

Review on Problems/challenges that patients face with current inhaler devices and opportunities/future approaches for open innovations

Abdullahi A. Shamsuddeen^{1,*}, Gaddafi I. Danmaliki², Mustapha Gan³ and Mustapha G. Sulaiman⁴

¹*Department of Chemistry, Sokoto state University, P.M.B 2134, Sokoto state, Nigeria*

²*Department of Biochemistry, Usmanu Danfodiyo University, Sokoto, Nigeria*

³*Department of Microbiology, Sokoto state University, P.M.B 2134, Sokoto state, Nigeria*

⁴*Department of Chemistry, School of Applied Sciences, University of Huddersfield, HD1 3DH, UK*

Corresponding Author email: shamsudden.ahmad@ssu.edu.ng

Abstract: Inhalation is the most efficient route of delivery for chronic obstructive pulmonary disease and anti-asthma drugs. Different types of inhaler devices are used for the treatment of COPD and these includes; Nebulisers, Pressurised Metered Dose Inhalers (pMDIs), and Dry Powder Inhalers (DPIs). Many patients encounter problems of wheezing, chest tightness, cough, breathlessness among others. These problems occur either as a results of; incorrect choice of inhaler device, poor technique, wrong diagnosis, concurrent smoking, inadequate understanding and proper education on how to use the device, nonadherence etc. These review article highlighted the future approaches for innovations in order to counter these problems. Some of these innovations highlighted includes; use of teaching aids, use of complete electronic compliance monitoring, physical demonstration to patient on how to use the device and also giving complete education in the correct use of the device.

1.0 Introduction

An inhaler is a medicinal tool utilised for distributing medication into the body through lungs. It is mostly utilised in the therapy of chronic obstructive pulmonary disease (COPD) and asthma which are the most frequent respiratory conditions characterised by continuous airway inflammation and bronchial obstruction (Scichilone et al, 2015). There are different types of inhaler devices use for the treatment of chronic aforementioned diseases and the commonly used ones include; dry powder inhalers (DPIs), pressurised Metered dose inhalers (MDI) and nebulisers. Nebulisers, pressurised metered dose inhalers (MDIs) and dry powder inhalers (DPIs) each have advantages and disadvantages, depending on factors such as the patient's age, severity of condition, situation (e.g. hospitalised versus out-patient), and ability to operate the device. A different inhalation technique and breathing pattern is required for each type of inhaler to reach optimal delivery of drug to the lungs (Haughney et al, 2010).

1.1 Metered Dose Inhaler (MDI)

The pressurised MDI was the first portable and small piece of equipment for pulmonary drug delivery. The device consist of a metal canister, which contains the medication as a pressurised aerosol, with a crimped cap that contains the drug

metering valve, the system is enclosed in an actuator through which the drug is inhaled.

Table 1. Approaches on how to use the pressurised metered dose inhaler

S/No	Correct approach for using pressurised metered dose inhaler (pMDIs)
1	The cap of the inhaler mouthpiece should be taken off
2	Inhaler should be shake
3	The device should be hold upright
4	Patient should breath out all the way
5	Patient should place the device mouth piece between the lips
6	The inhaler should be fired after starting a very slow and very deep breath in
7	Continue to breathe in very slowly until your lungs are full
8	Remove the inhaler from your mouth and hold your breath while counting to 10 or as long as possible
9	Breathe out slowly

(Sanchis et al, 2013)

Limitations of this device include; there is no risk of contamination of the lungs using this device and dose-to-dose reproducibility is high but inaccurate drug delivery can also be caused by the drug deposit on the device parts (Kaialy, &Nokhodchi, 2015)

1.2 Nebulisers

Until the pressurised MDI was developed in 1955, nebulisers were the only free device for delivering inhaled aerosol drugs. Various types are in use today, particularly pneumatic jet nebulisers, which are powered by a gas source that aerosolises the drug solution and delivers it to the patient via a mouthpiece or face mask. These are widely utilised to treat patients unable to utilize a portable inhaler due to lack of co-ordination, in cases such as disability, infancy, hospitalisation or severe illness. Limitations of this device include; the device has the ability to provide high doses to seriously ill patient but its limitation is high cost, risk of epidemic and degradation (Cazzola et al, 2012)

1.3 Dry powder inhalers (DPIs)

DPIs are breath-actuated, lowering the need for patients to co-ordinate their breathing and device actuation exactly. These equipmentalso offer portability and fast treatment time, but do not require propellants and newer designs incorporate dose counters.

