Formoterol dry powder in asthma

The paper by Dr A Wallin et al (June 1993;48;611–4) on the action of formoterol causes some concern in the way the authors express the duration of bronchodilatation. The method quoted of using the median time with 20% or more of the maximum achieved bronchodilatation means that fairly minor degrees of effect, probably without clinical relevance, are used for the criteria for duration of action. For example, from their fig 2 the baseline FEV\textsubscript{1} would seem to be approximately 1·8 l. The maximum FEV\textsubscript{1} achieved for 24 \mu g formoterol was approximately 2·2 l, a bronchodilatation of 0·4–1·0% of which is 0·08 l. Therefore bronchodilatation of 1·8 l to 1·88 l or 4·4% of baseline was taken to estimate duration of action. This compares with a bronchodilatation of 0·27 l if the criterion of a 15% improvement from baseline is used. If this later value is employed there is only produces bronchodilatation for approximately 4–5 hours, which may not be statistically different from salbutamol.

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AUTHORS' REPLY We are grateful to Dr Bright for his comments and calculations on the duration of bronchodilatation. If you use the definition time with FEV\textsubscript{1} > 15% over baseline we have no disagreement with him. However, as mentioned in the discussion we did not use this definition because of the moderate reversibility in our data with patients on inhaled steroids. The mean reversibility of FEV\textsubscript{1} was 23%, the median 19%, and the lowest 15%. If you use the definition of duration as time with FEV\textsubscript{1} > 15% over baseline, you cannot usefully express duration if the patient's maximum bronchodilatation was 15%. Even with a median reversibility of 19% the duration calculated in this way remains misleading. Another problem with defining duration based on change of FEV\textsubscript{1} in relation to baseline is the natural variability of lung function in asthma.

In fig 3 in our paper the FEV\textsubscript{1} in the salbutamol and placebo groups declined spontaneously. For those treated with placebo the decline was from 1·8 l (baseline) to 1·59 at 12 hours. If we take formoterol 24 \mu g as an example the FEV\textsubscript{1} was 1·81 l 12 hours after dosing, which was 18% over the placebo baseline (1·59) at that time. For formoterol 12 \mu g at 12 hours the corresponding value was 11%. When deciding if a drug has any clinical effect one should consider the natural variation of asthma. In this study we have done that by calculating duration as time with >20% of maximum achieved bronchodilatation, or measuring duration of action on inhaled long acting \beta\_2 agonists has been advocated by Arvidsson et al and has recently been described in detail elsewhere.\footnote{Arvidsson P, Larsson S, Löfdahl C-G. Objective and subjective bronchodilatation in over 12 hours after inhaled formoterol; individual responses. \textit{J Asthma} 1993;30:459–65.}

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Thorax 1994 49: 95
doi: 10.1136/thx.49.1.95-a