



INHALER THERAPY IN ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Asthma and chronic obstructive pulmonary disease (COPD) are obstructive lung diseases that are characterized by chronic inflammation and an increase in mucus production and are highly prevalent conditions. Despite recent advances and multiple available therapies, there remains a significant unmet medical need. Over the past 40 years, the introduction of new classes of safe and effective therapy is insufficient. In spite of the high burden of asthma and COPD among patients, there are fewer new approved therapies in comparison to cardiovascular, metabolic and neurological diseases due to few drug candidates and a higher failure rate in the development of respiratory medicine. Lung diseases are among the leading causes of death globally with asthma being one of the most prevalent respiratory diseases, which affects people of all ages but, despite effective therapies available, many patients are poorly controlled and have a low quality of life. COPD is currently ranked as the fourth cause of death worldwide and predicted to become the third leading cause of death in 2030. The development of more effective treatments is urgently needed in order to reduce the high mortality rate and the enormous suffering from asthma and COPD. Various inhalation devices with different classes of medications are the foundation as therapies in both asthma and COPD. This article gives a comprehensive review of promising inhaled therapies in the treatment of asthma and COPD.

KEYWORDS: Asthma, Bronchodilator, Chronic obstructive pulmonary disease, Inhalation.

INTRODUCTION

Asthma and chronic obstructive pulmonary disease (COPD) are common chronic conditions that comprise approximately 78% of direct health care costs associated with respiratory diseases in the European Union.^[1] In the UK alone, 5.4 million patients are currently receiving treatment for asthma; of these, 1.1 million are children.^[2] Over three million people die of COPD worldwide each year, an estimated 6% of all deaths worldwide.^[3] The delivery of drugs by inhalation is an integral component in the treatment and management of patients with both diseases. Over the past 30 years, there has been unprecedented growth in the market for inhaled therapy, with annual sales having increased from \$7 billion in 1987 to \$36 billion in 2014 and with over 90 billion inhaled doses prescribed to patients in a single year.⁴ Unlike systemic treatments, inhaled medicines are rapidly directed to the airways, allowing for rapid onset. Targeting a drug directly to the lungs allows for lower doses to be administered, limiting potential side effects. There is a large choice of inhalers; in 2011, more than 230 different device-drug combinations were available to prescribers in Europe, with 48 different inhaler products

in the UK alone, each with its own specific design characteristics.^[4,5] The most common device types sold in Europe in 2011 were pressurized metered-dose inhalers (pMDIs; 47.5%), followed by dry powder inhalers (DPIs; 39.5%) and nebulizers (13%), although distribution between inhalers differed considerably between countries. Therefore, choosing the most appropriate device to meet individual patient needs is an important consideration in clinical practice.^[6]

Inhalation devices in asthma and COPD

A Variety of different drug and inhaler combinations are available for the management of asthma and COPD, thereby increasing the likelihood of finding an appropriate option for each individual patient.^[7] Inhaler devices vary in several ways, including how the inhaler dispenses the medication, whether the treatment is passively or actively generated (eg, using propellant, mechanical, or compressed air), aspects of the drug formulation (eg, solution, dry powder, or mist), whether the inhaler contains medication in a single- or multi-dose, and whether the device is disposable or refillable. Each inhaler device also has unique design

characteristics, meaning that there is the option to tailor choice to meet the patient's specific needs.^[8]

Dry powder inhalers

DPIs were first introduced in 1970, and the earliest models were single-dose devices containing the powder formulation in a gelatine capsule, which the patient loaded into the device prior to use. Since the late 1980s, multi-dose devices have been available, giving the same degree of convenience as a pMDI.^[9]

All currently marketed DPIs are breath-actuated and no propellants are needed to generate the aerosol.^[10] The patient's inhalation through the device is used to disperse the powder formulation and to deliver it into the lungs. However, patients can make crucial errors with a DPI; for instance, by failing to load a dose correctly or by exhaling into the DPI so that the dose is blown away.^[11] Unless clearly instructed, some patients might not know that they must firmly seal their lips around the mouthpiece, causing them to attempt an "open mouth" inhalation technique that will not deliver any dose. The Turbuhaler™ DPI, and possibly other DPIs in which doses are metered from a bulk powder reservoir, must be kept upright (held vertically) when loading a dose before inhalation, so that the dosing chamber will fill under gravity.^[12]