Table 2. Procedures for using DPIs

S/No	Correct procedure for using dry powder inhaler
1	The mouthpiece cover should be remove
2	Sit upright or stand
3	Prime the inhaler according the manufacturer's instructions
4	Exhale completely, away from the mouthpiece
5	Put the mouthpiece between your teeth and close your lips around it
6	Inhale as rapidly and forcefully as possible, attempting to breathe in faster as you go
7	Take the inhaler out of your mouth
8	Hold your breath for about 10 s or as long as you can
9	Breathe out slowly.
10	Replace the cover

(Laube et al, 2011; Sanchis et al, 2013)

Table 1 above highlighted the correct approaches on how to use DPIs. Advantage and limitation of this device are;it does not need propellant andit is suitable and simple to use but its disadvantages is the molecular property of an active ingredients when drug formulations are in suspension, can cause it to combine with the canister, resulting in drug deposition on the canister wall (Kaialy, &Nokhodchi, 2015)

Good inhalation capacity requires many characteristics such asease of processing, stability, reproducibility and availabilityat the site of action. Particle deposition in the respiratory tract is affected by many physical properties of the aerosol such as size, density, shape and flowability (Kaialy, &Nokhodchi, 2015; Telko, & Hickey, 2005).

In recent years, different transformations have improved the performance and efficiency of the inhaler devices. In association with the technological advancement, the significance of patient ability to utilise the device properly and the teaching part of the physician herein, received much acknowledgement. On top of this, new device substances have been advanced, such as substances characterized by a prolonged time of action. Therefore, the advancement of inhalation treatment enlarged inside pharmaceutical companies active in the discipline, frequently - but not repeatedly - associates a new instrument with a new functional substance (Ninane et al, 2015; Lavorini, 2014;Cazzola et al, 2012).

2.0Patient challenges with current inhaler devices and future innovations

Inhalation is the best route of delivery for chronic obstructive pulmonary disease (COPD) and anti-asthma drugs. The inhaled route offers a more rapid onset of action

as therapeutic agents are administered directly to the lungs, allows smaller doses to be utilised and has a better efficacy to safety ratio in contrast to systemic therapy (Virchow, 2008; NHLBI, 2006). Although, the present level of asthma handling falls short of these goals worldwide for long-term management. Regardless of the availability of effective therapies, asthma remains a disease that is insufficiently controlled. Numerous patients with usual symptoms of asthma complain of wheezing, breathlessness, chest tightness, cough, asthma related sleep disturbance and require unscheduled vital care visits and emergency hospital admission due to asthma exacerbations (Virchow, 2008; Rabe et al, 2004). All of these problems that patient encounter are as a result of either; incorrect choice of inhaler device or poor technique, intentional or unintentional nonadherence, wrong diagnosis, concurrent smoking, under treatment, or lack of understanding and proper education on how to utilise the device etc. The purpose of this literature search was to highlight the challenges that patient face with current inhaler devices and to come out with future approaches for innovations in order to overcome these problems. These challenges and future innovations are highlighted as follows;

2.1 Lack of patient education and understanding on how to use an inhaler device

Patients play a major role in determining the triumph or failure of treatment. Education entails demonstration, simplification, and repetition should include comprehension of why the patient needs the inhaler, how the inhaler works, and the steps required to use it correctly (Virchow et al, 2008).

Old patients often suffer from cognitive impairments, visual problems or hearing or other physical disabilities (e.g., tremors, arthritis, and poor coordination) that significantly affect their capacity to comprehend and follow treatment regimens (Sanchis et al, 2013).

Malani and his co-workers in (2011) discovered that 54 % of out-patients were unable to use a pMDIs efficiently after the directives has been read to them or having the correct use of pMDI demonstrated to them. Common challenges experienced by patients using pMDIs included stopping inhalation upon release of the aerosol (24 %), deficiency coordinating aerosol release with inspiration (54 %) and inspiring through the nose whilst actuating the inhaler in the mouth (Melani et al, 2011).

Some healthcare professionals generally lack the acceptable knowledge and skills in using different inhaler technique, for this reason, academic and educational interventions should be design to train the trainer and also healthcare professional inhaler knowledge should be improve (Price et al, 2013). Pharmacist should be employed/assign in to show the patients on how to use the inhaler because research has revealed that pharmacist who participated in a single session education

workshop showed considerably better knowledge and skills than a control group and that this education was retained at a very high level (Price et al, 2013).

