Expert Opinion

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Adherence monitoring in drug delivery

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Adherence monitoring is an important issue in inhaled drug delivery. Adherence is commonly found to be low and poor adherence is associated with increased mortality and morbidity and increased use of health services. Improving adherence is essential to maintaining disease and symptom control for patients and decreasing health costs. Feedback on actual adherence has been shown to increase subsequent adherence. In addition, education programs, reminder systems and increased patient–clinician interaction can also improve adherence. However, improved adherence is not sufficient if inhalation devices are being used incorrectly; the emphasis must be on devices being used in accordance with both the prescribed regimen and the instructions for use. As a result of technological advancements, drug delivery devices that both monitor adherence and address poor inhaler technique are now available. These devices combine monitoring systems with various feedback mechanisms in order to 'coach' the patient to use the device correctly. Some devices also incorporate connectivity to communicate accurate adherence and inhaler technique data to the clinician. This editorial considers current and future adherence monitoring devices and the impact that such technology could have on improving the patient's adherence and inhaler technique.

Keywords: adherence, connectivity, inhaler technique, monitoring

Expert Opin. Drug Deliv. (2010) 7(10):1127-1131

1. Introduction

The term adherence relates to the frequency and dose of medication that patients take in relation to their prescribed regimen; this is commonly presented as the number of doses taken (i.e., one inhalation or one tablet) as a percentage of the total number of doses prescribed over a set period. Adherence is an important factor in the effectiveness of most self-administered medication regimens. For inhaled medications, adherence is commonly found to be low, at ~ 50% [1]. Inhaled medication is an important treatment mode for asthma and chronic obstructive pulmonary disease (COPD). World Health Organization figures estimate a worldwide patient population of 300 million for asthma and 210 million for COPD, demonstrating the magnitude of these patient groups [2,3]. As a result, these patient groups have a significant impact on overall healthcare budgets and therefore improving adherence is important to healthcare economics. When poor inhaler technique is taken into consideration alongside low adherence, this represents a significant reduction in the amount of medication being received compared with the amount being prescribed. Developments in technology are increasingly moving towards providing devices that deliver medication reliably and efficiently, monitor adherence and address poor inhaler technique.

Low adherence results in poor symptom and disease control and is associated with a range of negative effects, from lost work or school days to increased

10.1517/17425247.2010.517520 © 2010 Informa UK, Ltd. ISSN 1742-5247

Article highlights.

- Low adherence is associated with increased morbidity and mortality and should be monitored using electronic monitoring devices.
- Correct inhaler technique is integral to inhaled drug delivery and newer inhalation devices contain feedback systems to 'train' patients to use them correctly.
- Several devices are currently available and in development; these range from simple devices that record actuation to 'intelligent' devices that record adherence and inhaler technique data and provide feedback on correct use.
- Connectivity is becoming increasingly important to home monitoring systems.

This box summarizes key points contained in the article.

morbidity and mortality [4]. A key study by Milgrom *et al.* found adherence to asthma medication to be only 13.7% in children who suffered an exacerbation that required a course of oral corticosteroids compared with 68.2% in those who did not [5]. Other studies have shown poor adherence to be associated with increased emergency department visits and hospitalization [4]. As a result, low adherence impacts on patients' health, quality of life and healthcare costs. Improving adherence would have direct health benefits for patients and economic benefits for healthcare services.

