Delivery of inhaled beta agonists by metered-dose inhaler in ventilated patients – a survey of current practice

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For many years nebulisers have been the standard method of delivering beta agonists in ventilated patients, but metered-dose inhalers are increasingly seen as an effective alternative. Metered-dose inhalers are cheaper and less likely to cause infection. Clinical studies have shown inhalers to be as effective as nebulisers, but their use demands careful attention to detail. Minor alterations in inhaler technique can alter the delivered dose six-fold, varying from 0 to 38% of the total dose. We surveyed the frequency of metered-dose inhaler use and assessed the adequacy of the techniques currently employed. Our survey showed that only a minority (25%) of units were using inhalers, but that of these, 84% were using a dose or technique that was unlikely to deliver a therapeutic dose.

Keywords: *metered-dose inhalers; ventilators; salbutamol; intensive care unit*

Introduction

In a recent editorial in *JICS*, McAuley and Matthay pointed out that '…. the failure of drug delivery via the inhaled route is suggested to be one of the key factors implicated in the failure of other potentially useful drug therapies in ARDS.'[1] One of the problems with inhaled therapy in ventilated patients is that a relatively trivial change in technique can result in large changes in dose administered.[2-4] This is particularly true of metered-dose inhalers (MDI). If an inhaler is used incorrectly, there can be negligible drug delivery even after 100 doses.[5] In contrast, if used correctly, drug delivery can be up to 38%, which is comparable with non-intubated patients using the same technique.[4] The most important factors influencing drug delivery are use of humidification, synchronisation with inspiration, a delay between doses and use of a spacer.[4,6,7] If inhalers are to be effective, it is important that clinicians understand the principles behind their use and factors affecting their performance. Our survey aimed to assess how successfully intensivists use MDIs.

Methods

The Directory of Critical Care 2008 (CMA Medical Data, Loughborough) listed 302 adult ICUs in the UK. Each unit was contacted by telephone and a member of the nursing staff was asked about the use of beta agonists according to a pre-defined questionnaire (**Figure 1**). In ICUs where the staff were unable to answer at the time of initial enquiry, the unit was re-contacted until 100% of units had replied.

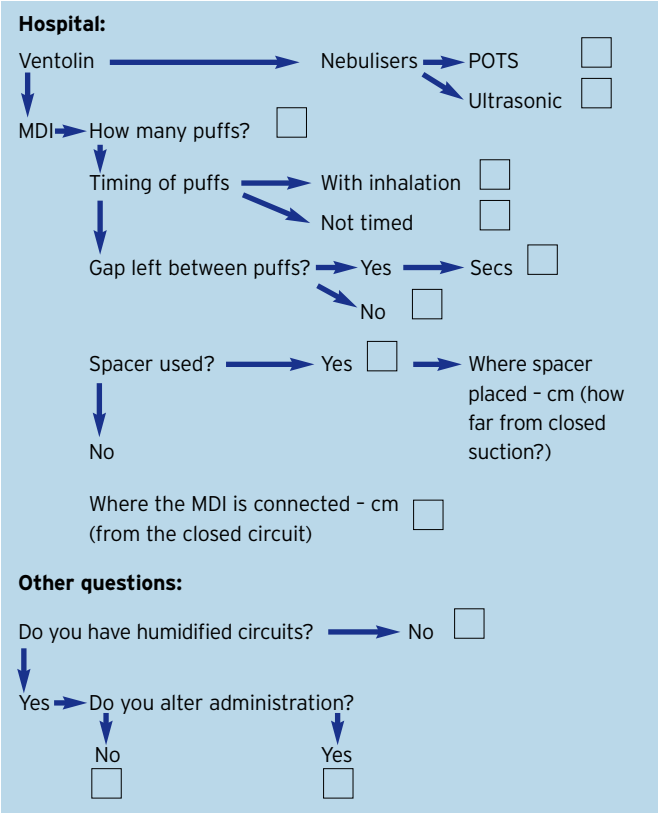

Figure 1 Telephone questionnaire regarding the use of inhaled beta agonists. MDI – metered-dose inhaler. POTS – jet nebuliser.

Results

All 302 UK ICUs regularly prescribed beta agonists for their patients. Two hundred and seventy-five (91%) used nebulisers (of which 225 (82%) used jet nebulisers, 28 (10%) ultrasonic nebulisers, and 22 (8%) used both). Twenty-seven (9%) ICUs used MDIs, and the remaining 47 (16%) used both inhalers and nebulisers.

Variable	Percentage effect on dose	No. of units (%)
Humidification	↓ 50	61 (82)
Synchronisation with inspiration	↑ 30	67 (91)
15 sec gap between dose	↑ 72	19 (25)
Use of spacer	↑ 70-75	20 (27)

Table 1 Number of units (total n=74) using different variables affecting inhaler drug delivery.

Prescribed dose (puffs)	No. of units (%)
1-5	51 (69)
5-10	7 (6)
10-15	12 (19)
Over 15	3 (4)
Unknown	1 (2)

Table 2 Prescribed doses of beta agonists using inhalers.

