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Nebulizers, inhalers, and spirometers for Chronic Obstructive Pulmonary Disease (COPD) and asthma- An updated review

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***Abstract*---Background:** Asthma and chronic obstructive pulmonary disease (COPD) are prevalent chronic conditions significantly impacting healthcare costs and patient quality of life. Inhalation therapy plays a crucial role in managing these diseases, with a wide array of devices available for medication delivery. **Aim:** This review aims to update the understanding of nebulizers, inhalers, and spirometers in managing asthma and COPD, highlighting device usage, patient adherence, and clinical outcomes. **Methods:** A comprehensive literature review was conducted, focusing on the effectiveness, usability, and patient adherence associated with various inhalation devices, including nebulizers, pressurized metered-dose inhalers (pMDIs), and dry powder inhalers (DPIs). Patient preferences and common user errors were also analyzed. **Results:** Findings indicate a significant prevalence of incorrect inhalation techniques, which adversely affect treatment outcomes. Despite the growing market for inhalation devices, non-adherence remains a challenge, particularly among patients with cognitive impairments. User errors were common across all device types, highlighting the need for improved patient education and device selection tailored to individual capabilities. **Conclusion:** Optimizing inhalation techniques and enhancing patient education are essential for improving clinical outcomes in asthma and COPD management. Future strategies should focus on personalized device selection and ongoing support to foster adherence and correct usage.

***Keywords*---**Asthma, Chronic Obstructive Pulmonary Disease, Inhalation Therapy, Nebulizers, Pressurized Metered-Dose Inhalers, Dry Powder Inhalers, Patient Adherence.

Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are prevalent chronic conditions that constitute approximately 78% of direct healthcare expenses associated with respiratory diseases in the European Union [1]. In the UK, 5.4 million individuals are currently receiving treatment for asthma, of which 1.1 million are children [2]. Globally, over three million people die from COPD each year, representing an estimated 6% of all deaths worldwide [3]. The delivery of medications through inhalation is a crucial element in the management and treatment of both conditions. Over the last three decades, there has been significant growth in the inhalation therapy market, with annual sales increasing from $7 billion in 1987 to $36 billion in 2014, along with over 90 billion inhaled doses prescribed annually [4]. Unlike systemic treatments, inhaled medications

are quickly directed to the airways, allowing for rapid therapeutic effects. Targeting drugs directly to the lungs enables the use of lower doses, thereby reducing the likelihood of adverse effects. The variety of inhalers is substantial; in 2011, more than 230 different device-drug combinations were available to prescribers in Europe [5], with 48 different inhaler products in the UK alone [6], each with specific design features [7, 8]. In 2011, the most common types of devices sold in Europe included pressurized metered-dose inhalers (pMDIs; 47.5%), followed by dry powder inhalers (DPIs; 39.5%) and nebulizers (13%), although the distribution of inhalers varied significantly among countries [5]. Consequently, selecting the most appropriate device to fulfill individual patient needs is a critical consideration in clinical practice.

