Journal of Pharmacovigilance and Drug Safety (JPDS)
ISSN (Print) : 0972-8899
DOI : 10.21276/JPDS

Journal of Pharmacovigilance and Drug Safety

An Official Publication of Society of Pharmacovigilance, India.

Review Article

Developments in Inhalational Devices: Consequences for the Treatment of Chronic Obstructive Pulmonary Disease

Vibhu Pandey[1], Jameel Ahmad[2]

[1]Junior resident,[2]Professor,
Department of Pharmacology,
J. N. Medical College, Faculty of Medicine, AMU, Aligarh, U.P

Received: 28.11.24
Accepted: 09.12.24

Corresponding Author

Dr. Jameel Ahmad
Assistant Professor,
Department of Pharmacology,
JNMC, AMU,
Aligarh (202002), U.P., India

ABSTRACT

Background: *Inhaled therapies are essential for managing symptoms and preventing exacerbations of Chronic Obstructive Pulmonary Disease (COPD), a cause of morbidity and mortality that is prevalent throughout the world. In order to enhance patient outcomes, innovative inhaler designs have been developed in response to limitations in classic inhaler technologies, such as inadequate drug delivery and poor adherence.* ***Objective:*** *This review focuses on advancements in smart inhalers, particle engineering, and usability enhancements, aiming to explore recent breakthroughs in inhaler technology and their potential impact on the management of COPD.* ***Methods:*** *A thorough literature review was performed to locate peer-reviewed studies, clinical trials, and reviews published in the last ten years. Focus was directed towards technologies that improve drug delivery, adherence monitoring, and patient usability.* ***Outcomes:*** *Innovative technologies, like smart inhalers, incorporate digital feedback and adherence monitoring, facilitating personalized treatment. Innovations in device design, such as soft mist inhalers and advanced dry powder inhalers, improve drug deposition efficiency and tackle patient-specific issues, including diminished inspiratory effort in elderly individuals. Enhanced usability features, such as optimized dose actuation mechanisms, have shown promise in improving adherence and minimizing errors.* ***Summary:*** *Advancements in inhaler technology offer transformative potential in COPD management, aligning with trends toward personalized and patient-centred care. By addressing barriers to effective therapy, these innovations improve drug delivery, enhance adherence, and reduce exacerbation rates. Further research is needed to integrate these technologies into routine clinical practice and assess their long-term impact on patient outcomes.*

Keywords: *COPD, inhaler technologies, smart inhalers, drug delivery, adherence, personalized medicine.*

How to cite this article: Vibhu Pandey *et al;* Developments in Inhalational Devices: Consequences for the Treatment of Chronic Obstructive Pulmonary Disease, J Pharmacovig Drug Safety, 2024;21(1):1-5.

Source of Support: Nil, **Conflict of Interest:** None.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) impacts more than 200 million individuals globally, constituting a considerable strain on healthcare systems and the quality of life of patients.[1] Management strategies emphasize symptom control, prevention of exacerbations, and deceleration of disease progression, with inhaled therapies serving as a fundamental component of treatment. Conventional inhalers, comprising pressurized metered-dose inhalers (pMDIs) and dry powder inhalers (DPIs), have demonstrated efficacy but are constrained by issues such as inadequate adherence, improper technique, and diminished drug delivery efficiency.[2] This review analyses novel inhaler technologies designed to address these limitations, thereby improving COPD management. Chronic Obstructive Pulmonary Disease (COPD) is defined by persistent inflammation, airway remodelling, and progressive restriction of airflow. Exacerbations and symptom variations are prevalent, caused by heightened airway resistance and hyperinflation. Efficient drug delivery to distal airways is essential for regulating inflammation, facilitating bronchodilation, and alleviating symptoms. Inhalers, as the principal drug delivery mechanism, guarantee the effective administration of

Access this article online	
Website: www.journalofsopi.com	**For Reprints**
DOI: 10.21276/jpds.2024.21.02.01	**Contact at editorjournalsopi@gmail.com**

medications such as bronchodilators and corticosteroids to the lungs. However, their efficacy relies on proper implementation and adherence.