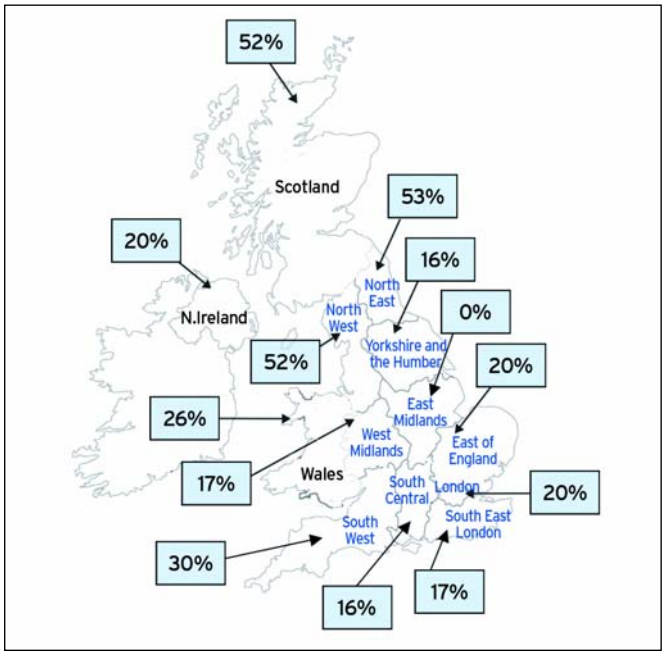

Figure 2 Regional use of MDIs in ventilated patients.

Of the 74 units using MDIs, 20 (27%) used a spacer; sixty-seven (91%) timed drug delivery with inspiration and 19 (25%) left at least 15 seconds between actuations. Ten units (14%) avoided humidified circuits; three (4%) used humidified circuits but stopped humidification before drug administration (see **Table 1**). The commonest prescribed dose was 1 to 5 puffs used in 51 (69%) of ICUs (**Table 2**). When all factors were considered, only 12 out of 74 (16%) ICUs were likely to be using the inhalers correctly to deliver therapeutic doses. The use of inhalers showed large regional variation (0 to 53%) (**Figure 2**), with a national average of 25%. A small number of hospitals spontaneously commented that inhaler use had been employed in the past but abandoned due to perceived lack of efficacy.

Discussion

This survey shows that 84% of units are using a technique that will deliver less than 25% of the recommended dose, which equates to approximately 10% of the prescribed dose. The reasons for ICUs adopting one technique over another were not explored but probably reflected local established practice.

Degradation of drug delivery using metered-dose inhalers is influenced by:

Humidification

Active humidification decreases inhaled drug delivery by about 50%.[6] It has an equally large effect on nebuliser performance, but because of the larger absolute dose its clinical impact is diminished.[8] Humidification affects drug delivery by altering the physical characteristics of the aerosol particles.[6] Particles are normally deposited by a mixture of inertial impact, sedimentation, and Brownian motion. Inertial impact tends to occur in the large bronchi, sedimentation in the smaller bronchi and Brownian motion in the alveoli. The smaller the particle, the more likely it will reach the distal lung. Active humidification causes particle swelling and hence deposition by inertial impact and sedimentation. The impact of passive humidification, eg with a humidifying filter, has not been tested.[4] Problems can also occur if the particles are too small and are lost in exhalation. The percentage of drug lost in exhalation is greater in intubated patients than in non-intubated patients (4.8% versus 1.0%).[6] The reason for this difference is not known.

Synchronisation with inspiration

Timing inhaler actuation with inspiration increases drug delivery. Bench studies show a 30% decrease in dose if delivery is not timed with inspiration.[7] A difference of one second between actuation and start of inspiration is enough to decrease delivery by 35%.[9] Delivering the dose as the tubing of the circuit expands is thought to be the best method[2] but no studies have examined the ability of staff to time drug delivery in this way.

Timing

Inhaled drugs should be delivered at the start of inspiration and 15 seconds left between actuations.[2] Giving doses rapidly one after the other may seem an attractive option, but an *in vitro* study showed a 72% reduction in dose if no gap was left.[7] Subsequent work has shown that leaving 15 seconds between actuations maximises drug delivery.[6] Fewer than half of ICUs waited 15 seconds or more between doses.

Use of a spacer

Using a spacer is key to success in both ambulatory and ventilated patients. It is 'fundamental in improving the efficacy of bronchodilator therapy given by MDI.'[5] In our survey only twenty (27%) units used a spacer. The effect of not using a spacer can be offset by increasing the prescribed dose; however only seven (9%) units used a dose large enough to compensate for the absence of a spacer. A spacer reduces the velocity of the MDI plume and allows evaporation of the propellant, which increases drug delivery.[8,9] The use of a spacer results in between four- and six-fold increase in drug delivery. This boosts

delivery to around 30-35% of prescribed dose.[4] Alternatives have been suggested such as the use of a bidirectional actuator,[9] but information on its effectiveness is limited.

In addition, there are other less well-understood variables in drug delivery using metered-dose inhalers. Differences in equipment affect drug delivery, as well as patient variables such as spontaneous *versus* mandatory respiration, tidal volume and respiratory rate. Several clinical studies were performed in the 1990s on sedated and paralysed patients receiving mandatory ventilation, but since then there has been a change in the way patients are ventilated with increased emphasis on low tidal volumes and augmenting spontaneous respiratory effort. All these are likely to alter drug delivery.

Conclusions

The indications for beta agonists in intensive care are the subject of current research. The ALTA study questioned the use of inhaled beta agonists in ARDS, and the results of the BALTI-2 study are awaited with interest. This survey shows that when using inhalers, the majority of ICUs may be using them incorrectly and so not delivering drug optimally. If beta agonists are thought to be important in the treatment of ARDS, it is vital that they are delivered properly.

Whether nebulisers or inhalers will prove the best way to deliver beta agonists in the future is open to question, and a survey of nebuliser practice may reveal similar deficiencies. Further technological developments such as improvements in ultrasonic nebulisers may make older technologies obsolete. In the meantime, whatever equipment is used, must be used correctly to deliver effective patient treatment.

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