Correct utilization of inhalation devices and adherence to prescribed regimens are essential factors for achieving better clinical management and enhanced quality of life [9–11]. Non-adherence is a significant health challenge; however, both asthma and COPD exhibit lower adherence rates compared to other chronic conditions [12]. The negative consequences of poor adherence to COPD medication have been well documented in the TOwards a Revolution in COPD Health (TORCH) study, which found a significant association with increased mortality and hospital admissions due to exacerbations [13]. Among COPD patients discharged from hospitals, adherence to medication has been found to be low, with cognitive impairment and the severity of airway obstruction being significant negative influences [14]. It is recognized that numerous factors present challenges to patients regarding inhaler use, including inhalation technique and pulmonary function. In patients with asthma or COPD, incorrect inhaler technique is linked to a 50% increased risk of hospitalization, more frequent emergency department visits, and heightened use of oral corticosteroids [15]. User errors are prevalent, regardless of the device employed. A study involving 3,393 devices used for continuous COPD treatment in 2,935 patients identified critical errors during inhalation tests, including issues with Breezhaler® (Novartis AG, Basel, Switzerland), Diskus® (GlaxoSmithKline, London, UK), Handihaler® (Boehringer Ingelheim Pharma, Ingelheim am Rhein, Germany), pMDIs, Respimat® (Boehringer Ingelheim Pharma), and Turbuhaler® (AstraZeneca, Cambridge, UK) in 15.4%, 21.2%, 29.3%, 43.8%, 46.9%, and 32.1% of patients, respectively [16]. However, a recent systematic review found 299 definitions for “critical error,” underscoring the necessity for a consensus on what constitutes an inhaler critical error [17]. It is also advised that patient preferences for devices should be considered when prescribing an inhaler [10], though healthcare professionals must be aware that patients frequently overestimate their competence in operating a device correctly [18]. Factors influencing patient preferences include simplicity and convenience (e.g., size and durability) as well as user experience (e.g., taste and side effects) [19]. Enhanced inhaler technique is not necessarily achieved through higher satisfaction with a device, a healthcare professional’s belief that the patient is engaged in the device selection process, or a patient’s comfort in using a device publicly [20]. Given the considerable expenses associated with managing asthma and COPD on a global scale, optimizing the use of inhalation devices and techniques is crucial [21]. Strategies to accomplish this include delivering high-quality education for both patients and the multidisciplinary team (MDT) involved in asthma management, utilizing device

technology effectively, and implementing techniques specifically designed to support adherence.

Inhalation Devices in Asthma and COPD

A diverse array of drug and inhaler combinations is available for the management of asthma and chronic obstructive pulmonary disease (COPD), enhancing the likelihood of identifying a suitable option for each patient. Inhaler devices differ in various aspects, including the method of medication delivery, whether the treatment is generated actively or passively (e.g., through propellant, mechanical means, or compressed air), the characteristics of the drug formulation (e.g., solution, dry powder, or aerosol), the device's capacity for single or multiple doses, and whether the device is disposable or refillable [21]. Each inhaler possesses unique design features, allowing for customization to meet individual patient needs [22]. However, these variations also pose challenges in ensuring that patients are adequately informed about the proper use of their devices and that they receive sufficient education and support to maintain correct usage. This challenge is exacerbated by the fact that patients often receive multiple devices that operate in distinct manners. The necessity of using various inhalers, each requiring different inhalation techniques, has been shown to negatively impact clinical outcomes in patients with COPD [23] and asthma [24]. Patients who recognize the importance of their inhaler in managing asthma demonstrate higher levels of correct inhaler utilization [21]. Nonetheless, it is essential that, beyond understanding the necessity of using an inhaler for disease control, patients are also educated on the importance of correct usage [25]. Thus, from the patient's viewpoint, the selection of an inhalation device is likely as crucial as the selection of the treatment itself [21]. The most commonly utilized devices include nebulizers, pressurized metered-dose inhalers (pMDIs), dry powder inhalers (DPIs), and soft mist inhalers (SMIs).

Nebulizers

Nebulizers represent one of the oldest categories of inhalation devices. Typically, they are used primarily in emergency situations for acute treatment or in chronic disease management for children or elderly patients who may struggle to use an inhaler with a spacer due to coordination issues [10, 26–28]. Once activated, nebulizers are straightforward to operate and provide a convenient method for delivering higher doses of medication to the airways when necessary [26]. Because nebulizers eliminate the requirement for patients to coordinate inhalation with actuation, they are particularly advantageous for individuals with cognitive, neuromuscular, or ventilation impairments [26–28]. More than 50% of patients opting for nebulizers instead of other inhalation devices do so because of physical or cognitive disabilities [26, 27, 29]. However, most nebulizer devices tend to be bulky and cumbersome, necessitating regular maintenance, extending drug delivery time from seconds to 10–15 minutes, and requiring thorough cleaning for sterilization [27]. Research indicates that in the acute management of conditions, nebulizers yield outcomes comparable to those of pMDIs with spacers [30]. However, when compared to DPIs, nebulizers may offer advantages for COPD patients with inadequate inspiratory flow [31]. A new portable nebulizer (Lonhala™ Magnair™, Sunovion Pharmaceuticals Inc., Marlborough, MA, USA)

has recently received approval from the US Food and Drug Administration (FDA) for administering glycopyrrolate within 2–3 minutes, allowing patients to breathe normally during treatment [32].

