

Measurement of peak inhalation rates with an In-Check Meter[®] to identify an elderly patient's ability to use a Turbuhaler[®]

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Abstract Dry powder inhalers are designed with resistance to airflow so that a respirable cloud of particles is generated during inhalation. Some of these devices require a certain inhalation rate to produce a consistent dose of respirable particles. The aim of the study was to determine the inhalation rate of elderly patients with chronic obstructive pulmonary disease (COPD) when they inhale through a Turbuhaler[®] and assess the potential of the In-Check Meter[®] to identify inhalation rates. Their peak inhalation rate using a normal inhalation, pre- and post-counselling, was measured using a Turbuhaler Trainer[®] and an In-Check Meter[®]. Spirometry was also measured. Seventy-four COPD patients with a mean (SD) age of 79.7 (8.4) years and forced expiratory volume in 1 sec (FEV₁) 41.9 (12.8)% predicted. Pre-counselling 14 obtained a rate of <30 l min⁻¹ with the Turbuhaler Trainer, 31 from 30 to 40 min⁻¹, 23 between 40–60 l min⁻¹ and 6 >60 l min⁻¹. The median (range) peak inhalation rates with the In-Check Meter[®] were 50 (50–70), 70 (50–130), 100 (60–200) and 225 (200–250) l min⁻¹. Post-counselling 7, 16, 41 and 10 achieved the respective peak inhalation rates using the Turbuhaler Trainer[®]. Similarly, the In-Check inhalation rates were 50 (50–60), 70 (50–130), 90 (60–200) and 250 (200–270) l min⁻¹. The results highlight the potential of the In-Check Meter[®] to identify patients' inhalation rates through dry powder inhalers. © 2001 Harcourt Publishers Ltd

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INTRODUCTION

Dry powder inhalers (DPIs) are more expensive than a metered-dose inhaler (MDI) but their use is increasing because they are easier to use, are breath-actuated, environmentally friendly and most have a dose counter. Internally, they are designed so that a patient's inhalation rate produces sufficient force to generate a cloud of drug particles capable of delivery into the airways. This force is generated by resistance in the device. It has been shown that each type of inhaler device has a different resistance (1,2).

In-vitro studies have shown that dose emission from a Turbuhaler[®] for budesonide (3) and terbutaline (3,4) is related to the inhalation rate and subsequently with total lung deposition (5,6) and response to terbutaline (6,7) and budesonide (8). Studies using other devices with

a high resistance have shown that dose emission is related to inhalation rate (9–11) and response (11). However, it is difficult to compare bronchodilation between doses, devices and inhalation methods because of maximal response obtained during most single studies. Newman *et al.* (12) highlighted this issue using asthmatic subjects. They reported that although lung deposition, measured by gamma scintigraphy, was 12.3% for a MDI and 23.5% when the MDI was attached to a spacer there was no difference in the forced expiratory volume in 1 sec (FEV₁) response.

Studies in asthmatics (13,14) and chronic obstructive pulmonary disease (COPD) (15) have shown that over half of the patients studied cannot use the Turbuhaler[®] with the recommended most desirable rate of >60 l min⁻¹ (5,16). In these studies (13–15) spirometry values were not able to identify which patients could use this device with the desirable rate. The relationship between inspiratory and expiratory airflow is not strong enough to predict whether patients are able to generate an inhalation rate for optimal drug delivery from an inhaler to the airways (17,18). Hirsch *et al.* (19) have shown how

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FEV₁ correlates to improved bronchodilation when using a Turbuhaler[®]. The product information leaflet explains that the inhalation technique used should include an inhalation that is 'as deep and hard as possible'. However patients with a reduced inspiratory capacity may not generate the necessary inhalation rate that is required for consistent and reliable dose emission. In the past measurements of inhalation rates through an inhaled device have required sophisticated equipment. Recently an In-Check Meter[®] (Clement Clarke Ltd, Harlow, U.K.) has been introduced to determine inhalation rates. This device is similar in design and appearance to a peak expiratory flow meter except that an inhalation is performed instead of a forced exhalation. Using a normal inhalation technique this In-Check Meter[®] is a simple and quick method to measure the inhalation rate of patients. In this study we have evaluated the potential of this meter to identify how patients use a Turbuhaler[®], with and without counselling, according to the manufacturer's patient information leaflet.

