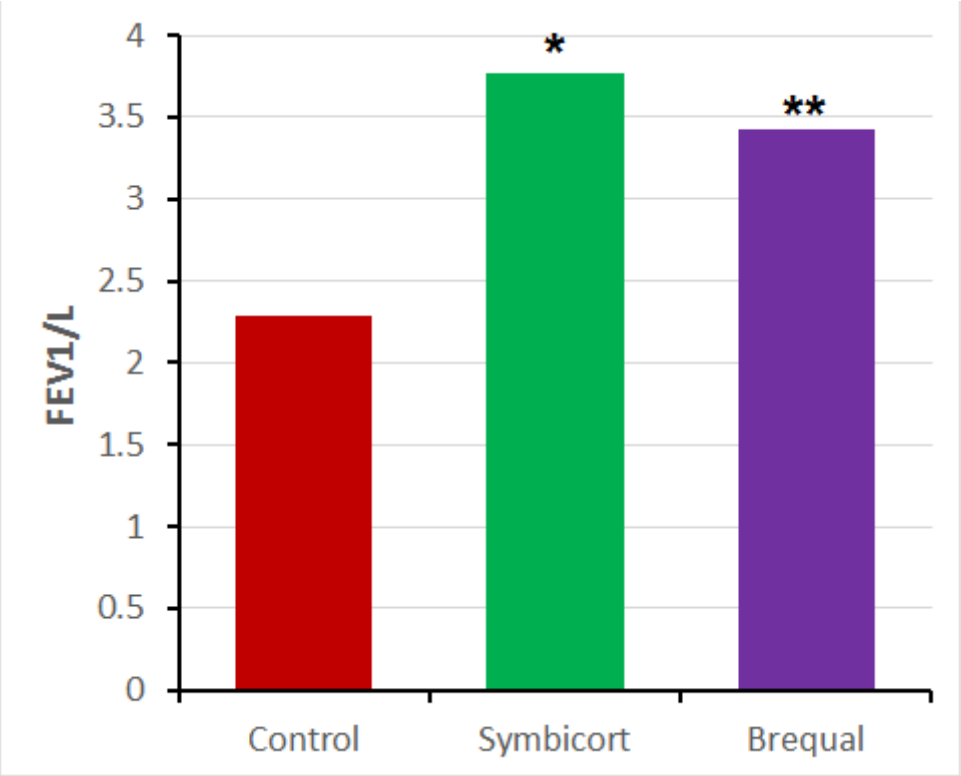

Figure (3-1) shows differences in FEV1 levels.

- * Symbicort Vs. Control significant difference (P = 0.00001)
- ** Brequal Vs. Control significant difference (P = 0.00001)
- Symbicort Vs. Brequal significant difference (P = 0.00001)

3.2 The Effects of Control, Symbicort and Brequal on number of asthma exacerbation

This marker showed to be highly increased in control group where ($p < 0.05$) significant versus low levels in treated groups with significant difference between them and with control group ($p < 0.05$).

Differences in number of asthma exacerbation are summarized in figure (3-2).