Pressurized Metered-Dose Inhalers

The pressurized metered-dose inhaler (pMDI) is a widely utilized device, largely due to the extensive range of medications it can deliver and its relatively low cost. In recent years, there has been a shift from chlorofluorocarbon (CFC) pMDIs, which are now nearly obsolete, to primarily hydrofluoroalkane (HFA) pMDIs. Current HFA solutions include long-acting β2-agonist formoterol, corticosteroids such as ciclesonide (CIC), beclomethasone dipropionate (BDP), and flunisolide, as well as a combination of BDP and formoterol in a single inhaler [33]. Both BDP and CIC formulations feature extra-fine particles (≤2 μm mass median aerodynamic diameter), which are linked to reduced oropharyngeal deposition and improved lung deposition [33]. Preparations containing extra-fine inhaled corticosteroids (ICS) have significantly higher chances of achieving asthma control and lower exacerbation rates at markedly lower doses compared to fine-particle ICSs [34]. Patients transitioning to extra-fine particle ICS preparations experienced a reduced risk of pneumonia, acute COPD exacerbations, and respiratory events [35]. Common errors among pMDI users include inhaling too rapidly (rather than slowly and deeply), failing to tilt the head properly, not emptying the lungs before inhalation, and not holding the breath after inhalation [11, 21]. Additionally, patients often struggle to accurately gauge the remaining number of doses; some pMDI devices still lack a dose counter despite FDA recommendations made in 2003. A study examining patient satisfaction with their pMDI revealed that 52% felt “extremely unsure” and 10% “somewhat unsure” about the amount of medication left [8]. Although the inclusion of dose counters in many devices addresses this issue, patients must still recognize the importance of monitoring their remaining medication [36].

Dry Powder Inhalers

Dry powder inhalers (DPIs) were introduced as user-friendly alternatives to CFC- and HFA-driven pMDIs [37]. Breath-actuated DPIs aim to mitigate challenges related to coordinating inhaler actuation and inhalation [15, 38]. There are three primary systems: capsule-based pre-metered single-dose devices; multi-unit dose inhalers (preloaded with blister foil by the manufacturer); and multiple-dose inhalers that utilize an in-built mechanism to dispense a single dose with each actuation from a powder reservoir [38, 39]. Effective DPI usage necessitates correct priming and loading of each dose [40]. DPIs rely on the user's inspiratory flow to empty the drug system, and failure to generate an adequate inspiratory flow is the most common critical error, occurring in 26% to 38% of cases [11, 15]. Other frequent errors include improper device positioning during dose loading, failing to tilt the head correctly, insufficient inspiratory effort, and not clearing the lungs prior to inhalation [11, 21]. It is increasingly acknowledged that many patients with asthma and COPD struggle to achieve the optimal inspiratory flow rates required for effective drug delivery and clinical benefits [41]. Furthermore, DPIs are sensitive to heat and moisture, necessitating precautions to avoid

humidity. This sensitivity limits their use in hot and humid climates, highlighting the importance of proper storage conditions [42, 43].

Pressurized Metered-Dose Inhalers (pMDIs)

Pressurized metered-dose inhalers (pMDIs) are widely utilized due to their ability to deliver a diverse array of medications at relatively low costs. There has been a significant shift from chlorofluorocarbon (CFC) pMDIs, which are now largely outdated, to hydrofluoroalkane (HFA) pMDIs. Current HFA formulations include long-acting β2-agonist formoterol and various corticosteroids such as ciclesonide (CIC), beclomethasone dipropionate (BDP), and flunisolide, along with a combination of BDP/formoterol in a single inhaler BDP and CIC formulations feature extra-fine particles (mass median aerodynamic diameter < 2 μm), which promote enhanced lung deposition and minimize oropharyngeal deposition. The use of inhaled corticosteroids (ICS) significantly increases the likelihood of asthma control and reduces exacerbation rates, especially at lower doses compared to fine-particle ICS. Moreover, patient to extra-fine particle ICS preparations face a reduced risk of pneumonia, acute exacerbations of chronic obstructive pulmonary disease (COPD), and respiratory incidents. However, common user errors include inhaling too quickly, improper head positioning, failure to exhale before inhalation, and not holding breath post-inhalation. Many patients struggle to gauge the clearly with older pMDI models lacking a dose counter, as noted by a study where 52% of participants felt “extremely unsure” about their medication supply.