METHODS

Local Ethics Research Committee approval was obtained and patients gave informed, written consent. All were elderly with chronic obstructive pulmonary disease (COPD), either inpatients or outpatients attending their first appointment post-discharge. At the time of measurement all in-patients had been stabilized and were ready for discharge. Also spirometry measurements were similar to those measured over the previous 6 months. Subjects inhaled through a Turbuhaler Trainer[®] (Astra Draco, Lund, Sweden) using their normal inhalation technique. They were given the patient information leaflet and allowed to study the instructions for 5 min. The Turbuhaler Trainer[®] categorizes the peak inhalation rate (PIFR-T) as <30, 30–40, 40–60 and >60 l min⁻¹ according to none, one, two or three green lights. *In-vitro* measurements ($n = 22$) identified that the mean

(SD) rate to illuminate one, two and three lights of the Turbuhaler Trainer[®] was 28.8 (1.1), 39.6 (2.2) and 60.6 (1.9) l min⁻¹. Patients then used the same inhalation technique using the In-Check Meter[®] (PIFR-IC) (Clement Clarke) and their peak inhalation rate was recorded. They were then counselled how to use the Turbuhaler[®] according to the manufacturer's instructions in the patient information leaflet with particular attention drawn to inhale through their mouth as 'deeply and hard as they could'. Measurements with the Turbuhaler[®] (PIFR-T) and In-Check Meter[®] (PIFR-IC) were then repeated. Finally, spirometry (best of three forced expirations) was measured.

RESULTS

Seventy-four (44 females) with a mean (SD) age of 79.7 (8.4) years, FEV₁ 41.9 (12.8)% predicted and PEFR 50.4 (17)% predicted completed the study. Their mean (SD) FEV₁ and PEFR was 0.51 (0.36) and 177 (70) l min⁻¹, respectively. Ten were outpatients, the remainder were inpatients ready for discharge. Fifty-one patients used an MDI (13 with a spacer), 16 a Turbuhaler[®], six a breath-activated MDI and one had an Accuhaler[®]. Table I provides a summary of inspiratory and expiratory flow data pre- and post-counselling. Table I shows that only six of the 74 patients could inhale through the Turbuhaler[®] at a rate of >60 l min⁻¹ and that counselling enabled another four to achieve the optimal inhalation rate of >60 l min⁻¹ through this device. Only two of the 16 patients who used a Turbuhaler[®] could achieve this optimal rate. Statistical analysis (Kruskal–Wallis) showed significant differences ($P < 0.001$) for PIFR-IC, PEFR and FEV₁ for each PIFR-T category. However, Fig. 1 and Table I highlight that only those patients who could inhale at a rate of >200 l min⁻¹ through the In-Check Meter[®] (PIFR-IC) could use the Turbuhaler[®] (PIFR-T) with an inhalation rate >60 l min⁻¹. The mean (SD) PIFR-IC for the PIFR-T categories of <30, 30–40, 40–60 and >60 l min⁻¹ prior

TABLE I Median (range) inspiratory and expiratory data

PIFR-T	<i>n</i>	PIFR-IC (l min ⁻¹)	PEFR (l min ⁻¹)	FEV ₁ (l)
(a) Pre-counselling				
<30	14	50 (50–70)	110 (60–150)	0.67 (0.33–1.15)
30–40	31	70 (50–130)	150 (110–200)	0.76 (0.51–1.51)
40–60	23	100 (60–200)	200 (100–350)	1.03 (0.56–2.00)
>60	6	225 (200–225)	240 (230–350)	0.37 (1.10–1.48)
(b) Post-counselling				
<30	7	50 (50–60)	100 (60–150)	0.51 (0.33–0.98)
30–40	16	70 (50–130)	150 (60–360)	0.79 (0.41–1.25)
40–60	41	90 (60–200)	180 (110–350)	0.78 (0.51–2.00)
>60	10	250 (200–270)	290 (100–350)	1.31 (0.82–1.70)