Traditional inhalers face challenges related to diminished compliance stemming from device complexity and the likelihood of patient errors. Approximately 70% of patients improperly utilize inhalers, resulting in diminished therapeutic efficacy.[3] Common errors include inadequate coordination of inhalation with actuation in pressurized metered-dose inhalers (pMDIs) and insufficient inspiratory efforts in dry powder inhalers (DPIs).[4]

Conventional inhalers frequently exhibit inconsistent drug delivery, particularly in the small airways. The requirement for propellants in pressurized metered-dose inhalers (pMDIs) presents environmental issues; conversely, dry powder inhalers (DPIs) may be less efficacious in patients with significant airflow restriction.

A multitude of patient-related factors affects the device's efficacy. The improper use of the device is primarily influenced by age-related deterioration in dexterity and cognitive abilities. Comorbidities, such as arthritis, further restrict proper device handling in elderly populations.[4]

Advancements in Inhaler Technologies

1. Smart Inhalers

Smart inhalers incorporate digital technology to enhance patient adherence and simplifies the complexities of device operation. These smart inhalers incorporate embedded sensors and connectivity capabilities aimed at resolving issues associated with patient adherence and correct usage, prevalent in COPD management.[5] These inhalers are particularly beneficial for assessing patient adherence to their medication regimens. These sensors monitor critical parameters, including dosage consumption, inhalation flow rates, and the timing of inhaler activation. If a patient misses doses or uses improper technique, the inhaler records this data for assessment. The objective of incorporating embedded sensors into the design of smart inhalers is to monitor and document essential data regarding patient usage of their inhalers. The aim is to ensure accurate oversight of medication usage and administration, which are essential for effective COPD management.[6] The primary parameters tracked by these smart inhalers include dosage frequency, inhalation flow rates, and the timing of inhaler activation. The sensors maintain a log of each activation, ensuring patient compliance with their prescribed medication regimen. They monitor adherence to the prescribed medication regimen (e.g., twice-daily) and identify any missed doses. The sensors evaluate the intensity and uniformity of inhalation, facilitating the assessment of the drug's effective delivery to the lungs. An inadequate inhalation flow may suggest that the patient is not receiving sufficient medication, potentially compromising disease management. The device accurately logs the time a dose is administered, offering insights into patient adherence to their dosing regimen (e.g., taking medication consistently at the same time daily). Variations in timing may indicate possible adherence problems or imply the necessity for modifications in patient schedules. If a patient consistently skips doses or uses the inhaler improperly (e.g., not inhaling strongly enough), the inhaler logs this information. This information is retained for examination by the patient and healthcare professionals, facilitating focused interventions such as retraining on appropriate techniques or modifications to the treatment strategy.[6] The advanced smart inhalers are designed to seamlessly connect with smartphones via Bluetooth, enabling a two-way information exchange between the inhaler and the user. These novel devices exhibit essential functions by providing real-time feedback, allowing patients to receive immediate insights regarding their inhaler technique or adherence via a mobile application. The notifications can indicate improper usage, such as insufficient inhalation or missed doses, enabling prompt corrective actions. The inhaler functions as a medication reminder, equipped with programmed applications that dispatch alerts when it is time to administer a dose, thereby diminishing the probability of overlooked medications. These reminders can be customized to align with the patient's schedule and treatment protocol. The application offers a comprehensive record of previous inhaler usage, enabling patients to track their adherence patterns over time. A weekly or monthly adherence summary can aid patients in visualizing their progress and understanding the importance of consistency. The applications associated with these inhaler devices frequently incorporate educational components, including videos or detailed instructions, to instruct patients on the proper inhaler technique. They may also offer personalised recommendations based on specific usage patterns, such as modifying inhalation techniques for enhanced drug delivery.[7] The connectivity of these smart inhalers to smartphones enhances patient engagement by integrating reminders, feedback, and educational resources, thereby empowering patients to actively manage their condition. The documentation of patient usage data aids in comprehending the influence of proper technique on symptomatology and disease progression. The collected data from these inhaler devices can facilitate interventions provided by healthcare professionals. The data collected from patients' personal devices can be shared directly with healthcare providers, offering detailed insights into a patient's adherence and inhalation technique. For example, if a patient consistently fails to use the inhaler properly, the provider can offer targeted retraining or adjust the treatment plan. The timely interventions based on this data can help prevent exacerbations and improve disease control. Healthcare professionals can use the collected data from each device to make individualized treatment decisions, such as modifying the inhaler type, changing medication timing, or addressing issues like poor inspiratory effort. By addressing adherence and technique issues early, smart inhalers can significantly reduce the risk of COPD exacerbations, which are often caused by suboptimal medication delivery or missed doses.[8] The combination of embedded sensors and smartphone connectivity in smart inhalers revolutionizes COPD management by addressing adherence and usage challenges. These features not only empower patients to take control of their health but also enable healthcare providers to deliver personalized, data-driven care, improving outcomes and reducing healthcare costs.

