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INVESTIGATING THE EFFECTIVENESS OF DIFFERENT INHALER DEVICES IN DELIVERING MEDICATION TO PATIENTS WITH OBSTRUCTIVE LUNG DISEASES

Alduwayyikh Ziyad Shujaa, Alshammari Saad Khulaif, Alenezi Bander Abdullah , Alotaibi Adel Aeydh, Alsaif Khalaf Abdulrahman K , Alotaibi Ahmad Bandar, Almutairi Faisal Nawar, Alanazi Salem Mohammed, Alanazi Muhana Abdulkarem, Alharbi Shaiem Abdullah, Almutairi Fahad Saud, Alrashidi Majed Alfalayah

Abstract:

Patients with asthma and COPD experience a significant burden, often leading to recurrent hospitalizations owing to exacerbations. There are many factors contributing to the inadequate disease management in people with asthma and COPD. It is linked to health care providers not following guidelines and patients not properly using inhalers or following treatment plans. This study intends to provide information on inhaler technique and its influence on quality of life (QoL) and symptom management in a standard sample of patients with chronic lung disease from a randomized controlled trial focusing on medication adherence.

Chronic obstructive pulmonary disease (COPD) is a significant economic burden and necessitates consistent and continuous therapy. Inhalation therapy is advised for all illness stages to deliver active molecules straight to the target site of action and reduce unwanted side effects. Inhalers are essential for effectively managing people with COPD, and selecting the right one is just as critical as choosing the medication. The primary parameters affecting inhaled medication deposition in the airways are the patient's inhalation flow rate, aerosol velocity, and the size of inhaled drug particles. These factors eventually influence the quantity of medicine that reaches the intended spot, consequently affecting the patient's functional and clinical reactions. Patients' proficiency and knowledge in using inhalers have a direct impact on the effectiveness of the treatment. However, in daily clinical practice, insufficient attention is paid to the characteristics of various inhalers and patients' proficiency in using the device. Clear recommendations are essential to assist healthcare professionals in recommending and prescribing the most suitable inhaled drug/device product. This review attempts to give the most recent research about the significance of the inhaler device in treating individuals with COPD.

Key Words: Diabetes, antidiabetic drug, skeleton, bone, bone health

Introduction:

Chronic obstructive pulmonary disease (COPD) represents a major global concern for national healthcare systems, being ranked as the fourth leading cause of death in the world and significantly affecting the quality of life of patients [1, 2]. COPD is characterized by persistent airway inflammation and bronchial obstruction and requires regular and ongoing treatment. Inhalation therapy is the mainstay of treatment in patients with COPD, where bronchodilators (beta-2 agonists, anti-muscarinic agents) and anti-inflammatory drugs (corticosteroids) are recommended by international strategy documents at any stage of the disease [3]. In contrast, oral treatments such as theophylline, phosphodiesterase-4 inhibitors and corticosteroids are only occasionally used.

Indeed, inhaled treatment has several advantages over oral therapy as inhalation allows the delivery of active molecules directly to the target site of action, whilst minimizing adverse sideeffects. Furthermore, a lower drug dose is needed to achieve the therapeutic effect via the inhaled route and the onset of action is more rapid, in contrast with oral administration [4].

Inhalers, therefore, play a crucial role in the management of patients with COPD and it is being recognized that the choice of the inhalation device appears to be as important as that of the drug molecule [5]. Indeed in daily clinical practice, pulmonologists usually focus on the pharmacological properties of the various respiratory drugs in selecting the best possible therapeutic option, but little consideration is given to the features of the different inhalers and to the ability of the patient to use the device, which are topical issues [6]. In fact it is often underappreciated that incorrect inhalation technique by the patient is directly associated with increased healthcare resource utilization [7–9].

Furthermore, with increasingly constrained societal healthcare budgets and expiring patent protection for many branded medications, there is emphasis on the development of generic inhaled drugs that are therapeutically equivalent to the original registered products but may differ in their formulation and the design of the inhalation device. This growing scenario poses practical clinical questions about the potential impact of switching from branded to generic inhaler products in managing patients with COPD [10]. Indeed, the estimated 10 new drug product launches in COPD over the next 2 years [11, 12] will lead to even more confusion, and apathy, in respiratory prescribing, as there are currently more than 250 inhaler products in pharmaceutical formularies [13] and direction is greatly needed to help healthcare professionals advise and prescribe the ‘appropriate’ inhaled drug/device product for patients.

The present review article aims to provide the latest evidence on the importance of the inhaler device in the management and treatment of patients with COPD, and specifically to collect data to support decisions on the appropriate choice of device by healthcare professionals. It also addresses and contrasts the advantages and limitations of different available inhalation device options.

Background:

Asthma and Chronic Obstructive Pulmonary Disease (COPD) are common chronic respiratory conditions in the general population.[14] Asthma and COPD are chronic respiratory disorders that are currently untreatable but manageable. However, the severity of each condition in patients is significant, leading to recurrent hospitalizations owing to worsening symptoms. Even with good medication options and evidence-based guidelines, disease control remains inadequate in patients with these two chronic obstructive lung disorders.