Dry Powder Inhalers (DPIs)

Dry powder inhalers (DPI as user-friendly alternatives to CFC- and HFA-driven pMDIs. Breath-actuated DPIs aim to simplify the coordination needed for action and inspiration. The primary types include capsule-based single-dose devices, multi-unit dose blisters, and multiple-dose inhalers equipped with a built-in mechanism to dispense a single dose. For effective DPI usage, proper priming and loading are essential. DPIs rely on the user's insert the medication, and insufficient inspiratory effort is a prevailing error, occurring in 26% to 38% of cases. Other common mistakes include incorrect device positioning during loading, inadequate head tilt, and failure to exhale fully here is growing recognition that many patients with asthma and COPD struggle to generate the necessary inspiratory flow for optimal drug deliverinical benefits. Additionally, DPIs are sensitive to heat and moisture, limiting their use in humid climates.

Soft Mist Inhalers (SMIs)

Soft mist inhalers (SMIs) provide an also pMDIs and DPIs, enhancing drug delivery to the lungs and improving patient adherence. The Rhaler by Boehringer Ingelheim is the sole SMI currently available for asthma and COPD. It operates without propellants, utilizing a compressed spring to generate a slow-moving aerosol cloud. The Respimat® is less susceptible to moisture due to its solution-based aerosol, making it more suitable for humid environments. While the inhalation technique mirrors that of a pMDI, the aerobated to HFA-driven pMDIs. Research by Dal Negro et al. demonstrated that the SMI's dynamic characteristics

result in a more facilitating easier patient use due to the slower jet emission and uniform droplet composition. The extended expulsion timspimat® (approximately 1.2 secishes the likelihood of poor coordination between actuation and inhalation, potentially leading to better lung deposition and reduced throat drug impaction. Scintigraphy study that the Respimat® achieves higher lung deposition (up to 50% more) and lower oropharyngeal deposition compared to HFA-based pMDIs, attributed to the small particle size produced. Overall, the Respimat® Soft Mist™ inhaler offers a clinical practice, addressing some limitations associated with other inhaler types.

Inhaler Selection in Clinical Practice

The choice of inhaler is influenced by several factors, including pulmoon (inspiratory flow and breathing technique), device handling, the use of spacers, required inhaler techniques, and patient preferences. Proper inhaler technique is crucial for ensuring optimal drug delivery to the lungs and peripheral airways, which is essential for achieving disease control. As treatment efficacy correlates with patient preferences is vital; tailored inhaler selection can enhance satisfaction, adherencsical barriers impacting device handling are well-documented. Special consideration is needed for children, the elderly, and individuals with conditions such as joint pain, osteoarthritis, and muscle weakness can hinder device manipulation. Moreover, cognitive impairments and physical limitations can affect the abiliectively, particularly regarding creating a proper seal around a spacer. For children, inhaler selection must consider age and capability, as well as challenges associated with manual dexterity. The use of spacers in children can alleviate the need for coordination during actuation. Inhaled is also affected by factors such as inspiratory flow, aerosol velocity, and particle size. These issues can significantly reduce drug deposition in the lungs, particularly in young children and older adults, who often face difficulties in coordinating actuation with inhalation.

The CRITical Inhaler mistaKes and Asthma controL sKAL), one of the largest investigations into inhaler technique, analyzed data from 3,660at insufficient inspiratory effort was prevalent among DPI users (32%-38%) and associated with uncontrolled asthma. In pMDI usersiming (24.9% of patients) correlated with uncontrolled asthma.

