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Poor Inhaler Adherence and Techniques – How Can We Improve It?

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Abstract

Purpose of Review Chronic obstructive lung disease is a leading cause of death and morbidity in the elderly. Inhaled therapy is the mainstay of treatment (Global Strategy for diagnosis, management and prevention of chronic obstructive lung disease, 2020). There has been a significant growth in the number of new inhaler devices. These devices are ever-improving and welcomed. This brings an increasing challenge of choosing the right device for the patient. Non-adherence has been shown to have a significant effect on morbidity and mortality. Recent research has shown that COPD patients with poor adherence and technique have a higher mortality and tend to be elderly, have impaired cognitive function and greater co-morbidities (Vestbo, et al., Thorax 64:939-43, 2009; Cushen, et al., Am J Respir Crit Care Med 197:1630-1633, 2018). This article is a review of inhaled therapy devices available. In particular it looks at challenges in the elderly population and approaches to same.

Recent Findings Recent research has worked to try to understand and overcome challenges with inhaler adherence and techniques. In particular attention is turning to use of inhaler sensor technology. Improved nebulised technology including long acting pharmacological treatments are also providing new solutions to these challenges.

Keywords Inhaler · Elderly · Geriatric · Adherence · Poor inhaler technique · Obstructive lung disease inhalers

Introduction

Inhaled therapy devices have been in development as far back as ancient Egyptian times [4]. Despite the emergence of many inhalation therapy devices, particularly over the last three decades, there are still many challenges both financially and with clinical outcomes. Billions of dollars are estimated to be lost in the United States each year due to incorrect device use [5]. There is evidence that incorrect use of inhalers is higher in the older population [6]. In 2009 Vestbo et al. looked at adherence with inhaler treatment, via assessing dose counters. This was an analysis of the TORCH study data, a large multi centre randomized placebo control led trial (6112 patients). It found that inhaler adherence was associated with significantly reduced risk of death and hospital admission in exacerbations of COPD. 11.3% of good adherence patients died compared to 26.4% with poor adherence [2••]. With evidence that both adherence and technique tend to be lower in the elderly, it is important to understand why and how we can improve inhaled drug delivery in this population.

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Inhaled Therapy Devices - an Overview

Successful delivery of an inhaled drug is dependent on many important factors which help to understand why it is not often as simple as it first looks. The three principle inhaled therapy targets, inhaled corticosteroid (ICS) receptors, bronchodilator receptors for long acting muscarinic receptors (LAMA) and long acting beta agonists (LABA) are present throughout the lung. Receptors for LAMA/LABA drugs are predominantly in the conducting airways which facilitate air delivery but not gas exchange. ICS receptors are present in all airways including gas exchange areas i.e. alveoli which extend to the lung peripheries. Appropriate sized particles, follow a generated airstream to the lung with minimum deposition to oropharynx and larynx. This successful delivery is dependent on many factors including inspiratory effort and timing and also breath holding after inhalation is important to enhance deposition in the peripheral airways. Non deposited particles are exhaled [7].

There are now four principle ways to deliver inhaled therapy in modern day medicine, pressurized metered dose inhalers (pMDIs), dry powder inhalers (DPIs), soft mist inhalers (SMIs) and nebulisers, (see Table 1 below). There are online video resources to help familiarize oneself with the ever growing number of inhaler devices [8].

pMDIs were first introduced in 1956. In the late 1980s the breath-actuated pressurized metered-dose inhalers (BA-pMDI) were developed to try to overcome one of the main challenges with pMDIs, the coordination required between actuation and inhalation. DPIs were first available in the 1940s and there are now three main categories as shown in Table 1. They require a greater inspiratory effort than the pMDI but less coordination. It was not until the 1990s that DPI development really emerged with second generation pre loaded inhalers. SMIs which deliver the aerosolised drug as a fine mist at a slow velocity first became commercially available in 2004 [4, 9, 10].

Nebulisers were a significant advancement in inhaled therapy, producing a fine droplet form of the medication for inhalation. They have been in development since the mid-1800s the first model being a jet nebuliser, a technology commonly in use today. While widely used its main drawback is the time required for dose delivery. Ultrasonic nebulisers were next developed using piezo electric crystals generating aerosol particles.