Soft mist inhalers

The development of soft mist inhalers (SMIs) has opened up new opportunities for inhaled drug delivery. SMIs use liquid formulations similar to those in nebulisers, but are generally multi-dose devices that have the potential to compete with pMDIs and DPIs in the portable inhaler market. While a number of SMIs are known to be in development,^[13] the only device currently marketed is Respimat[®] Soft Mist™ Inhaler (Boehringer Ingelheim GmbH & Co. KG, Ingelheim, Germany). This device contains sufficient doses of a bronchodilator formulation for 1 month's dosing, stored in a fluid reservoir.^[14]

Inhaler device preferences

After demonstration and self-testing of all 10 placebo inhaler devices, 41% of the study participants chose one of the devices they already used in everyday life as a preference. This might have an impact on the further results. 7.6% opted for an inhaler they had used in the past and another 50.4% preferred an inhaler they had never used. Multi-dose dry powder inhalers (Diskus[®], Forspiro[®], Genuair[®], Nexthaler[®], Spiromax[®], Turbuhaler[®]) were favoured significantly more often than other inhaler devices ($p = 0.017$).^[15]

Limitations

We prospectively collected data from a sample of hospitalized and ambulant asthma and COPD patients. Our study offers insight into eliciting possible patient preferences for inhaler devices. Nevertheless, the results should be interpreted within the context of study limitations. This is a cross-sectional clinical study. This

means that the data were collected at a single point in time. As a result, the study gives a less comprehensive impression than a longer-term observation.^[16] Based on our results, no statement can be made as to whether the error rates in device use or inhaler preferences change over time. Because correct handling of an inhaler prescription is usually only checked once, but not repeatedly, by a healthcare professional, the design we chose may most closely reflect real life. Both inpatient and outpatient treatments were included. Since this is a monocentric study, a bias in patient recruitment cannot be ruled out, and results may not be extrapolated to other regions and populations.^[17]

Our study examined widely used, but not all, inhalers available on the German market. With a total of 10 devices, a large number of different inhalers was tested in order to get the most comprehensive picture possible. However, this also meant that patients had to answer a variety of questions.^[18] Though randomizing the demonstration and testing order of the devices, signs of fatigue in the test subjects with the devices queried later cannot be ruled out and may have resulted in less variance in results between devices.^[19] Asthma and COPD patients were not naive to inhalation therapy. Therefore, it would be beneficial to know how dry-powder inhaler design interacts with the airway dynamics of patients.^[20,21]

Pressurised metered-dose inhalers plus spacer devices

Spacer devices are attachments to the inhaler mouthpiece with a volume ranging from 20–750 mL. Their design and performance has been discussed in detail elsewhere.^[21,22] Many have a one-way valve in the mouthpiece, which prevents the patient blowing the dose away after firing. However, inhalation must be strong enough to trigger the one-way valve; otherwise, no dose will be delivered. Spacers overcome coordination problems because inhalation can take place either as the device is fired into the spacer or after a short pause, with the latter method being recommended for some models.^[23] Cold Freon problems are unlikely with spacer devices because the point of aerosol generation is more remote from the mouth compared with a pMDI. Tidal breathing from the spacer after firing a dose may be acceptable for some models^[24] but multiple actuations, long delays between firing and inhaling, and the accumulation of static charge on some plastic spacer devices are likely to reduce the dose available for inhalation.^[25,26] Ideally, each pMDI dose should be inhaled separately from the spacer. Specific handling and washing techniques for different spacers are generally recommended to minimize static charge build-up. While spacers are good drug-delivery devices, they suffer from the obvious disadvantages of making the entire delivery system less portable, compact and convenient than a standard pMDI.^[27]

CONCLUSION

A variety of inhaler devices are now available to deliver Inhaled drugs to patients with COPD. The inhaled drug Delivery field is a dynamic one, with many inhalers available Already and new ones being introduced on a regular basis. The Plethora of inhaler devices available, requiring different Inhalation techniques for optimal drug delivery, may confuse patients and healthcare providers alike, a situation described as “device dementia”.

Drug delivery from all inhaler devices depends on how the patient prepares the device and then inhales from it. The relative difficulties in completing these two steps correctly can be shown on a scale, with pMDI being the easiest to prepare (and hardest to inhale from correctly) and nebulizers at the opposite end.

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