The clinical impact of these smart inhalers has shown significant improvements in medication adherence-studies report adherence improvements of 20-30%. Regular use of these devices diminishes COPD exacerbations and decreases hospitalization days, thereby preventing missed doses, resulting in improved disease management and fewer complications. Immediate feedback aids patients in correcting improper techniques, thus improving patient involvement and education.

2. Soft Mist Inhalers (SMIs)

Soft Mist Inhalers (SMIs) signify a notable progression in inhaler technology, enhancing drug delivery efficacy and user-friendliness for individuals with chronic respiratory conditions such as COPD. In contrast to conventional inhalers, SMIs produce a slowly dispersing, fine aerosol mist through a spring-loaded mechanical mechanism instead of utilizing propellants. This design facilitates improved medication deposition in distal airways, which is essential for the effective management of conditions such as COPD.[9] A primary benefit of SMIs is their diminished reliance on inhalation technique. pMDIs necessitate exact synchronization between actuation and inhalation, whereas SMIs generate a gradual mist that patients can inhale effortlessly, markedly reducing the likelihood of improper technique. This feature renders SMIs especially advantageous for elderly patients or individuals with diminished inspiratory capacity, as conventional inhalers frequently do not achieve optimal outcomes.[10] Moreover, SMIs exhibit superior efficiency in medication delivery, attaining lung deposition rates of up to 60%, in contrast to the 10-20% achieved by pMDIs. This efficiency not only decreases the necessary dosage but also mitigates systemic side effects, enhancing patient safety and comfort.[11] Clinical trials have shown that SMIs, like the Respimat device, yield better results than conventional inhalers. Patients with COPD utilizing SMIs have demonstrated a reduction in exacerbations and enhanced lung function relative to those employing pMDIs or DPIs, especially among the elderly demographic.[12] Moreover, patients consistently express a preference for SMIs over alternative inhaler types due to their user-friendliness and the soothing, less irritating quality of the mist.[11] Despite these advantages, SMIs have specific limitations. They are generally more expensive than traditional inhalers, which may limit their accessibility, particularly in low-resource settings. Effective utilization necessitates appropriate training, although the learning curve is less pronounced compared to other inhaler types.[13] SMIs tackle significant challenges in inhaler utilization by improving drug delivery, diminishing reliance on inhalation technique, and decreasing total dosage requirements. With increasing clinical evidence validating their effectiveness, SMIs are set to become fundamental in the treatment of COPD and other chronic respiratory disorders.[14]