Patient factors, such as preferences and satisfaction, significantly influence inhaler choice and usage. Beyond ease of ussuch as portability, device noise, taste, treatment duration, and conso matter. Engaging patients in the selection process can improve adherence; for example, research by Small et al. revealed that higher satisfaction levels with inhalers were linked to improved compliance and better hees, including fewer exacerbations and healthcare visits. In studies exploring inhaler preferencesnts consistently expressed a desire for smaller, portable devices and emphasized the necessity of dose couroper training from healthcare professionals. Overall, patient preference for inhaler types varies widely, influenced factors.

Training and Education to Support the Use of Inhalers

Misuse of inhalers ranks among the most frequently reported obstacles to adherence. According to Melani et al. [15], the most pronounced associations between inhaler misuse were linked to older age, lower educational attainment, and inadequate instruction on inhaler technique. It is important to recognize that even the most user-friendly devices necessitate proper education and demonstration, which several studies have indicated are often insufficient. Education is a modifiable factor, and healthcare professionals should customize their guidance to meet individual patient needs while ensuring their own knowledge is current [7]. When a new device is introduced in clinical settings, the assertion that it is user-friendly may imply that education and training are unnecessary. However, patients still need training and skills enhancement for any device [15, 52], and their inhaler technique should be evaluated regularly, particularly for those with poor asthma control, even if they are using devices deemed easy to operate [56]. Although training can improve inhaler use, many patients tend to revert to incorrect techniques after a short period [73, 74]. The Global Initiative for Asthma (GINA) recommends strategies to promote effective device use, such as demonstrating inhaler techniques and providing retraining during follow-up visits [10]. A Cochrane review assessed various interventions and found that while many studies showed post-intervention improvements in the number of individuals using the correct inhaler technique, it could not be confirmed whether these improvements led to clinical benefits [51]. The authors advised healthcare professionals to regularly ask patients to demonstrate their inhaler technique and make necessary corrections, as well as refer them for training when available.

Role of Pharmacists:

1. Patient Education and Counseling: Pharmacists are essential in providing education about the correct use of inhalation devices. They can offer personalized demonstrations and instructions on inhalation techniques, which is crucial given the prevalence of user errors. By helping patients understand how to properly use nebulizers, pressurized metered-dose inhalers (pMDIs), and dry powder inhalers (DPIs), pharmacists can enhance adherence and improve treatment outcomes.

2. Medication Management: Pharmacists play a critical role in managing the medication regimen for patients with asthma and COPD. This includes:

- **Medication Reconciliation**: Ensuring that patients understand their prescribed medications, potential side effects, and interactions with other drugs.
- **Dosing Adjustments**: Evaluating the effectiveness of inhalation therapy and making necessary adjustments in collaboration with healthcare providers to optimize patient outcomes.

3. Monitoring and Follow-Up: Pharmacists are well-positioned to monitor patients' use of inhalation devices and their adherence to therapy. They can conduct follow-up assessments to:

- Identify and address issues related to incorrect inhaler techniques.
- Evaluate the effectiveness of the current treatment plan and make recommendations for changes if needed.
- Assess the impact of cognitive impairments on adherence and device use.

4. Collaborating with Healthcare Teams: As part of a multidisciplinary healthcare team, pharmacists collaborate with physicians, nurses, and respiratory therapists to ensure comprehensive care for patients with asthma and COPD. Their expertise in pharmacotherapy allows them to contribute valuable insights into medication selection and management strategies tailored to individual patient needs.

5. Tailored Device Selection: Pharmacists can assist healthcare providers in selecting the most appropriate inhalation device based on the patient's abilities, preferences, and specific medical conditions. This personalized approach can help mitigate the challenges associated with the variety of inhalers and ensure that patients receive devices that are manageable for them.

6. Research and Continuous Improvement: Pharmacists can contribute to research efforts focused on improving inhalation therapy adherence and outcomes. By staying updated on the latest evidence and guidelines regarding inhalation devices, they can advocate for best practices and help implement educational initiatives within their healthcare settings.