To monitor adherence a reliable, accurate recording system is required. Electronic monitors have been shown to be the most accurate method of monitoring compared with other techniques available, including canister weights, prescription refill records and a variety of self-report methods [6,7]. Jentzsch *et al.* compared adherence rates using four different methods and found mean adherence to be 97.9% using self/parent report, 70% using pharmacy records, 51.5% using a Doser and 46.3% using canister weights [7]. Jentzsch *et al.* concluded that canister weights and the electronic monitor were the most accurate. Furthermore, electronic monitors can provide data in a timely, convenient way either directly to the patient or to their clinician. In addition to recording adherence data, electronic monitors can also play a role in improving adherence and, in some cases, inhaler technique, ensuring that the treatments taken are taken correctly. In a study by Nides *et al.*, a Nebulizer Chronolog was used to record adherence and the results showed that providing feedback on actual adherence can improve subsequent adherence [8]. Adherence monitoring has also been used to highlight the effectiveness of other types of intervention to improve adherence, including home-based interventions, education programs and reminder systems. It has also been shown that increased patient–clinician interaction is important, and a study by Wilson *et al.* found that increased involvement of the patients in the decision-making stage regarding their treatment can increase adherence and asthma control [9]. Using some of these methods, a range of studies have shown that adherence can be increased up to 79 – 88.8% [8,10-12]. An approach that combines an effective monitoring system with other methods shown to improve adherence should be considered.

However, improving adherence alone does not necessarily increase the amount of drug that is received by the patient. Poor inhaler technique results in little or no medication being successfully received and is a widespread problem; studies have found that 14 – 90% of patients do not use their pressurized metered dose inhaler (pMDI) effectively [13]. Giraud and Roche found that inhaler misuse, and particularly poor coordination, is associated with poor asthma control in patients using pMDIs to administer inhaler corticosteroids [13]. Everard presses the need for both adherence to the medication regimen and correct inhaler technique in order to achieve 'true compliance': the prescribed number of doses taken correctly [14]. Consequently, comprehensive, frequent training on device use by healthcare professionals is considered an important aspect of care and is incorporated in care guidelines for asthma and COPD. However, Self *et al.* conducted a review of studies into the skill of different groups of healthcare professionals in using asthma inhalation devices and found that only 7 – 28% of physicians, 4 – 66% of nurses and 85 – 92% of respiratory therapists demonstrated a correct technique, using a range of devices [15].

Evidently there are several issues to consider in developing an effective adherence system, related to the patient, the clinician and the device. The following key steps provide a framework for developing such a system through addressing the issues outlined above.

- The chosen method of monitoring must provide accurate data on which objective clinician decisions can be based.
- The patient requires training with the device, both initially and at regular intervals during treatment.
- The device is intuitive to use and provides feedback when used correctly, as correct use is a prerequisite to improving adherence.
- The device is capable of providing adherence data in a timely manner, which can be shared with the patient and healthcare professional.

2. Basic adherence monitoring devices

There is a range of devices available for the monitoring of adherence with varying capabilities. The Doser (Meditrack, Easton, MA, USA) is the most widely known basic monitor and is used in clinical trials and sold commercially in the US. The Doser is a simple device attached to a pMDI that counts and stores when the pMDI is actuated. It also provides a countdown as to when the pMDI is empty. Several versions of the MDILog (LifeLink Monitoring, Norcross, GA, USA) have been used in trials on monitoring and improving adherence. However, several studies have raised questions regarding the accuracy of these devices, particularly the earlier versions,

which had problems with battery drainage [16]. The Smartinhaler (Nexus6 Ltd, Auckland, New Zealand) is a basic adherence monitoring device that also incorporates other features related to adherence, including optional reminder systems and a choice between covert or overt monitoring. There are five different Smartinhalers, designed for use with different inhalers, all of which are commercially available. The Smartinhaler has also been used in several studies to provide an accurate insight into actual adherence [10,17]. It is important to note that basic devices such as the Doser cannot record whether the inhaler technique was correct, only that the inhaler was actuated.