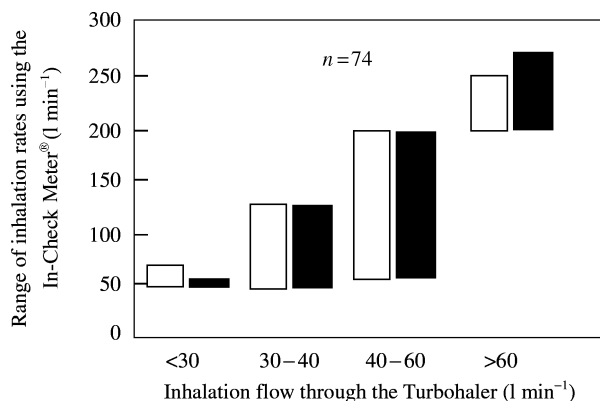


Fig. 1. The range of peak inhalation rates obtained with the In-Check Meter[®] before (□) and after (■) counselling for the inhalation rates measured using a Turbuhaler Trainer[®] ($n = 74$).

to counselling were 53.6 (6.3), 73.9 (19.3), 117.3 (47.6) and 226.7 (20.7) l min⁻¹, respectively. After counselling the respective PIFR-IC rates were 51.4 (3.8), 73.1 (70.7), 102.6 (37.2) and 232.0 (22.0). Statistical analysis (Mann-Whitney) showed no difference for PIFR-IC, FEV₁ or PEFR before and after counselling for each PIFR-T category. Correlations between either PIFR-T or PIFR-IC with spirometry were weak.

DISCUSSION

There is evidence that there is a link between the fine particle mass emitted from an inhaler with total lung deposition (20). However, this may not be shown by measurements of clinical effect due to maximal response (12). For dry powder inhalers that emit a flow dependent respirable dose, there is evidence of a reduced clinical effect at low inhalation flow rates when using these inhalers (6,8,11,19). For some inhalers there is an optimal, i.e. desirable / most favourable rate for inhalation (6,16). It is important to identify the patients who can use each individual device. The In-Check Meter[®] is a simple and easy to use measurement which identifies inhalation rates and thus is a useful aid.

Peak inhalation rates rather than a peak inspiratory rate from a forced manoeuvre were measured during this study to mimic how patients use inhalers. Dewar *et al.* (15) reported that 41% of their COPD patients could inhale at the optimal rate through a Turbuhaler[®]. Their patients were younger although the PEFR was similar to that of this study. Also, Dewar *et al.* (15) used the Turbuhaler[®] attached to a vitalograph in reverse mode and counselled their patients to make forced inhalations. Clark and Hollingworth (1) have highlighted that during these measurements the technique to be used with each inhaler should be assessed not a forced manoeuvre. A short sharp suck will provide a greater inspiration

than that during more prolonged inhalation through an inhaler.

A value of > 60 l min⁻¹ has been quoted as the most favourable inhalation rate when using a Turbuhaler (5,6,16,18). The National Institute of Clinical Excellence (NICE) has produced a report that identifies the high resistance of the Turbuhaler[®] and that it 'needs a relatively high inspiratory flow of 60 l min⁻¹ for optimal drug delivery' (21). The measurements with the Turbuhaler[®] indicate that most elderly COPD patients may not obtain the nominal dose because they cannot generate the optimal inhalation rate of > 60 l min⁻¹. Pre-counselling 14 patients and post-counselling seven could not generate > 30 l min⁻¹. Although the patients inhaling between 30-60 l min⁻¹ through the Turbuhaler[®] do not obtain the nominal dose their condition can be managed by titration according to response. However, this could be difficult to perceive for those that are irreversible and cannot be applied to the anti-inflammatory agents. Using unnecessary extra reliever doses complicates management plans and increases the medication costs. Furthermore when patients deteriorate their inspiratory effort will decrease (22) and thus they will obtain a reduced dose which may aggravate the deterioration. These, patients with insufficient inspiratory effort should, therefore, be prescribed an inhaler with less resistance. The In-Check measurements highlight how these patients can easily be identified.