Verbal and written instructions, inhaler education intervention, physical demonstrations, strategies for enhancing efficacy of inhaler such as; use of training aid, use of multimedia computer presentations and telepharmacy counselling with an interactive video should be delivered by trained community pharmacist so as to significantly enhance the patient inhaler technique (Price et al, 2013). Another future innovation that should be taken to overcome most of this problems is to give complete education to the patients on how to use the device so that they use the instrument properly, use correct inhaler tool, identify when the canister is empty and of extremely important, take the medications as they have been authorised (Redding, 2010; Rubin, 2010). Another basic concept is the nature of the education conveyed. Verbal instruction combined with physical demonstration has been found to be the most effective patient training technique in the correct use of inhaler (Price et al, 2013). Repeating this education overtime increases the proportion of patients returning to follow-up visits who maintained correct technique (Redding, 2010).

The role of healthcare experts in inhaler use is critical both in achieving initial correct inhaler system, furthermore in maintaining this correct use over time. Inhaler device training should be delivered to patients by healthcare experts. Skill level, frequency and nature should be illustrated. System validation of training and inhalation assessment should additionally be proposed for healthcare experts who prescribe inhalers (Walsh et al, 2011).

2.2 Non-adherence to prescriptions by patient

The unwitting non-adherence that happens when a patient does not know the correct inhaler technique or does not comprehend the difference between a rescue and controller medication is common in real life. The vast majority of patient challenges to current inhaler devices are as a result of non-adherence because they overlooks prescriptions. Adherent patients take medications as recommended, whereas “non-adherent” patients neglect regardless of their willingness and acceptance of therapy (Melani et al, 2011).

The issue of patient age is particularly essential in unintentional non-adherence. Young children generally rely on others for delivery of drugs and most of the time they are unable to communicate their perception of symptom severity (Ninane et al, 2015). In these patients, the common utilisation of nebulizers makes the administration of asthma drugs particularly tedious and time consuming. However, other factors, including fear of stigmatisation at school, fear of side effects, and fear of dependence can significantly decrease adherence in school-age children. As psychological distress is connected with non-adherence, accurate screening for

unhealthy behaviours should be part of a comprehensive approach to adolescents with asthma (Laube et al, 2011). In elderly patients, unintentional non-adherence to inhalation therapy represents another issue that may lead to significant impairment of symptom control (Cordts and Steckel, 2012).

To overcome these problems for future innovations, adherence is critical for the clinical outcomes, as well as correct device, and this has driven demand for more user-friendly devices. Treatment effectiveness is strongly dependent on the willingness and capacity of the patient to perform the prescribed therapy, particularly for chronic or long-term therapies. Training and practice are required to enhance delivery of the inhaled drug to the targeted site. Unfortunately, this aspect is often ignored in daily practice and can negatively influence the outcomes (Scichilone et al, 2015).

Electronic compliance monitoring and motivation (automated) reminders can be a helpful solution for patients that choose to refrain from taking the drugs, to only take the medication from time-to-time or to knowingly utilise the wrong inhalation device. The reasons for patient conduct should also be addressed (Price et al, 2013). Patients should also be offered a self-monitoring system and a tool which will enable a professional instructor to provide feedback. In the future electronic monitoring and evaluation systems used in combination with inhalation devices will make this much easier to achieve (Kaialy and Nochodchi, 2015). Biomarkers identification which could deduce the dose of medication received by target tissues could also be a potential future research objective (Madkour, & Galal, 2015).

2.3 Poor inhaler device or incorrect choice of the device

Inhaler plays an important role in the management of chronic respiratory diseases. The choice of the device by the patient can be essential as the choice of the medication. Ideally, patient should utilise one device for all their inhaled therapies but most patients were given the wrong device for the right reason and that has caused an issue of the medication unable reach the targeted site (Crompton et al, 2000). Frequently patients face problems of poor coordination, sore throat (large portion of the medication will be deposited back to the mouth instead of the lungs), absence of dose counter to some inhaler devices etc. (Dekhuijzen et al, 2014).

Poor inhaler device leads to poor treatment response. Any enhancement in inhalation therapy therefore has the potential to enhance the outcome of asthma therapy without introducing excessive new equipment modalities (Virchow et al, 2008). Not all patients accomplish reasonable control with currently available prescription, but there is little evidence to suggest that new medications which are currently under development will put the disease in complete remission in the majority of patients (Virchow et al, 2008).

Lack of inhaler instructions and poor inhaler devices are a major cause of poor disease control, influencing as they do the most of drug that reaches the lung for treatment. Consequence of poor inhaler devices include a decrease in pulmonary deposition with a concomitant reduction in bronchodilator effect. This is a regrettable situation since the inhaled medication are the most effective therapy available for COPD and asthma (Melani et al, 2011).