Although quieter and faster than jet nebulisers they are not suitable for delivery of all drugs, particularly heat labile compounds. The latest development in nebulisers is vibrating mesh design which is more efficient for drug delivery as well as being quiet and portable [10, 11].

Challenges in the Elderly

In older patients inhaler use can be challenging due principally to physical, sensory and cognitive decline. These patients may have difficulty in correctly using a handheld device due to poor fine motor control or weakness resulting from comorbid conditions such as loss of dexterity with arthritis and stroke and neurodegenerative conditions such as Parkinson's disease. Physical decline in thoracic musculoskeletal structure and function and declining lung function make inhalation and breath holding more difficult. Impaired cognitive function from stroke and dementia can impede learning and memory in the use of what appear relatively simple devices. Visual and hearing impairment can compound this. Finally drug interactions and side effects can be more prevalent in the elderly. The following sections aim to review these challenges with approaches to selecting a suitable device for individual patients. Figure 1 below suggests approaches to common scenarios.

Poor Technique

It is useful to assess the patient's natural technique and coordination. If the patient has difficulty with coordination of actuation and inhalation of pMDIs then DPIs offer a good solution as the device is triggered by inhalation alone. An adequate inspiratory effort is needed, discussed in the next section. If this is not achievable then pMDIs with a spacer device can be considered. It is important to hold the spacer with the inhaler upright while using. Cleaning of the spacer needs to be done regularly including allowing the device to dry after [12]. An alternative to the spacer is a BA pMDI.

Poor Inspiratory Effort

Inspiratory effort is an important factor in DPI use and age has been shown to be an important determinant in inspiratory flow through DPIs. In order to optimize inspiration patients need to be in good posture, either sitting upright or standing. This is not always possible in elderly patients. Older age in particular with chronic lung disease results in deterioration of lung

Table 1 Inhaled Therapy Devices

Inhaled Therapy Devices	
Pressurized Meter Dose Inhalers (pMDIs)	*Triggered by patient. Slow gentle inhalation. Option with spacer*
Dry Powder Inhalers (DPIs)	*Require patient inspiratory effort to aerosolise dry powder*
1st Generation	Single dose, capsule manually loaded
2nd Generation	Multi-dose, dry powder pre-loaded
3rd Generation	Piezo electric crystals help aerosolise dry powder
Soft Mist Inhalers (SMIs)	*Deliver aerosolised mist as fine mist and slow velocity*
Nebuliser	*Require patient normal tidal volume only to deliver*
Jet nebuliser	Compressor to aerosolise liquid
Ultrasonic nebuliser	Piezo electric crystals generate aerosol
Vibrating mesh design	Vibrating plate generates aerosol with reduced delivery time

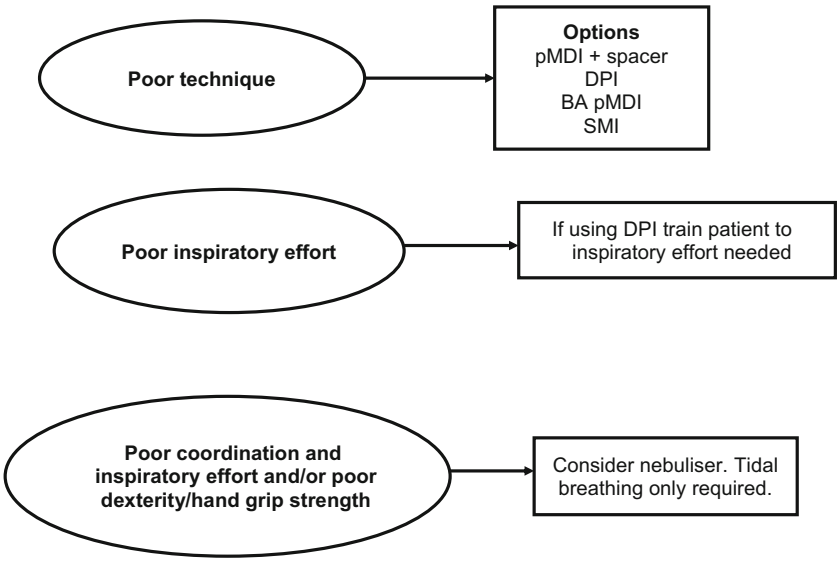

Fig. 1 Considerations when choosing inhalation device. One to one education and re-education is important

function, with increased weakness of respiratory muscles, change in chest shape, reduced chest wall compliance and changes to the lung parenchyma and airways [13, 14].

