In vitro evaluation of an asthma dosing device: The smart-inhaler

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Summary Monitoring devices attached to pressurised metered dose inhalers provide an important objective measurement of patient adherence with asthma medications in clinical and research settings. The Smart-inhaler is a relatively new device that has not been previously validated. This study examines the accuracy of the Smart-inhaler in a bench-top experiment and compares it with a previously validated device, the Doser. Ten Smart-inhalers and five Dosers were actuated twice on two occasions per day for 30 days (120 doses). Six Smart-inhalers were also actuated 30 times in rapid succession to examine the ability of the Smart-inhaler to detect "dumping". Five Smart-inhalers failed to detect the first one or two doses. However, when the aerosol canister was placed more firmly in the device, actuating the device in the process, the following two doses were recorded accurately in all ten devices. Otherwise all ten Smart-inhalers and five Dosers recorded all actuations faithfully and there were no spurious recordings. The six Smart-inhalers recorded all 30 doses delivered in rapid succession. The Smart-inhaler and Doser are both highly accurate at measuring actuated doses and no spurious doses were recorded in an in vitro setting.

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Introduction

The Smart-inhaler (Nexus 6, Auckland, NZ) is a device that has been developed to measure adherence with inhaled asthma medications. Adherence is important both in clinical and research settings. Poor adherence with asthma management plans and treatment regimens has been associated with poor disease control, an increased risk of hospital admission and an increased mortality rate. Objective monitoring of adherence is often necessary as patient and parental reports of adherence are often inaccurate and tend to overestimate the number of doses of medication.

KEYWORDS
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In addition a physician’s subjective impressions of their patients’ adherence may be equally unreliable.²,⁵,⁶ There are a number of devices that have been developed to objectively measure adherence with inhaled asthma medications including the Doser (Meditrack, Hudson, MA, USA) and MDI log (Westmed, Colorado, USA).⁹ Some patients who suspect they are being monitored may discharge their medication prior to clinical review in an attempt to hide non-adherence, a practice sometimes referred to as “dumping”.¹⁰ Monitoring devices ideally should be able to monitor adherence covertly, accurately record the time that each dose was taken, store data over a reasonable time period (more than 30 days), detect multiple successive actuations (dumping), not interfere with the dose of delivered medication and provide access to data so that it may be downloaded to a personal computer.

The aim of this paper was to assess whether the Smart-inhaler was able to accurately record actuations using a range of pressurised metered dose inhalers (pMDIs) distributed by GlaxoSmithKline (GSK) compared with a known record of actuations. The relative accuracy of the Smart-inhaler was compared with the Doser (Meditrack, Hudson, MA), a previously validated monitoring device. Six Smart-inhalers were actuated in rapid succession to determine how the Smart-inhaler would record “dumping”.

Methods

The Smart-inhaler replaces the plastic holder of a standard pMDI (Fig. 1). It incorporates a switch that is activated each time the canister is depressed within the device. The devices supplied for this study were orange, similar to a Fluticasone pMDI (Flixotide, GSK). The device has a similar shape to a standard pMDI with a compartment behind the canister containing the battery and electronics. The device connects to a laptop computer through a cradle and serial communication link. A web-based programme is used to configure the device, set the device clock and download data. The website is protected by a secure password and data are stored centrally and on the user’s computer. The web-based software can track specific devices and data can be entered into the same database from multiple trial sites. The web-based software calculates adherence on the basis of two doses given twice daily. A standard report presents the number of subjects from each group, the mean percentage of compliance and the difference between the two groups. The graphic function presents the mean compliance of each group as a bar graph. The number of doses actuated by each Smart-inhaler either on a daily, weekly or annual basis may be graphed. However, data may also be downloaded into a standard spreadsheet for more detailed analysis.

The Doser is a monitoring device that has been previously validated (Fig. 2).⁹,¹¹ The Doser attaches to the top of a pMDI with a plastic sleeve. It records the number of doses actuated in a 24 h period and also counts backwards from a pre-selected number of doses. The Doser CT (clinical trials version) has a 45-day memory and may be set so that screen contained within the device is blank. Data from a Doser can be read from the screen but cannot be downloaded for further analysis. The Doser can attach to most products, although it does not attach well to Sodium cromoglycate (Intal, Aventis), Nedocromil sodium (Tilade, Aventis) or Ipratropium bromide (Atrovent, Boehringer Ingelheim) as the canister may not actuate effectively if used with these devices.¹²

Part one

Ten Smart-inhalers were configured using web-based software as per the manufacturer’s instructions. Two devices were attached to a pMDI containing Salbutamol 100 µg (Ventolin, GSK, Vic), Fluticasone propionate 50 µg (Flixotide), Fluticasone propionate 125 µg, Fluticasone propionate 50 µg/Salmeterol xinafoate 25 µg (Seretide), or Fluticasone propionate 125 µg/Salmeterol xinafoate 25 µg.
Five Doser CT devices were activated, the number of doses was set at 200 and the device was set in the clinical trials mode as per the manufacturer’s instructions. The number of doses was purposely set at a number higher than would be used during the study to ensure that if additional spurious doses were recorded the device would not reach zero before the conclusion of the experiment. Each Doser was attached to one of the same five different pMDIs as above.

Each device was actuated twice on two separate occasions during a 24h period for 30 consecutive days (120 doses). Each device was weighed prior to and following each pair of actuations. This was performed to detect if accidental actuation had occurred between dosing and to confirm that two doses had been actuated on each occasion. The time stamps recorded by all Smart-inhalers were accurate when compared with the manual log. All five Dosers were 100% accurate.