The results indicate how counselling can improve the inhalation technique but the changes were only small and thus when the healthcare costs are considered it will not be cost effective. Studies have questioned the value of inhalation technique training because many patients revert to their poor inhaler technique when they get home (23-25). When a patient uses an inhaler the inspiratory flow generated is dependent on the capacity of their respiratory muscle and the resistance within their airways (26,27). The pre-counselling values were therefore close to the maximum they could achieve and suggest that this group of patients would not benefit from counselling about their technique. The patient's unable to achieve the most favourable inhalation rate when they inhaled 'as deep and hard as you can' will not be able to achieve the full benefit when they use a Turbuhaler[®]. Other dry powder inhalers also have a most desirable inhalation rate. Thus, if the Turbuhaler Trainer[®] was used alone then blindly prescribing another inhaler is not the ideal solution. The In-Check Meter[®] used in this study was the first version introduced and thus all inhalation rates were measured with no resistance to airflow. The study highlights how this simple meter can be used to identify a patient's natural (untrained) inspiratory effort. Recently, a new version, the In-Check Dial, has been introduced which can mimic the resistance of a selection of inhaled products. The accuracy of this new version to identify inhalation rates, when set for different inhalers, has been

reported (28). Using a single meter rather than one for each inhaler provided by the manufacturer will be easier to use in the clinic. The inhalation rate of uncounselled patients through different inhalers can now be measured using the In-Check Dial. From the results obtained using this device the most suitable inhaler, without technique training, for each individual can be identified. The ideal device would be one where the inhalation rate obtained is towards the middle of the most desirable range for that inhaler to account for the natural intra-individual variability of inhalation rates (28). We now have studies in progress to evaluate the potential of the In-Check Dial in the clinic as an aid to prescribing.