Conclusion

Inhalation devices, including nebulizers, pMDIs, and DPIs, are fundamental in managing asthma and chronic obstructive pulmonary disease (COPD). This updated review reveals that while these devices provide crucial therapeutic benefits, significant challenges remain regarding their correct usage and patient adherence. As asthma and COPD prevalence continues to rise, necessitating effective medication delivery methods, it becomes increasingly essential to optimize these devices' use and educate patients. The variability in device types and their operation can lead to substantial confusion among patients, contributing to poor adherence rates. Incorrect inhalation techniques are prevalent, with studies indicating that even with education, a considerable proportion of patients do not utilize these devices effectively. This trend highlights the need for standardized training protocols that emphasize not only the importance of inhalers in managing their conditions but also the techniques required for effective medication delivery. Furthermore, patient preferences play a significant role in adherence. Devices must be selected based on individual patient capabilities, preferences, and specific clinical needs. For instance, nebulizers may be better suited for patients with physical or cognitive impairments, while pMDIs and DPIs may be appropriate for others. Therefore, healthcare professionals must consider these factors during device selection and emphasize the importance of proper technique, as poor inhaler technique can lead to exacerbated symptoms and increased healthcare costs. Future strategies should prioritize comprehensive patient education initiatives, fostering a greater understanding of inhalation devices and their significance in managing asthma and COPD. Collaboration between healthcare providers, patients, and device manufacturers can enhance inhalation therapy's overall effectiveness. Ongoing research and innovation in inhalation technology are also crucial, ensuring that devices meet the evolving needs of patients while maintaining ease of use and effectiveness. Ultimately, addressing the barriers to proper inhalation device use and enhancing patient adherence will lead to improved health outcomes for individuals suffering from asthma and COPD, reducing the burden on healthcare systems and improving patients' quality of life.

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الملخص:

الخلفية :يعد الربو ومرض الانسداد الرئوي المزمن (COPD) من الحالات المزمنة الشائعة التي تؤثر بشكل كبير على تكاليف الرعاية الصحية وجودة حياة المرضى. تلعب العلاجات بالاستنشاق دورًا حاسمًا في إدارة هذه الأمراض، مع توفر مجموعة واسعة من الأجهزة لتوصيل الأدوية.

الهدف :تهدف هذه المراجعة إلى تحديث الفهم حول أجهزة النيبوليزر، البخاخات، ومقاييس التنفس في إدارة الربو وCOPD، مع تسليط الضوء على استخدام الأجهزة، وامتثال المرضى، والنتائج السريرية.

الطرق :تم إجراء مراجعة شاملة للأدبيات، مع التركيز على الفعالية، وسهولة الاستخدام، وامتثال المرضى المرتبط بأجهزة الاستنشاق المختلفة، بما في ذلك النيبوليزر، والبخاخات الجرعية المضغوطة(pMDIs) ، وبخاخات المساحيق الجافة .(DPIs) كما تم تحليل تفضيلات المرضى والأخطاء الشائعة التي يرتكبها المستخدمون.

النتائج :تشير النتائج إلى انتشار كبير للتقنيات غير الصحيحة للاستنشاق، مما يؤثر سلبًا على نتائج العلاج. على الرغم من السوق المتزايد لأجهزة الاستنشاق، لا يزال عدم الامتثال يمثل تحديًا، خاصة بين المرضى الذين يعانون من إعاقات معرفية. كانت الأخطاء الناتجة عن المستخدمين شائعة عبر جميع أنواع الأجهزة، مما يبرز الحاجة إلى تحسين تعليم المرضى واختيار الأجهزة الملائمة لقدرات الأفراد.

الخلاصة :يعد تحسين تقنيات الاستنشاق وتعزيز تعليم المرضى أمرًا أساسيًا لتحسين النتائج السريرية في إدارة الربو و .COPDينبغي أن تركز الاستراتيجيات المستقبلية على اختيار الأجهزة بشكل شخصي والدعم المستمر لتعزيز الامتثال والاستخدام الصحيح.

الكلمات المفتاحية :الربو، مرض الانسداد الرئوي المزمن، العلاج بالاستنشاق، أجهزة النيبوليزر، البخاخات الجرعية المضغوطة، بخاخات المساحيق الجافة، امتثال المرضى.