3. Features beyond adherence monitoring

To address the issue of poor inhaler technique and the inability of simple devices to monitor whether medication has been successfully received, some newer devices have the ability to 'train' the patient to use the device correctly, providing feedback on any errors in use and ensuring the patient receives a complete dose. For example, the I-neb Adaptive Aerosol Delivery (AAD) System (Philips Respironics, Chichester, UK) has a software program that displays real-time visual feedback on the patients' breathing pattern, coaching them to perform the slow, deep inhalations required for one of the two breathing modes [18]. This is an example of how a device can become 'interactive'. This is an important development as Fogg, in his book on persuasive technology, suggests that interactive experiences can be a contributing factor to the ability of technology to influence the actions of those who use it [19]. The I-neb AAD System also has a range of audible, visual and tactile feedback mechanisms to alert the patient to errors in the use of the device and also to signal completed treatments, guiding the patient towards correct device use. In addition, the I-neb AAD System contains a Patient Logging System that compiles data on both adherence and inhaler technique, which can be used to address problems with either the prescribed regimen or the use of the device.

Another device that addresses technique is the AERx iDMS (Aradigm Corp, Hayward, CA, USA), a second-generation delivery device used in clinical trials primarily for the delivery of inhaled insulin. The AERx iDMS contains technology that regulates the patient's breathing to improve the efficiency of drug delivery, provides visual feedback, and generates an electronic dosing record. Technology such as this is integral to the development of an effective monitoring system that both monitors and improves the efficacy of inhaled medication regimens.

The incorporation of connectivity has extended further the capabilities of such devices, for example the I-neb Insight Online System allows patients to upload their data onto a server, providing remote access to their adherence and device use data to their clinician. The ability to monitor remotely such information consequently provides the opportunity to intervene. SmartinhalerLive™ is a similar service developed by Nexus6 that 'uses wireless communications technology to provide real time data collection and reporting from drug delivery devices including asthma and COPD inhalation devices' [20]. Connectivity is another tool that Fogg considers important to the potential of persuasive technology; for example, creating the potential for social comparison whereby patients can access the adherence rates and behavior of other patients with the same disease and treatment, which could further influence behavior. In addition, connectivity combined with device mobility creates the potential to intervene at the opportune time.

Several guidelines for the treatment of respiratory diseases also include the use of adherence and device use monitoring systems. The Cystic Fibrosis Trust 2009 guidelines specifically recommend inhalers that give feedback on correct use of the device and incorporate the ability to provide adherence data to clinicians, allowing them to work with patients to improve adherence [21]. Adherence monitoring is also included in the guidelines for the treatment of asthma and COPD, demonstrating the increasing understanding that monitoring adherence is an important aspect of treatment using inhaled medications [22,23].

4. Current advanced adherence monitoring devices and new developments

As discussed, more advanced devices that combine adherence monitoring with systems designed both to monitor and to influence incorrect use of the device are available. The I-neb AAD System is commercially available in the UK and provides feedback on use, records adherence and inhaler technique, and has the capability to connect to the I-neb Insight Online System. The AERx iDMS has been mostly used in clinical trials for the delivery of insulin and is not yet commercially available. Aradigm also developed the SmartMist System; launched in 1998, the SmartMist was for use with a pMDI and incorporated indicator lights and breath-control technology to guide patients to a successful inhalation as well as a monitoring system for peak flow. However, the SmartMist was not a commercial success. The Akita^2 (Activaero GmbH, Gemünden, Germany) is a nebulizer system mainly used in clinical trials and includes smart card technology to record adherence and breathing pattern data.

As technology advances, new devices are also being developed for the market. The MicroDose Dry Powder Inhaler (DPI) (MicroDose Therapeutx Inc., NJ, USA) uses a high frequency piezo transducer and other electromechanical elements to ensure delivery independent of flow rate, coordination or orientation of the device. The MicroDose DPI uses indicator lights to provide electronic dose feedback and confirmation of delivered dose. In 2009, a collaboration with Nexus6 was announced to evaluate the possibility of incorporating SmartinhalerLive technology into the MicroDose DPI in order to provide real-time adherence and inhaler technique data to the patient and clinician [24]. Cambridge Consultants

Ltd (Cambridge, UK) have focused on connectivity in the development of the Vena wireless medical device, which would allow patient adherence to be monitored using wireless technology for data transfer. David Blakely, Head of Drug Delivery at Cambridge Consultants, highlights the use of the device to 'close the loop between a patient and their healthcare provider' [25]. Closing this gap through the availability of adherence data could improve adherence through increased accessibility to actual adherence and communication between patient and clinician. The Sensohaler (Sagentia Ltd, Cambridge, UK) uses acoustic analysis to measure and monitor drug delivery characteristics and provides feedback on correct use to the user and his/her clinician.