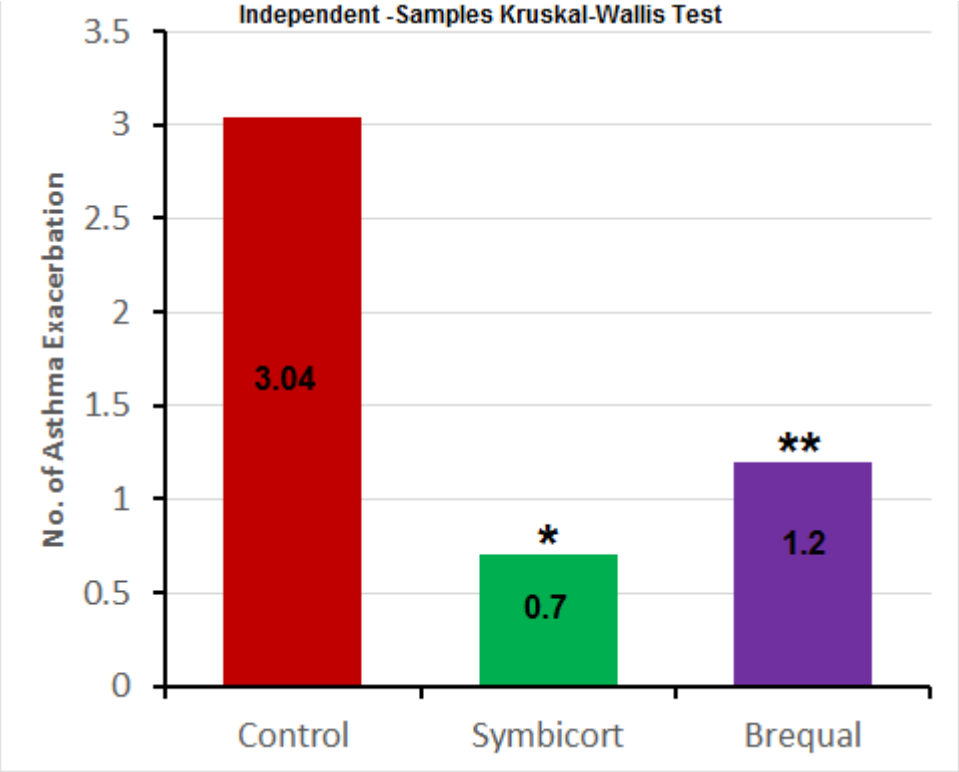

Figure (3-2) shows differences in number of asthma exacerbation.

- * Symbicort Vs. Control significant difference (P = 0.00001)
- ** Brequal Vs. Control significant difference (P = 0.00001)
- Symbicort Vs. Brequal significant difference (P = 0.00001)

3.3 The Effects of Control, Symbicort and Brequal on number of emergency department visits (ED visit)

Number of ED visit was significantly increased ($p < 0.05$) in control group as compared to drug groups that exhibited significant low level ($p < 0.05$) of this marker in our patients.

Differences in ED visits are summarized in figure (3-3).