There are many factors contributing to the inadequate disease management in people with asthma and COPD. One significant factor is the improper use of inhaler devices, leading to negative health consequences such as higher hospitalization rates and inadequate disease management. [15,16,17]

Inhaled medicine is crucial in treating individuals with asthma and COPD. This method allows for the direct delivery of the medication into the airways. Thus, significant concentrations in a specific area can be reached while minimizing the chances of negative effects across the body [18]. Various consecutive actions are required to correctly apply these devices. Failure to perform one or more stages correctly might significantly decrease the delivery of the administered chemical, therefore affecting the medication's effectiveness and safety.[19] Research indicates that 50–80% of the people examined do not use their inhaler devices correctly.[20,21,22,23] They frequently overestimate their ability to inhale properly or may be unaware of their inappropriate use of inhaled medication.[24]

Thus, it is advisable to regularly evaluate the inhaling technique according to national and international norms to make corrections if needed.

This cross-sectional analysis aims to provide data on inhaler technique and its influence on quality of life and symptom control in a standard group of patients with chronic lung disease from the Adherence-Trial [25]. The longitudinal Adherence-Trial aimed to study the impact of a personalized intervention involving a daily alarm clock and phone call reminders on adherence to inhaled therapy in asthma and COPD patients. The trial also sought to assess the influence of this intervention on exacerbations and quality of life.[25]

Choosing Inhaler:

The objective of therapy for COPD patients is to achieve complete symptom management and prevent disease exacerbations by administering the appropriate inhaled medication dosage to the specific site of action in the lungs, while minimizing or avoiding any negative side effects.[3] Although inhaled therapy is crucial for treating COPD patients, existing literature does not have a consistent agreement on the criteria for selecting and prescribing inhalation devices. Conversely, healthcare professionals typically feel at ease treating patients based on the pharmacological characteristics of the drug. In 2005, Dolovich and colleagues published evidence-based guidelines on behalf of the American College of Chest Physicians (ACCP) and

the American College of Asthma, Allergy, and Immunology (ACAAI). The guidelines aimed to provide recommendations on selecting inhaler devices and evaluating the outcomes of aerosol therapy. [26] Their systematic review and meta-analysis of randomized controlled trials found no significant difference in efficacy outcomes among devices in various clinical settings. Adverse side-effects were minimal and mostly associated with a higher drug dose. The authors recommended that the selection of an aerosol delivery device should consider various factors, including drug availability and administration time, patient age and ability to use the device correctly, convenience in outpatient and inpatient settings, costs, and physician and patient preference. A recent position paper by a collaborative task force of the European Respiratory Society (ERS) and the International Society for Aerosols in Medicine (ISAM) outlined guidelines for selecting the most suitable inhaler device based on factors such as the patient's condition, inspiratory flow, demographic, clinical environment, and inhalation method.[27] Less than 2% of the Global Initiative for Obstructive Lung Disease (GOLD) strategy paper for COPD patients addresses device-related issues.[28] The new GINA strategy document for asthma emphasizes the evaluation of the patient's breathing technique and the selection of the suitable device as a crucial element in their treatment protocols.[29]

The key factors affecting inhaled drug deposition in the airways are the patient's inhalation flow, aerosol velocity, and inhaled drug particle size. These factors determine the amount of drug that reaches the airways and consequently affect the patient's functional and clinical responses.[30] Therefore, the selection of an inhalation device for individuals with COPD should primarily be based on these factors.

Method:

The Adherence-Trial was a single-blind randomized controlled trial. The study details have been previously published [25]. The study examined the compliance with inhaled medication over a

six-month period in individuals with asthma and/or COPD who had at least one exacerbation in the previous year. The study took place in an outpatient setting from January 2014 to March 2017. The investigator secured written consent from patients to affirm their willingness to partake in the trial. Adherence was assessed by electronic data capture devices that record the date and time of each inhalation device use and transmit this information daily via wireless connection to an online database. All participants underwent a training course prior to the baseline visit. The training course aimed to offer a review of inhalation techniques to ensure all participants had a consistent understanding of other disease and were using their medicine accurately. The course commenced with a concise overview of asthma and COPD. Subsequently, the most commonly utilized devices were introduced and briefly showcased. Issues and errors related to the use of the devices were clarified. A short film produced by the "Deutsche Atemwegsliga" in Bad Lippspringe, Germany, [26] demonstrated the proper use of the separate gadgets. At the conclusion of the course, participants were provided with the chance to inquire about the equipment. Following the training course, patients were assigned randomly to either

the intervention or control group. The intervention group was provided with a daily alarm clock and received reminder support calls if medication adherence was not followed or if the use of rescue medication increased. Participants were evaluated through clinical visits every two months during the trial. Refer to Figure 1 for a comprehensive overview of the study protocol. The trial was authorized by the local ethics council (registration number: EK-269/13) and registered on ClinicalTrials.gov with the identifier NCT02386722 before it began.

