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Dear Editor

Response to Prof. Borgström re: paper by Arvidsson et al. (Respir Med 2000; 94: 574–577)

We have received the letter by Prof. Borgström, employed by AstraZeneca R&D in Lund, regarding our recently published study comparing the effects of salbutamol given either by the Turbuhaler® or the Diskus® device (1). Prof. Borgström is bringing up a series of unrelated issues, but the key question is whether it is appropriate to use a cumulative dose–response design when comparing the clinical effects of bronchodilators.

Briefly, our study compared the effects of salbutamol given by two different inhalation devices, the Turbuhaler® and the Diskus®. We found that there were no, or very small, differences in the bronchodilating effects of salbutamol given by either device, in a dose range of 200–3200 μg. Importantly, we documented a clear dose–response relationship in FEV₁ over this dose range (2–2–2–51), which is important when comparing the potency of treatments.

Prof. Borgström argues that the initial dose of a β₂-agonist may influence the effects of a second dose, and thus that the results of findings at the higher levels of the dose–response curve may be more difficult to compare. Interestingly, however, Astra’s documentation for the Turbuhaler® is based on cumulative dose–response studies (2–5). Furthermore, there is a massive published documentation regarding the appropriateness of using cumulative dose–response designs in bronchodilator studies. In addition to these scientific arguments, it may however be even more important to remember that asthma patients, in real life, use multiple doses from an inhaler when they experience worsening of asthma. Thus, cumulative dosing may very well be appropriate when comparing the effects of different inhaled drugs. Regardless of this, we found no difference in the effects of salbutamol Turbuhaler® or Diskus® at the lowest dose used (200 μg). Also, a study performed in Southampton, U.K., showed no clinically relevant differences in maximal bronchodilating effect when therapeutic doses of salbutamol were given via Turbuhaler® either as two consecutive doses or as two divided doses separated by different time intervals (6).

We were careful to compare the same microgram doses, in contrast to some more recent publications evolved from studies sponsored by AstraZeneca (7,8). We did this to avoid any advantage for any of the used inhalers. Our conclusion must be, however aggravating it may be for Prof. Borgström, that there is no or little difference in the effects of salbutamol given by either Turbuhaler® or Diskus®, in the types of patients we have included in the present study.

Prof. Borgström had some additional comments. One of these has been addressed in a recent erratum. Importantly, it is not required to reference studies published only as abstracts, as these have not been peer reviewed. It is extensively argued that the Turbuhaler® gives better peripheral deposition than other devices, and in a publication by Thorson et al. at AstraZeneca, it is stated that ‘the systemic availability of budesonide, calculated as a geometric mean and expressed as percentage of the metered dose, was 38% for Turbuhaler® and 26% for p-MDI’ (9).

We are not stating that there is a greater peripheral to central deposition, but rather a greater total peripheral lung deposition, using the Turbuhaler® device. This argument, extensively used at scientific meeting and in marketing situations, may however be untrue as described in Prof. Borgström’s letter, thus arguing against any improved therapeutic ratio of a drug given by Turbuhaler® vs. any other device.

Importantly, we have high respect for Prof. Borgström’s competence in this field, but we feel that it also must be important to consider clinical implications of studies comparing different devices. ‘In vivo veritas’ as stated by Prof. Borgström previously (10).

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