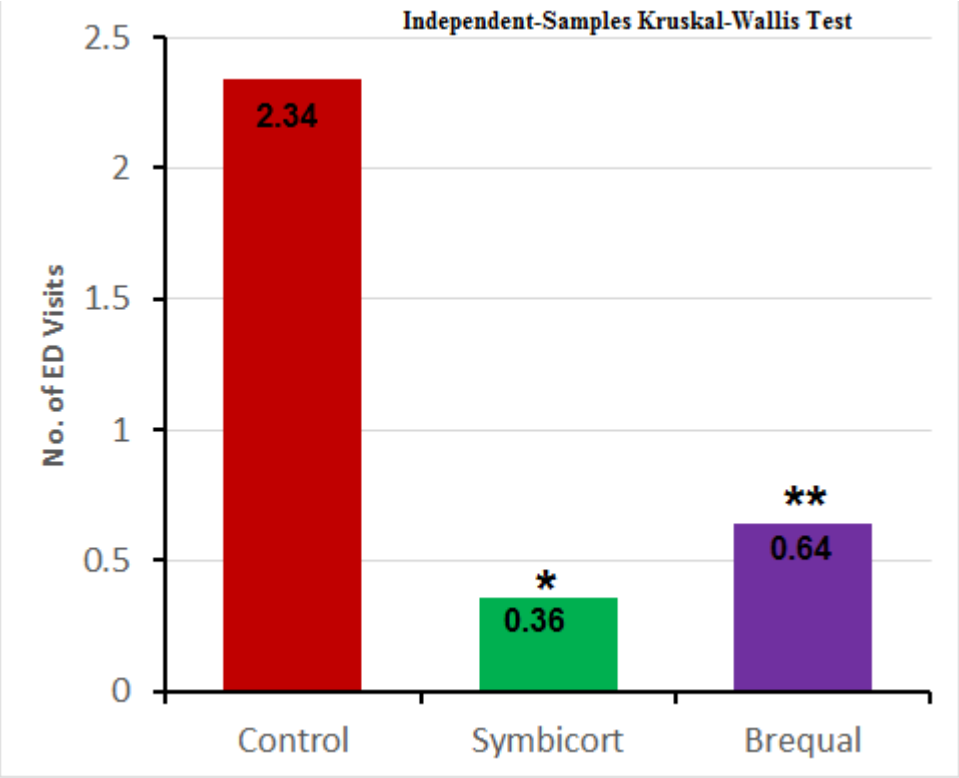

Figure (3-3) shows differences in number of ED visits.

- * Symbicort Vs. Control significant difference (P = 0.00001)
- ** Brequal Vs. Control significant difference (P = 0.00001)
- Symbicort Vs. Brequal significant difference (P = 0.025)

3.4 The Effects of Control, Symbicort and Brequal on incidence of Pneumonia

Pneumonia incidence was significantly inhibited in symbicort and brequal groups ($p < 0.05$) while in control group, it was significantly increased ($p < 0.05$).

Differences in pneumonia development are summarized in figure (3-4).

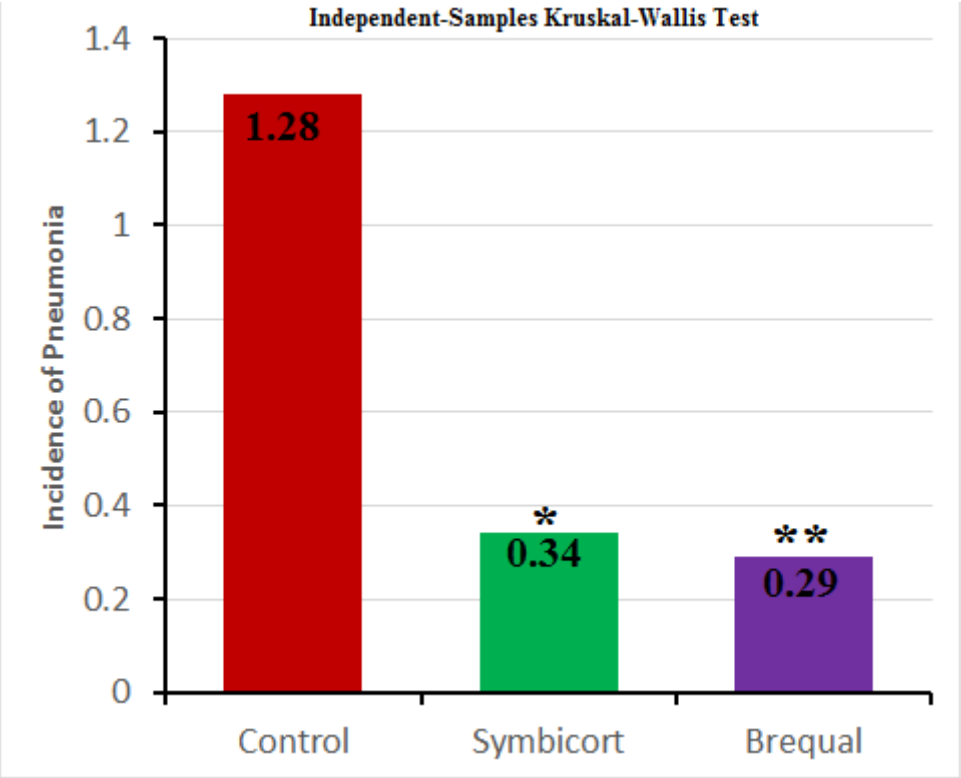

Figure (3-4) shows differences in Pneumonia incidence.