Measurements:

Sociodemographic variables: Sociodemographic characteristics like age, gender, marital status, and education level were collected using a standard questionnaire during the initial visit. Smoking status, pack years (py), and body mass index (BMI) were documented at this appointment. Furthermore, inquiries on diseases such as allergies, frequency of exacerbations in the past 12 months with corresponding antibiotic treatments, use of systemic corticosteroids, visits to the emergency department, and hospitalizations were made. If patients were unable to provide information about the occurrences, the treating physician was consulted. Furthermore, the present inhaled drug was documented. The lung disorders (asthma, COPD, or ACO) identified were based on existing medical records and were not reassessed for this research.

Pulmonary function: Spirometry was utilized to assess forced vital capacity (FVC) and forced expiratory volume in one second (FEV1). Pulmonary gas transfer information was obtained by measuring the diffusing capacity of the lung for carbon monoxide (DLCO). All tests were conducted in accordance with the European Respiratory Society's recommendations [32]. The EasyOne Pro gadget from ndd Medizintechnik AG in Zürich, Switzerland was utilized.

Assessment of the device app: Each patient was required to demonstrate the inhaling method using a placebo device for all prescribed devices in order to identify fake device application. Correct usage was evaluated according to the study protocol using predetermined checklists specific to each kind of inhaler, which were derived from user guidelines and instruction box inserts provided by the manufacturers. [31] The inhaler approach was deemed correct when each step on the checklist was executed accurately. An erroneous execution of one or more phases deemed the technique flawed. Participants were given a score of "0" for each erroneous step and a score of "1" for each correct step. A critical error is when a step is completed incorrectly, leading to a significant reduction or complete inhibition of drug administration, which affects the effectiveness of the drug being supplied. [33] The device application was evaluated by a qualified pharmacist. For consistency, the device application was consistently examined by the same pharmacist to standardize error observation. Additionally, during the training, the pharmacist frequently viewed films of inhalers for certain device kinds to improve their proficiency in evaluation. The evaluation was conducted by one observer, assessing intra-observer variability.

Asthma Control Test (ACT): The ACT questionnaire was used to evaluate asthma control. The questionnaire validation confirmed the reliability and validity of scores derived from the ACT,

indicating its capability to identify patients with poorly managed asthma. It is a validated tool for assessing asthma control that may be easily administered to evaluate the amount of asthma control, with or without the need for lung function testing. The ACT score varies from 5 and 25. Values from 5 to 15 imply "very poor controlled asthma," 16 to 19 signal "not well controlled asthma," and 20 to 25 represent "well controlled asthma."[35]

Effects of COPD symptoms: COPD patients' health state was assessed using the COPD Assessment Test (CAT). The CAT is an established, condition-specific questionnaire consisting of eight items rated on a six-point difference scale. It is designed to assess the effect of lung disease on the health status of patients. Scoring between 0 and 10 indicates a low impact, 11-20 represents a medium impact, 21-30 signifies a strong impact, and 31-40 indicates a very significant impact of the condition on an individual's health status.[36]

Results:

Incorrect inhaling technique varied from 0% to 53% depending on the kind of inhaler. COPD patients who applied the device incorrectly had a higher CAT total score than those who applied it correctly (P = .02). In addition, COPD patients who used the device incorrectly had a higher likelihood of experiencing coughing (P = .03) and increased breathlessness when walking uphill or climbing stairs (P = .02). COPD patients who utilized their devices correctly had a significantly higher mean FEV1% predicted at baseline compared to those who used their devices incorrectly (P = .04). No significant difference was seen in asthma patients.

Discussion:

Patients demonstrated a higher rate of improper application while using metered dose inhalers and dry powder inhalers like Turbohalers and Breezhaler, compared to devices such as Discus and Ellipta®, which were more frequently used correctly. Device application did not affect the ACT score or lung function metrics in asthma patients. Incorrect device application in COPD patients negatively affected the CAT score. Moreover, individuals who used their devices accurately had an improved forced expiratory volume in one second (FEV1).

Conclusion:

In individuals with COPD, inhalation therapy is the primary form of treatment. In recent years, major advancements and innovations have been made in device engineering and formulations, as indicated by collected data. Physicians have access to a wide range of device categories, each with features that ensure successful aerosol administration for treating COPD. It appears that there is no perfect inhaler as each one has its own strengths and weaknesses. Effective inhalation and drug delivery to the target site depend on various parameters that influence patients' reaction to treatment. When selecting an inhaler, it is important to examine factors such as aerosol velocity, medication particle size, pulmonary function, inhalation flow, dexterity, cognition, and patient preferences. Regrettably, there has been less effort to raise awareness among healthcare providers about the importance of these factors. Despite ample trustworthy facts in literature,

international plan documents and respiratory scientific associations offer limited and ambiguous suggestions. This condition leads to decreased effectiveness of inhalation therapy and a squandering of financial resources. Efforts are crucial to enhance healthcare provider knowledge and education on inhalation devices to maximize therapeutic benefits for patients and improve doctor-patient satisfaction with aerosol therapy.

Properly inhaling the recommended drug is linked to enhanced health condition and respiratory capacity. Health practitioners should be prompted by these results to give guidance on proper inhalation technique and to consistently assess the patients' inhalation technique

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