REFERENCES

- Clark AR, Hollingworth AM. The relationship between powder inhaler resistance and peak inspiratory condition in healthy volunteers. Implications for *in-vitro* testing. *J Aerosol Med* 1993; **6**: 99–110.
- Richards R, Sanders M. Need for a comparative performance standard for dry powder inhalers. *Thorax* 1993; **48**: 1186–1187.
- Ross DL, Schulz RK. Effect of inhalation flow rate on the dosing characteristics of dry powder inhalers (DPI) and metered dose inhalers (MDI). *J Aerosol Med* 1996; **2**: 215–226.
- Malton A, Sumbly BS, Dandiker Y. A comparison of *in-vitro* drug delivery for salbutamol Diskus and Terbutaline Turbuhaler. *J Pharm Med* 1996; **6**: 35–48.
- Borgström L, Bondesson E, Morén E, Trofast E, Newman SP. Lung deposition of budesonide inhaled via Turbuhaler: a comparison with terbutaline sulphate in normal subjects. *Eur Respir J* 1994; **7**: 69–73.
- Newman SP, Morén F, Trofast E, Talaei N, Clarke SW. Terbutaline sulphate. Turbuhaler effect of inhaled flow rate on drug deposition and efficacy. *Int J Pharm* 1991; **74**: 209–213.
- Engel T, Scharling B, Skovsted B, Heinig JH. Effects, side effects and plasma concentrations of terbutaline in adult asthmatics when inhaling from a dry powder inhaler device and different inhalation flows and volumes. *Br J Clin Pharmacol* 1992; **33**: 439–444.
- Engel T, Heinig JH, Malling H-J, Scharling B, Nikander K, Madsen F. Clinical comparison of inhaled budesonide delivered either pressurized metered dose inhaler or Turbuhaler. *Allergy* 1989; **44**: 220–225.
- Pitcairn GR, Lunghetti J, Ventura P, Newman SP. A comparison of lung deposition of salbutamol inhaled from a new dry powder inhaler at two flow rates. *Int J Pharm* 1994; **102**: 11–18.
- Pitcairn GR, Lim J, Hollingworth A, Newman SP. Scintigraphic assessment of drug delivery for the Ultrahaler Dry Power Inhaler. *J Aerosol Med* 1997; **10**: 295–306.
- Nielson KG, Skov M, Klug B, Iverson M, Bisgaard M. Flow dependent effect of formoterol dry powder inhaled from the Aerolizer. *Eur Respir J* 1997; **10**: 2105–2109.
- Newman SP, Talaei N, Clarke SW. Salbutamol aerosol delivery in man with the Rondo Spacer. *Acta Ther* 1991; **17**: 49–50.
- Johnson S, Miles JF, Weir DC, Hanley SP. Turbuhaler objective assessment of patient generated flow. *Thorax* 1996; **51**: A75.
- Hawksworth GM, Chrystyn H. Characterization of the inspiratory manoeuvre when asthmatics inhale through a Turbuhaler pre-and post-counselling in a community pharmacy. *Respir Med* 2000; **94**: 501–504.
- Dewar MH, Jamieson A, McLean A, Crompton GK. Peak respiratory flow through a Turbuhaler in chronic obstructive airways disease. *Respir Med* 1999; **93**: 342–344.
- Borgström L, Derom E, Stahl E, Wahlin-Böll E, Pauwels R. The inhalation device influences lung deposition and bronchodilating effect of terbutaline. *Am J Respir Crit Care Med* 1996; **5**: 1636–1640.
- Brown PH, Ning ACWS, Greening AP, McLean A, Crompton GK. Peak inspiratory flow through Turbuhaler in acute asthma. *Eur Respir J* 1995; **8**: 1940–1941.
- Engel T, Heinig JH, Madsen F, Nikander K. Peak inspiratory flow and inspiratory vital capacity of patients with asthma measured with and without a new dry powder inhaler (Turbuhaler) device. *Eur Respir Med* 1990; **3**: 1037–1041.
- Hirsch T, Pater-Keen M, Koch R, Leupold W. Influence of inspiratory capacity on bronchodilation via Turbuhaler or pressurized metered dose inhaler in asthmatic children. *Respir Med* 1997; **91**: 340–341.
- Olsson B, Asking L, Borgström L, Bondesson E. Effect of inlet throat on the correlation between the fine particle dose and lung deposition. In Dalby RN, Byron PR, Farr SY, eds. *Respiratory Drug Delivery V. USA*: Interpharm Press Inc, 1996; 273–281.
- Payne N, Beard S, Brucklebank D, Ram F, Wright J, Taylor R. Clinical and cost-effectiveness of inhaler devices for children with chronic asthma. Report commissioned by NHS R&D HTA Programme, on behalf of the National Institute for Clinical Excellence, August 2000. www.nice.org.uk/pdf/asthma.pdf.
- Pedersen S, Hansen OR, Fulsgang G. Influence of inspiratory flow rate upon the effect of a Turbuhaler. *Arch Dis Child* 1990; **65**: 308–319.
- Paterson IC, Crompton GK. Use of pressurised aerosols by asthmatic patients. *BMJ* 1976; **1**: 76–77.
- Crompton GK. Problems patients have using pressurised aerosol inhalers. *Eur J Respir Dis* 1982; **119**(Suppl): 101–104.
- Nimmo CJ, Chen DNM, Martinusen SM, et al. Assessment of patient acceptance and inhalation technique of a pressurized aerosol inhaler and two breath-activated devices. *Ann Pharmacother* 1993; **27**: 922–927.
- Selroos O, Pietinhalho A, Riska H. Delivery devices for inhaled asthma medication: clinical implications of differences in effectiveness. *Clin Immunother* 1996; **6**: 273–299.
- Ganderton D. General factors influencing drug delivery to the lung. *Respir Med* 1997; **91**: 13–16.
- Tarsin W, Hawksworth GM, Chrystyn H. The intra-individual variability of inhalation rates through two different dry powder inhalers. *Thorax* 2000; **55**(Suppl 3) A61.