- * Symbicort Vs. Control significant difference (P = 0.00001)
- ** Brequal Vs. Control significant difference (P = 0.00001)
- Symbicort Vs. Brequal insignificant difference (P = 0.07).

4.Discussion

4.1 Effects of Control on study parameters

FEV1 reveal lower values in control patients as compared to treatment groups, this decline in FEV1 is more likely due to persistent inflammation and airway remodeling (10).

Frequency of asthma exacerbations is commonly greater in control patients as related to those receiving treatment due to poor asthma control and airway inflammation. Those patients will be at high risk of morbidity and reduced quality of life (11).

Due to uncontrolled symptoms and exacerbations, control patients are more likely to visit the emergency department for acute symptom management (11).

Untreated asthma patients may be at risk of developing respiratory infections (e.g. pneumonia) due to poor asthma management and frequent exacerbation (12).

4.2 Effects of Symbicort on study parameters

In this presented research, it was found that the FEV1 values significantly increased in symbicort group as compared to control. Studies have shown that the use of Symbicort can lead to a significant improvement in the forced expiratory volume in one second (FEV1), an important indicator of lung function. In a randomized double-blind study, the results showed that patients using Symbicort experienced a significant increase in FEV1 ($P < 0.05$) compared to patients using placebo. The increase in FEV1 is primarily due to the bronchodilator effect of formoterol, which relaxes the smooth muscles in the airways, leading to their dilation and improved airflow (13).

Furthermore, results of this research shown that the number of asthma exacerbations and ED visits are significantly decreased in symbicort as compared to control ($P < 0.05$). A study done by Brown& Davis exhibited that patients using Symbicort experienced a significant decrease in the number of asthma exacerbations and ED visits compared to patients using placebo ($P < 0.05$). The reduction in asthma exacerbations and ED visits is attributed to the anti-inflammatory effect of budesonide, which reduces airway inflammation and prevents the occurrence of asthma attacks. Additionally, formoterol provides long-acting bronchodilation, which helps maintain open airways and reduces the frequency of exacerbations (14).

This study also shown that there is slightly increase in pneumonia incidence in symbicort group as compared to brequal but significantly decrease infection in treatment group related to control. Some studies have shown that the use of Symbicort may increase the risk of pneumonia in some patients. In an analytical study involving a large group of patients, the results indicated a slight increase in the incidence of pneumonia among patients using Symbicort. The increased risk of pneumonia is likely due to the immunosuppressive effect of budesonide, which can reduce the body's ability to fight off infections. This makes patients more susceptible to respiratory infections, including pneumonia (15).

4.3 Effects of Brequal on Study parameters

In the current study, it is found that FEV1 value was dramatically increased in Brequal group as compared to control one.

A study accomplished by Kayser et al have shown that the use of Brequal can lead to a significant increment in the FEV1, an important indicator of lung function. Bronchodilation effects of salmeterol improve airflow and thus increase FEV1 values (16).

Also, number of asthma exacerbations and emergency department (ED) visits were significantly reduced in brequal group ($p < 0.05$) as compared to control group in this research. Anti-inflammatory effects of fluticasone steroid effectively decrease airway inflammation and as a result, the number of asthma exacerbations and asthma attacks reduced considerably. Additionally, salmeterol provides long-acting bronchodilation, which helps maintain open airways and reduces the frequency of exacerbations (17).

Brequal result in significant reduction in pneumonia development as that in control group ($P < 0.05$). This drug decrease pneumonia incidence more than symbicort but this reduction is insignificant ($P>0.05$). Immunosuppressive effect of fluticasone corticosteroid reduces the body's ability to fight off infections. The same result was obtained by Jackson (2023) (18).