With DPIs the patient needs to inhale as deep and as hard as possible so they can overcome internal resistance to flow, aerosolise the powdered particles and also provide turbulent flow to de-aggregate the powdered formulation and prepare for lung deposition. A retrospective cohort study by Loh et al. showed that patients with a measured peak inspiratory flow rate (PIF) <60 L/min had a shorter time to COPD and all-cause readmission. Older patients had lower PIF [15]. Patients with severe airflow obstruction or mucus plugging can potentially have reduced deposition in the lung periphery, which may be particularly important for corticosteroids [7].

Assessment of inspiratory effort is important in deciding the correct inhaled therapy device for a patient. One option to consider when assessing inhaler technique is the In-Check DIAL G16 device. It is a specialized inspiratory flow meter, originally developed in the 1990's and can help train patients in inhaler use. It is able to simulate the resistance characteristics of different inhalers helping to guide the patient to the inspiratory effort needed for their device [16].

Poor Dexterity/Handgrip Strength

Reduced hand grip strength, measured using a dynamometer, has been shown to be a predictor of incorrect pMDI use [17]. New inhalers such as second generation DPIs have been shown to be easier to handle. The medication is preloaded and activated by inhalation as previously mentioned [18]. A fallback position for patients with uncorrectable handheld inhaler handling, coordination or insufficient inspiratory effort is use of a nebuliser. Once the device is in place tidal breathing only is required. They do require maintenance and also compared to inhalers they have longer drug delivery time for older devices.

Cognitive and Sensory Impairment

Dementia is common in the elderly and memory issues could be compounded by associated effects of obstructive lung disease such as hypercapnia and exacerbations of the primary lung disease. There is a long list of potential critical errors in inhaler use listed by Price et al. pMDI errors include failure to remove cap, actuation not corresponding to inhalation i.e. coordination, unable to tell when the device is empty. DPI potential errors include failure to slide the cover or mouthpiece levers fully, blowing into the device before inhalation and inhalation not forceful enough at the start [12].

Role for Cognitive Testing

Recall of correct inhaler use has been demonstrated to be poor in many patients despite instruction. In elderly patients with poor control of their airway disease it is worth considering cognitive testing. Once the most appropriate device is chosen it is likely that repeated training sessions will be required to reinforce correct technique [19]. Mini Mental State Exam (MMSE) and ability to copy intersecting pentagons (IP) have been shown to predict success with MDI inhaler technique. MMSE <24 or negative IP help predict elderly patients who will not be able to use a pMDI [20]. More recently cognitive impairment demonstrated by MOCA score has been associated with poor compliance and technique [21•]. Abbreviated mental test (AMT) score has been shown to be less useful in predicting successful pMDI use. Some patients with normal AMT score with poor inhaler technique have been shown to

have dyspraxia as measured by ideomotor dyspraxia score (IDS) [22].

Importance of Simplicity

Simplicity of the patient's treatment plan is important. It is not advisable to mix delivery devices if possible as the technique for different inhaler devices can be very different, in particular the technique required for pMDIs verses DPI. With pMDIs it is important for the patient to inhale slowly as opposed to DPIs where a good inspiratory effort is needed. Before changing devices one should always ensure patient technique is assessed for their current device. Patients prescribed multiple inhaler types have been shown to have worse outcomes than those prescribed additional inhalers requiring the same technique [23].

Importance of Education

Effective education in device use by nurse specialist or pharmacist is vital. Written and verbal instructions can improve patient technique but demonstration by a pharmacist has been shown to improve skill level considerably [12]. Crane et al. showed that that one to one demonstration and coaching of inhaler device technique is of greater benefit in improving inhaler technique in older people versus written information, even if it includes pictures alone. The study intervention group also received education including knowledge of their disease, their particular inhaler devices, why good technique is important and tips on improving it. If difficulty with the device was noted such as use affected by arthritis or inspiratory flow, other options were discussed with their practitioner [24].

Sensory Considerations

Other important considerations in the elderly are senses of hearing and vision. Some inhalers require you to inhale until a click is heard. Some first generation dry powder inhalers require capsule loading and most inhalers have counters to convey number of doses remaining, both need to be considered if visual impairment.