3. Advances in Dry Powder Inhalers (DPIs)

Dry Powder Inhalers (DPIs) have become a crucial advancement in respiratory treatment, providing an alternative to pressurized metered-dose inhalers (pMDIs). Recent advances in their design have addressed key limitations, such as the need for sufficient inspiratory flow and inconsistencies in drug delivery. These improvements have made DPIs more effective and user-friendly, especially for patients with severe COPD, who often struggle with traditional inhalers.[15] A significant development in DPIs is the formulation of engineered particles. Pharmaceutical researchers have enhanced aerosolization and deposition in the lungs by optimizing particle size, shape, and composition. These ultrafine particles improve delivery to the small airways, which are the primary site of obstruction in COPD. Engineered particles guarantee uniform drug efficacy irrespective of fluctuations in inspiratory effort, tackling a prevalent issue in patients with severe COPD.[16] A significant advancement is the integration of breath-actuated mechanisms. Conventional inhalers frequently necessitate manual synchronization of actuation and inhalation, posing difficulties for patients with diminished dexterity or cognitive abilities. Breath-actuated DPIs obviate this necessity by autonomously releasing medication upon patient inhalation. This mechanism enhances the usage process and ensures that the medication is delivered at the optimal point in the breathing cycle, thus maximizing lung deposition.[17] The influence of these innovations is significant. Next-generation DPIs provide markedly enhanced usability and drug deposition, even in patients with severe COPD who may exhibit impaired inspiratory flow. Clinical studies indicate that these devices improve pulmonary function and reduce the frequency of exacerbations by ensuring reliable and efficient medication delivery. Furthermore, they are associated with a decreased occurrence of side effects, as the improved delivery reduces drug accumulation in the oropharynx and systemic absorption.[18] Despite these advancements, some limitations remain. DPIs require a minimum inspiratory effort to effectively release the medication, which may still be challenging for the most severely affected COPD patients. However, continued research into particle engineering and device design is addressing this gap.[19] Advancements in DPIs, such as engineered particles and breath-actuated mechanisms, have markedly enhanced their efficacy and usability. These innovations are especially advantageous for patients with severe COPD, providing improved drug delivery, superior symptom management, and diminished exacerbation risk. As DPIs advance, they are poised to assume a more significant role in the individualized management of respiratory diseases.[20]

4. Particle Engineering and Aerosol Science

Progress in particle engineering has markedly enhanced the administration of inhaled therapeutics for chronic respiratory conditions such as COPD. A significant advancement in this field is the formulation of ultra-fine particles, which are tailored for improved deposition in narrow airways. These smaller particles have improved aerodynamic properties, allowing them to reach the peripheral parts of the lungs more effectively. This innovation resolves the problem of inadequate drug deposition, a constraint of previous inhaler technologies. Furthermore, the advancement of combination therapies, which administer bronchodilators and corticosteroids in a single inhaler, has improved patient convenience by minimizing the number of devices required for treatment. These advancements optimize treatment protocols and enhance adherence, which is essential for disease management.[21]

The implications of these innovations are substantial. Improving the targeting of medication to the lungs reduces systemic drug absorption, consequently lessening side effects like oral thrush or complications related to systemic corticosteroids. Improved lung deposition facilitates superior symptom management, thereby enhancing patients' quality of life.[22]

Patient-Centered Design Innovations

Modern inhalers increasingly incorporate ergonomic and accessible designs to cater to a diverse patient population. For individuals with reduced dexterity, such as those suffering from arthritis, inhalers featuring streamlined actuation mechanisms and enlarged dose counters enhance usability. Moreover, tactile feedback systems enable users to verify correct actuation, mitigating concerns regarding device misuse. To enhance user-friendliness for patients with visual impairments, clear labelling and auditory signals are incorporated into the devices.[13] Customization for specific needs is another area of innovation. Pediatric inhalers are engineered with reduced, age-appropriate dosages, whereas devices for elderly individuals or those with cognitive impairments typically incorporate auto-actuation or preloaded medication. Modular inhaler designs, adaptable to diverse inspiratory flow capacities, guarantee effective usage across all patient demographics.[17]

Integration into Personalized Medicine

The integration of inhaler technologies with digital platforms supports the broader trend toward personalized medicine. Smart inhalers equipped with data-tracking capabilities provide actionable insights into individual usage patterns. These data-driven interventions enable healthcare providers to identify adherence challenges, evaluate inhalation techniques, and customize treatment plans accordingly. Patients who regularly neglect doses can receive reminders via connected smartphone applications, enhancing accountability.[14]

Moreover, smart inhalers facilitate behavioral support by involving patients in self-management. Mobile applications linked to these devices frequently encompass educational resources, tailored advice, and progress monitoring tools. These features enable patients to comprehend their condition more effectively and comply with their treatment regimen.[23]