4.4 Comparative Analysis of Symbicort and Brequal in Asthma Management

Symbicort and Brequal are both combination medications used to control asthma symptoms and improve lung function. According to the results of current study, symbicort exhibits better asthma management than brequal. Several studies have compared the efficacy and safety of these two medications to determine which one might be more effective. Vogelmeier et al. (2017) found that both medications improved FEV1 significantly. However, Symbicort showed a slightly higher improvement in lung function compared to Brequal ($P < 0.05$). Patients using Symbicort had fewer asthma exacerbations and ED visits ($P < 0.01$) (19). The incidence of pneumonia was similar between the two group. Price et al. (2016) concluded that Symbicort was more effective in reducing asthma exacerbations and improving overall asthma control compared to Brequal. Symbicort showed a greater reduction in the use of rescue medications ($P < 0.05$). Both treatments had similar safety profiles, with no significant difference in the incidence of pneumonia (20). Rabe et al. (2015) demonstrated that Symbicort provided better control of asthma symptoms and improved quality of life scores compared to Brequal. The incidence of asthma exacerbations and ED visits was lower with Symbicort ($P < 0.01$). The risk of pneumonia was not significantly different between the two groups (21).

5.1 Conclusions

Based on these results, it can be concluded that Symbicort has a positive impact on improving lung function and reducing asthma exacerbations and ED visits, but it may increase the risk of pneumonia in some patients. Therefore, physicians should consider these factors when prescribing Symbicort to asthma patients.

5.2 Recommendations

We recommend the following:

1- **Preferred Use of Budesonide/Formoterol in Severe Asthma Patients**: Given the superior control of asthma symptoms and improvement in quality of life observed in the study, it is recommended to prioritize Budesonide/Formoterol for patients with moderate-to-severe asthma requiring effective maintenance therapy.

2- **Consideration for Reducing Asthma Exacerbations and Emergency Department Visits:** Physicians should consider Budesonide/Formoterol as the preferred treatment option in cases where reducing asthma exacerbations and minimizing emergency department visits is critical, as it demonstrated better performance in these aspects.

3- **Pneumonia Risk Monitoring:** Although the risk of pneumonia was not significantly different between the two treatments, it is still essential to monitor patients closely for potential respiratory infections, especially those with comorbidities or weakened immune systems.

4- **Individualized Treatment Approach:** While the results indicate an advantage of Budesonide/Formoterol, treatment decisions should be individualized based on the patient's specific clinical profile, including age, disease severity, comorbidities, and response to prior therapies.

5- **Further Research on Long-Term Outcomes:** The study highlights the need for additional long-term research comparing both combinations, particularly focusing on safety profiles, to provide a clearer understanding of the risks and benefits associated with each treatment.

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Appendix

Comparative Study on the Efficacy of Symbicort vs. Brequal in Iraqi Asthmatic Patients

Section 1: Demographic information

1. **Age:**
2. **Gender:** ☐ Male ☐ Female
3. **Weight:**
4. **Occupation:** ☐Student ☐ employed ☐unemployed ☐self-employed ☐ other
5. **Level of education:** ☐diploma ☐bachelor ☐master ☐PhD ☐other
6. **Location:** ☐urban ☐rural
7. **Marital status:** ☐single ☐married

Section 2: Medical history and health information

9- Have you ever been diagnosed with asthma? ☐ Yes ☐ No

10- If yes, at what age were you diagnosed? ☐

11- Do you have a family history of asthma? ☐ Yes ☐ No

12- Do you have any other medical conditions?

☐Diabetes ☐Cardiovascular disease ☐kidney disease ☐Other ☐none

13- Are you currently taking any medication for asthma with its name?

☐Yes ☐NO

Section 3: Lifestyle factors

14- How often do you engage in physical activity (e.g. walking, running etc.)?

☐Every day ☐3-5 times/week ☐1-2 times/week ☐rarely ☐never

15- How would you describe your diet?

☐Healthy and balanced ☐average, with a mix of healthy and unhealthy foods ☐unhealthy

16- Do you smoke? ☐Yes ☐ No

17- If yes, how many cigarettes do you smoke per day? ☐