Enhancement in inhaler innovation and design in combination with improvement in both patient and physician training can be the way forward in improving asthma management and control. In other words, an old but well known medication in a new, reliable inhaler is probably more useful than a new drug in an old inhaler device (Cordts, &Steckel, 2012)

Pressurised metered dose inhaler is the most frequently prescribed inhaler device worldwide despite the fact that most patient can't utilise it effectively. This is because pMDIs require good coordination of patient inspiration and activation to ensure correct inhalation and deposition of medication in the lung (Cordts, &Steckel, 2012). Patient mostly fail to continuously inhale slowly after activation of the inhaler. In addition patient often activate the device before inhalation or at the end of inhalation and conclude inhaler activation while breath-holding (Scichilone et al, 2015). Several improvements for future innovations should be made in pMDIs, improvements such as a change in propellant and actuation/coordination, so as to improve the deposition of medication in the lung (Melani et al, 2011)

A research of pMDI use in a group of 115 asthmatics demonstrated that 72 % of patients who received no directions were unable to use their device effectively compared to 45 % after physician training. Another research carried out in 207 patients uncovered that almost half of the patients (47 %) utilised their pMDIs insufficiently, ladies more frequently than men. Similarly, a Spanish investigation in patients, nurses and physicians (N = 1640) demonstrated that 91 % of patients were unable to use their pMDIs effectively compared with 85 % and 72 % of nurses and physicians respectively (Madkour, &Galal, 2015)

Larger devices which can be handheld effectively and which have clearer displays and larger actuators should be prescribe to elderly patients and younger patients may profit from using smaller devices for technical delivery systems (Giraud and Roche, 2002).

In real-life clinical settings, doctors often discuss on the properties of different drugs with their colleagues and patients, in order to agree on the best possible choice for the patient, whereas little thought is given to the properties of different inhalers and that has caused lots of problems to patients. Scichilone and his co-workers, (2015) highlighted that priority should be given to the choice of the appropriate technique,

based on patient needs and expectations, followed by the choice of the medication, based on the disease and its severity. The task force of the International Society for Aerosols in Medicine (ISAM) and the European Respiratory Society (ERS) provides a consensus statement and clear recommendations for choosing the best aerosol delivery device based on a level of inspiratory flow, patient's actuation-inhalation coordination and other clinical conditions; choosing the correct device is the primary step for optimal control of the disease (Scichilone et al, 2015; Laube et al, 2011).

Conclusion

Inhalation is the preferred route of delivery for anti-asthma and chronic obstructive pulmonary disease (COPD) drugs. The present level of asthma and COPD control worldwide now falls short for long-term management. In spite of the availability of effective therapies, asthma remains an illness that is insufficiently controlled. Challenges that patients experience are as a results of either; poor technique or incorrect choice of inhaler device, intentional or unintentional nonadherence, concurrent smoking, wrong diagnosis, under treatment, or lack of awareness and proper education on how to use the inhaler devices. This literature highlighted future approaches for innovations in order to overcome these problems. Approaches like improvement in inhaler technology and design in combination with improvement in both patient and physician education can be the way forward in improving asthma management and control, Electronic compliance monitoring and motivation (automated) reminders can be a helpful solution for patients that decides to refrain from taking the medication, to only take the medication from time-to-time or to knowingly use the wrong inhalation technique etc.

References

1. Cazzola, M., Page, C. P., Calzetta, L., & Matera, M. G. (2012). Pharmacology and therapeutics of bronchodilators. *Pharmacological reviews*, 64(3), 450-504.
2. Cordts, E., & Steckel, H. (2012). Capabilities and limitations of using powder rheology and permeability to predict dry powder inhaler performance. *European Journal of Pharmaceutics and Biopharmaceutics*, 82(2), 417-423.
3. Crompton, G. K., Dewar, M. H., Allbutt, H. M., & Innes, J. A. (2000, December). Inhaler preference and technique in inhaler naive subjects; a comparison of HFA and conventional devices. In *Thorax* (Vol. 55, pp. A61-A61). BRITISH MED ASSOC HOUSE, TAVISTOCK SQUARE, LONDON WC1H 9JR, ENGLAND: BRITISH MED JOURNAL PUBL GROUP.