Barriers to Implementation

Despite their benefits, advanced inhaler technologies face several barriers to widespread adoption. The substantial initial expenses associated with smart inhalers and advanced devices may restrict their accessibility, especially in low-resource environments where cost is a significant issue. The dependence on digital platforms for smart inhalers presents a challenge for elderly patients or individuals lacking technological proficiency.[24]

A further concern is the absence of regulatory and standardization frameworks for these devices. Discrepancies in standards among manufacturers may result in interoperability challenges, hindering integration into clinical workflows and electronic health records.[25]

Future Directions

To fully realize the potential of advanced inhaler technologies, several key areas need further development. Comprehensive clinical trials are essential to determine the long-term advantages of these devices, encompassing their effects on exacerbation rates, patient quality of life, and healthcare expenditures. These trials would yield substantial evidence to facilitate regulatory approval and incorporation into treatment guidelines.[26]

The integration of telemedicine presents a promising opportunity. By integrating smart inhalers with telehealth systems, healthcare providers can oversee patient compliance remotely and implement immediate modifications to treatment regimens. This method is especially beneficial in the management of chronic diseases such as COPD, as ongoing monitoring can avert complications.[9]

There is an increasing emphasis on sustainability in the development of inhalers. Numerous companies are developing eco-friendly designs, including inhalers with reduced carbon footprints or recyclable components, to mitigate the environmental impact of respiratory treatments.[14]

CONCLUSION

Innovations in particle engineering, patient-centric design, and digital integration have transformed inhaler technologies, providing substantial advantages for COPD management. Despite the persistence of challenges including cost, technological literacy, and regulatory obstacles, continuous innovation and research are expected to mitigate these impediments. These technologies correspond with the transition towards individualized and sustainable healthcare, guaranteeing enhanced patient outcomes and ecological accountability.

REFERENCES

1. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, Nair H, Gasevic D, Sridhar D, Campbell H, Chan KY. Global and regional estimates of COPD prevalence: Systematic review and meta–analysis. Journal of global health. 2015 Dec;5(2).
2. Turégano-Yedro M, Trillo-Calvo E, Navarro i Ros F, Maya-Viejo JD, González Villaescusa C, Echave Sustaeta JM, Doña E, Alcázar Navarrete B. Inhaler Adherence in COPD: A Crucial Step Towards the Correct Treatment. International Journal of Chronic Obstructive Pulmonary Disease. 2023 Dec 31:2887-93.
3. Jardim JR, Nascimento OA. The importance of inhaler adherence to prevent COPD exacerbations. Medical Sciences. 2019 Apr 1;7(4):54.
4. Usmani OS, Lavorini F, Marshall J, Dunlop WC, Heron L, Farrington E, Dekhuijzen R. Critical inhaler errors in asthma and COPD: a systematic review of impact on health outcomes. Respiratory research. 2018 Dec;19:1-20.