The canisters were removed from all Smart-inhalers and the set-up process was repeated to investigate why five of the Dosers had failed to record the first one or two actuations. In each case, a new canister containing Seretide 50/25 μg was inserted into a Smart-inhaler, but not pushed to the bottom. All devices were weighed with the canister in the device. The canister was then pushed firmly into the devices actuating the canister in the process. Two further doses were discharged from each device. All devices were weighed before and after each actuation.

Three actuations were recorded by nine devices. However, the actuation that occurred as the canister was inserted into the 6th device was not recorded. The change in weight before and after the first dose from the 6th Smart-inhaler was 68.9 μg which is reduced when compared with the other 29 doses (mean 72.4 μg, range 70.5–75.3 μg).

Part two

Six Smart-inhalers were configured using web-based software as per the manufacturer’s instructions. Each was attached to a pMDI containing either Salbutamol 100 μg, Salmeterol xinafoate 25 μg (Serevent), Fluticasone propionate 50 μg, Fluticasone propionate 125 μg, Fluticasone propionate 50 μg/Salmeterol xinafoate 25 μg or Fluticasone propionate 125 μg/Salmeterol xinafoate 25 μg. Each pMDI was actuated 30 times in rapid succession. Data from each device were then downloaded onto a laptop using the web-based software and compared with the known number of actuations.

Results

Part one

Five of the Smart-inhalers were 100% accurate with no additional or omitted actuations. One Smart-inhaler failed to record the first dose (Flixotide 125 μg) actuated and four Smart-inhalers failed to record the first two actuations (Flixotide 50 μg and Seretide 50/25 μg). However, the remainder of the actuations in all devices was recorded and no device had any spurious recordings. The time stamps recorded by all Smart-inhalers were accurate when compared with the manual log. All five Dosers were 100% accurate.

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Part two

The six Smart-inhalers correctly recorded all 30 doses. Interestingly when actuated in quick succession the time stamp revealed the same time to the second for all 30 doses which correlated with the time of the first actuation.
Discussion

A number of studies have measured adherence with inhaled asthma medications in several different populations and reported mean levels ranging from 50% to 86%.\(^2,6,13,14\) It is possible that mean rates of adherence within the general population are even lower. It is recognised that patients who participate in trials do not necessarily reflect the broader population and that subjects often behave differently when they believe they are being observed.\(^15\) Adherence is difficult to measure objectively and therefore its significance is often downplayed in both research trials and clinical practice. However, in both these settings adherence may prove to be a crucial piece of the puzzle when examining the failure of a treatment to have an effect or a superior effect of one treatment over another. The role in clinical practice may extend further. Monitoring adherence and providing feedback may improve adherence.\(^16\) Secondly adherence is a marker of other important health-related behaviours demonstrated by the improved outcome of patients who are more adherent within the placebo arm of a trial.\(^17\)

The Doser is a monitoring device that has been validated in two previous studies. Simmons et al.\(^11\) reported that when the dosing histories from ten Dosers were compared with known actuations dosed by laboratory technicians, 96.7% were in agreement. In this paper, 89% of disagreement related to unrecorded actuations. A second study by Julius et al.\(^9\) reported that when dosing histories from six Dosers were compared with known actuations, 94.3% were in agreement. In this study, the majority of Dosers recorded additional doses and reached zero prematurely. Once the preset number of doses reaches zero further actuations are not recorded. Prior to reaching this point none of the Dosers missed any doses. It is not clear from either study why the Dosers either failed to record actuations or spurious actuations were recorded.

In this study both the Smart-inhaler and Doser proved to be extremely accurate. None of the ten Smart-inhalers recorded any erroneous actuations. The canisters fit firmly into the devices and do not fall out. It would appear that it is possible to trigger an actuation without the canister being completely within the device or activating the switch. When the 10 Smart-inhalers were initially set up, each canister was placed in the device gently to prevent an erroneous actuation. After the first two actuations, no actuations were missed and each actuation was recorded with an accurate time stamp. When the set-up was repeated and the canisters were firmly pushed into the device no subsequent doses were missed. Thus the missed actuations likely relate to the manner in which the devices were set-up and this should not occur if the canister is actuated as it is inserted.

The Smart-inhaler offers the advantage of a time stamp with a resolution of seconds. This allows investigators to determine when doses were given during the day. It also allows investigators to determine if doses were given so close together that normal dosing would not have been possible. When doses are actuated in quick succession the time stamp is repeated. Both devices only record that a dose was actuated and not whether the medication was inhaled. The Smart-inhaler looks more like a normal inhaler than does a pMDI with the Doser attached. However, all patients who are familiar with their medication will recognise that the device is different from a standard pMDI. We are currently conducting a trial to investigate whether covert monitoring is possible with the Smart-inhaler. The other significant advantage of the Smart-inhaler is the capacity to download data, saving time and avoiding errors during the manual transfer of data into a database.

The principal limitation of Smart-inhaler is the cost. Thirty Smart-inhalers were purchased, along with a docking station and 12 months access to a trial database at a total cost of Aus$21,461. The cost per device was 14 times the cost of the same number of Dosers. Obviously this expense relates to the technology involved and the cost of setting up and maintaining the website and database for the period of the trial. The cost per device is reduced if a large number of devices is required per trial, and hence may be more cost effective for larger-scale clinical trials.

References

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