4. Dekhuijzen, P. R., Bjermer, L., Lavorini, F., Ninane, V., Molimard, M., & Haughney, J. (2014). Guidance on handheld inhalers in asthma and COPD guidelines. *Respiratory medicine*, 108(5), 694-700.
5. Giraud, V., & Roche, N. (2002). Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *European Respiratory Journal*, 19(2), 246-251.
6. Haughney, J., Price, D., Barnes, N. C., Virchow, J. C., Roche, N., & Chrystyn, H. (2010). Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory Medicine CME*, 3(3), 125-131.
7. Islam, N., & Gladki, E. (2008). Dry powder inhalers (DPIs) – a review of device reliability and innovation. *International Journal of Pharmaceutics*, 360(1), 1-11.
8. Kaialy, W., & Nokhodchi, A. (2015). Dry powder inhalers: Physicochemical and aerosolization properties of several size-fractions of a promising alternative carrier, freeze-dried mannitol. *European Journal of Pharmaceutical Sciences*, 68, 56-67.
9. Lavorini, F. (2014). Inhaled drug delivery in the hands of the patient. *Journal of aerosol medicine and pulmonary drug delivery*, 27(6), 414-418.
10. Laube, B. L., Janssens, H. M., de Jongh, F. H., Devadason, S. G., Dhand, R., Diot, P., & Chrystyn, H. (2011). What the pulmonary specialist should know about the new inhalation therapies. *European Respiratory Journal*, 37(6), 1308-1417.
11. Madkour, A., & Galal, I. (2015). Do Egyptian patients use their inhalers correctly? A checklist auditing for inhalation devices usage techniques. *Egyptian Journal of Chest Diseases and Tuberculosis*, 64(2), 497-504.
12. Melani, A. S., Bonavia, M., Cilenti, V., Cinti, C., Lodi, M., Martucci, P., & Neri, M. (2011). Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respiratory medicine*, 105(6), 930-938.
13. National Heart Lung and Blood Institute. (2006). Global initiative for asthma: global strategy for asthma management and prevention. NHLBI. In *WHO Workshop Report* (No. 95-3659).
14. Ninane, V., Vandevoorde, J., Cataldo, D., Derom, E., Liistro, G., Munghen, E., & Vincken, W. (2015). New developments in inhaler devices within pharmaceutical companies: A systematic review of the impact on clinical outcomes and patient preferences. *Respiratory medicine*, 109(11), 1430-1438.
15. Price, D., Bosnic-Anticevich, S., Briggs, A., Chrystyn, H., Rand, C., Scheuch, G., & Inhaler Error Steering Committee. (2013). Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respiratory medicine*, 107(1), 37-46.

16. Rabe, K. F., Adachi, M., Lai, C. K., Soriano, J. B., Vermeire, P. A., Weiss, K. B., & Weiss, S. T. (2004). Worldwide severity and control of asthma in children and adults: the global asthma insights and reality surveys. *Journal of Allergy and Clinical Immunology*, 114(1), 40-47.
17. Redding, G. J. (2010). Childhood bronchiectasis around the world. *Paediatric Respiratory Reviews*, 11, S73.
18. Rubin, B. K. (2010). Aerosol deposition and effectiveness: it's more than particle size. *Paediatric Respiratory Reviews*, 11, S25.
19. Sanchis, J., Corrigan, C., Levy, M. L., & Viejo, J. L. (2013). Inhaler devices—from theory to practice. *Respiratory medicine*, 107(4), 495-502.
20. Scichilone, N., Benfante, A., Bocchino, M., Braido, F., Paggiaro, P., Papi, A., & Sanduzzi, A. (2015). Which factors affect the choice of the inhaler in chronic obstructive respiratory diseases? *Pulmonary pharmacology & therapeutics*, 31, 63-67.
21. Telko, M. J., & Hickey, A. J. (2005). Dry powder inhaler formulation. *Respiratory care*, 50(9), 1209-1227.
22. Turner Richard, (2009) *Developments in respiratory delivery*, Available at: http://www.manufacturingchemist.com/technical/article_page/Developments_in_respiratory_delivery/43321 (Accessed: 15th November, 2015).
23. Virchow, J. C., Crompton, G. K., Dal Negro, R., Pedersen, S., Magnan, A., Seidenberg, J., & Barnes, P. J. (2008). Importance of inhaler devices in the management of airway disease. *Respiratory medicine*, 102(1), 10-19.
24. Walsh, J., Bickmann, D., Bretkreutz, J., Chariot-Goulet, M., & European Paediatric Formulation Initiative. (2011). Delivery devices for the administration of paediatric formulations: overview of current practice, challenges and recent developments. *International journal of pharmaceuticals*, 415(1), 221-231.