5. Iwanaga T, Tohda Y, Nakamura S, Suga Y. The Respimat® soft mist inhaler: implications of drug delivery characteristics for patients. Clinical Drug Investigation. 2019 Nov;39(11):1021-30.
6. Chan AH, Pleasants RA, Dhand R, Tilley SL, Schworer SA, Costello RW, Merchant R. Digital inhalers for asthma or chronic obstructive pulmonary disease: a scientific perspective. Pulmonary Therapy. 2021 Dec;7(2):345-76.
7. Aung H, Tan R, Flynn C, Divall P, Wright A, Murphy A, Shaw D, Ward TJ, Greening NJ. Digital remote maintenance inhaler adherence interventions in COPD: a systematic review and meta-analysis. European Respiratory Review. 2024 Dec 4;33(174).
8. Zabczyk C, Blakey JD. The effect of connected “smart” inhalers on medication adherence. Frontiers in Medical Technology. 2021 Aug 18;3:657321.
9. Usmani OS, Levy ML. Effective respiratory management of asthma and COPD and the environmental impacts of inhalers. NPJ Primary Care Respiratory Medicine. 2023 Jul 1;33(1):24.
10. Lavorini F, Usmani OS, Dhand R. Aerosol delivery systems for treating obstructive airway diseases during the SARS-CoV-2 pandemic. Internal and Emergency Medicine. 2021 Nov;16:2035-9.
11. Abadelah M, Chrystyn H, Larhrib H. Use of inspiratory profiles from patients with chronic obstructive pulmonary disease (COPD) to investigate drug delivery uniformity and aerodynamic dose emission of indacaterol from a capsule based dry powder inhaler. European Journal of Pharmaceutical Sciences. 2019 Jun 15;134:138-44.
12. Mahler DA. The role of inspiratory flow in selection and use of inhaled therapy for patients with chronic obstructive pulmonary disease. Respiratory Medicine. 2020 Jan 1;161:105857.
13. Lavorini F, Chudek J, Gálffy G, Pallarés-Sanmartin A, Pelkonen AS, Rytilä P, Syk J, Szilasi M, Tamási L, Xanthopoulos A, Haahtela T. Switching to the dry-powder inhaler Easyhaler®: a narrative review of the evidence. Pulmonary Therapy. 2021 Dec 1:1-9.
14. Global Initiative for Chronic Obstructive Lung Disease (GOLD) Guidelines 2024.
15. Morais-Almeida M, Pité H, Cardoso J, Costa R, Cordeiro CR, Silva E, Todo-Bom A, Vicente C, Marques JA. Asthma management with breath-triggered inhalers: innovation through design. Asthma research and practice. 2020 Dec;6:1-1.
16. Abiona O, Wyatt D, Koner J, Mohammed A. The optimisation of carrier selection in dry powder inhaler formulation and the role of surface energetics. Biomedicines. 2022 Oct 26;10(11):2707.
17. Cataldo D, Hanon S, Peche RV, Schuermans DJ, Degryse JM, De Wulf IA, Elinck K, Leys MH, Rummens PL, Derom E. How to choose the right inhaler using a patient-centric approach?. Advances in therapy. 2022 Mar;39(3):1149-63.
18. Levy ML, Carroll W, Izquierdo Alonso JL, Keller C, Lavorini F, Lehtimäki L. Understanding dry powder inhalers: key technical and patient preference attributes. Advances in therapy. 2019 Oct;36(10):2547-57.
19. Muralidharan P, Hayes Jr D, Mansour HM. Dry powder inhalers in COPD, lung inflammation and pulmonary infections. Expert opinion on drug delivery. 2015 Jun 3;12(6):947-62.
20. Malmberg LP, Rytilä P, Happonen P, Haahtela T. Inspiratory flows through dry powder inhaler in chronic obstructive pulmonary disease: age and gender rather than severity matters. International journal of chronic obstructive pulmonary disease. 2010 Aug 9:257-62.
21. Negi A, Nimbkar S, Moses JA. Engineering Inhalable Therapeutic Particles: Conventional and Emerging Approaches. Pharmaceutics. 2023 Nov 30;15(12):2706.
22. Biddiscombe MF, Usmani OS. Is there room for further innovation in inhaled therapy for airways disease?. Breathe. 2018 Sep 1;14(3):216-24.
23. O'Connor A, Tai A, Brinn M, Hoang AN, Cataldi D, Carson-Chahhoud K. Co-design of an augmented reality asthma inhaler educational intervention for children: Development and usability study. JMIR Pediatrics and Parenting. 2023 Jul 25;6(1):e40219.
24. Gaikwad SS, Pathare SR, More MA, Waykhinde NA, Laddha UD, Salunkhe KS, Kshirsagar SJ, Patil SS, Ramteke KH. Dry Powder Inhaler with the technical and practical obstacles, and forthcoming platform strategies. Journal of Controlled Release. 2023 Mar 1;355:292-311.
25. Needham M, Cocks P, Righton L. Next-Generation Pressurised Metered Dose Inhalers: a Holistic, Patient-Centred Approach to Sustainability. ONdrugDelivery Magazine. 2020 Sep(112):10-3.
26. Raj A, Kumar A, Dames JF. Tapping the role of microbial biosurfactants in pesticide remediation: an eco-friendly approach for environmental sustainability. Frontiers in Microbiology. 2021 Dec 23;12:791723.