5. Conclusion

There is no doubt that improved adherence can contribute to better disease management and decreased healthcare costs. Monitoring can improve adherence, but to achieve maximum benefit of the prescribed drugs, good inhaler technique is essential. In addition, there are other factors that can further enhance adherence which should be considered, including education programs, patient–clinician interaction and reminder systems. Advances in technology are increasingly providing options to patients and clinicians for devices that incorporate several of these methods, including 'training' patients to develop correct inhaler technique and providing the ability to download and transfer data on the use of the device to the clinician. The integration of connectivity into devices has generated the potential for regular home monitoring of all aspects of patient use of a device, as recommended in some national guidelines. Future developments indicate further emphasis on home monitoring and the availability of data, enhancing the vital link between patient and clinician while developing ever more effective drug delivery systems.

6. Expert opinion

As the world's demographics continue to shift and the average age of the population rises, the pressure on healthcare budgets increases. As a result, remote monitoring will become a key tool in home healthcare management. For those using inhaled medications, technological advancements have now made it possible to deliver effective monitoring at home, and the widespread adoption of broadband means that this can now be effectively implemented. The use of home monitoring in high-cost therapy areas such as cystic fibrosis, where the patient group is generally younger and computer literate, is gaining momentum where the business model is cost-effective in proportion to the pharmaceutical budget. In cystic fibrosis the value of monitoring to optimize patients' therapy has been recognized by the clinical teams supporting the patients and is now being adopted as a normal part of the patient management program, as well as in national healthcare guidelines.

Barriers to the adoption of home monitoring remain in other patient groups taking inhaled medication. Reimbursement has been a significant barrier to the implementation of home monitoring in the healthcare systems of developed countries. Initially, this requires socioeconomic studies to justify the reimbursement costs; even when these cost–benefit studies are completed, the reallocation of healthcare budgets by transferring funds from hospital to homecare budgets are needed before a service can be implemented. A significant challenge still remains in interfacing with older patients who are not familiar with this type of computer or mobile-based technology, or do not have the home IT infrastructure to support this type of service. In patient groups such as COPD, addressing this challenge will require both automated wireless monitoring systems to minimize the patient interaction required to collect the data, and allowing for the data to be shared with all the care providers interfacing with these patients. This significantly increases the capital cost required to implement these services, and as a result the only common system for monitoring of elderly patients is the emergency call button, most often paid for by a concerned relative.

When making decisions on siting patient data servers, further barriers also exist in the form of national data protection guidelines, which then interface with different national healthcare systems. The opportunity to share infrastructure is improving as more homes are connected to data services and the standardization of device data formats such as the CONTINUA initiative will also greatly assist in sharing data. The ability to connect to central healthcare data stores such as Google Health and MS HealthVault may also provide for more cost-effective data collection solutions to be implemented. As more home monitoring services are adopted and hence more healthcare providers are exposed to their value in providing support to remote patients, and as the barriers to implementation are reduced, the rate of adoption will increase rapidly; as has been seen with other Internet-based services, after a slow start over the last 10 years, the next 10 years will see exponential growth in home monitoring.

Acknowledgment

The author acknowledges L Pearce (PS5 Consultants Ltd, Portsmouth, UK) for editorial assistance.

Declaration of interest

This manuscript was sponsored by Philips Respironics. J Denyer is an employee of Philips Respironics.

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