Polypharmacy and its Implications

Polypharmacy is a common challenge in the elderly. A large UK cohort study by Hanlon et al. showed that multimorbidity is more common in patients with COPD compared to those without (17% vs 4%) and is associated with high levels of polypharmacy (52% taking ≥5 drugs). Common side effects found in COPD patients with comorbidity and polypharmacy are falls, constipation, urinary retention and CNS depression [25]. As inhaled therapy is locally delivered it may be overlooked when systemic side effects affect compliance. When prescribing a new inhaler, the patient's medication list should ideally be reviewed to avoid potential drug interactions and adverse drug events. Often, well-intentioned patients will volunteer a long list of medications but forget to include their inhaled therapies.

Generally inhaled beta-agonist and muscarinic antagonists are well tolerated however if a patient is not using their medication it is worth asking about potential side effects. Muscarinic antagonists potentially can cause side effects such as nasopharyngitis, dry mouth, constipation and urinary retention. Beta agonists have potential side effects such as headache, tremor and muscle cramps [26].

Inhaled corticosteroids (ICS) are indicated as per Global Initiative for Asthma (GINA) guidelines at step 1 of treatment [27]. In Chronic obstructive lung disease (COPD), ICS can be considered in the treatment of Group D patients as per Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [1]. As such ICS treatment is common in the elderly population with respiratory conditions and awareness and management of side effects is important to sustain effective inhaled therapy. Important potential side effects to consider are oral candida and pneumonia. Other potential side effects are osteoporosis, diabetes and cataracts. Candidiasis can be oral, pharyngeal and oesophageal and it is important to look for oral thrush, sore throat and advise on gargling and mouth rinsing. In general, consider using lowest effective dose to reduce these potential side effects [28].

The Future Direction of Inhaled Therapy in the Elderly

Technology to objectively access inhaler use to unlock the reasons for non adherence and failed therapy is beginning to appear in recent years and it may have a significant role to play in choosing the right inhalation device for individual elderly patients. Simple examples of this include counters installed in inhalers but these do not give any information on the technique of inhaler use. Mobile device use for direct observation of therapy (MDOT) is one new approach. This technology with remote feedback has been shown to improve asthma controlled test score (ACT) in a paediatric study [29].

The emergence of low cost sensors has led to development of SMART inhalers to objectively collect data on inhaler use, in particular technique and adherence [30]. An Inhaler Compliance Assessment (INCA) device has recently been developed, consisting of a microphone and associated hardware attached to the inhaler device allowing acoustic recordings which characterize inhaler actions.

These include drug priming, inspiratory effort, exhalation and the timing and sequence of those events. Errors including failure to prime, exhalation into the inhaler after priming, failure to generate sufficient inhalation flow, dose dumping, time of use and interval between dosing can be analysed [21, 31]. Such technology has many potential uses including assessment of patient technique, adherence and training in device use as well as potential for intelligent dosing and improving clinical trial design [30].

Finally, for older patients whom are unable to manage hand held inhaler devices, nebulisation may play a greater role in the future. Nebulisers do require maintenance and newer devices are expensive however the devices are becoming smaller, more portable and have more efficient drug delivery, in particular vibrating mesh nebulisers [32]. One issue with nebulisers which is changing is availability of long acting drug options. Previously LABAs such as Formoterol fumarate and Arformoterol tartrate were available but no LAMAs. Recently two LAMAs Glycopyrrolate bromide and Revefenacin have been developed [33•]. This will help with providing nebuliser therapy as an option for patients. Further research into the role of nebuliser therapy in the elderly would be helpful such as direct comparison of hand held inhaler device and nebuliser devices in the elderly, examining symptom management, exacerbation frequency and hospitalization.

Conclusion

Despite decades of technological development inhaled therapy remains a challenge in the elderly. Current research in this population is lacking particularly given the recent increase in the number and type of delivery devices available. Bedside assessment of cognitive function, co-ordination and inspiratory effort can help improve adherence and technique and inform the choice of device. Repeated education and feedback will remain important. As well as continued device improvement, built in sensor technology is likely to become more common and has the potential to help us improve the effectiveness of inhaled therapy. More research is needed on the specific potential of new nebuliser devices in the elderly and the new availability of long acting pharmaceutical agents will help this.

Compliance with Ethical Standards

Conflict of Interest None.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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