Inhalation of aerosols by children: an ongoing controversy

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In the observational report by Karen G. Schüepp et al. published in this issue [1] the investigators tested a customised suspension of radiolabelled Budesonide with a small droplet size of mean mass diameter (MMD) of 2.5 ± 1.25 µm nebulised by a new "eflow" device. The lung deposition was 36% which was significantly higher than the 8% deposition with a conventional nebuliser, which produced particles with a MMD of 4.2 ± 2 µm. Despite convincing visualisation of better deposition using gamma camera technology the results are preliminary and need verification as the authors have recommended.

The Respiratory Society (ERS) Guidelines on the use of nebulisers, compiled by members of an ERS task force and published in the European Respiratory Journal in 2001 list problems with the scientific background of clinical nebuliser use: shortage of clinical trials, quality of reporting of published trials involving nebuliser use, responsibility of manufacturers, responsibility of prescribers and technical aspects of the nebuliser [2]. Most of these problems are apparent in the paper by Karen G. Schüepp et al. Why does this paper reflect the problems listed by the ERS task force?

First, it serves apples, pears, oranges and bananas: using two sets of nebulisers which generated two sizes of droplets, applying the method to children with or without tightly fitted face masks, either crying or breathing quietly during nebulisation, it introduces at least six variables, which are distributed at random to the 6 children in this study. This implies that every child in this investigation constituted an "n of one" trial (ie, a trial including only one person). The single new finding is an improved deposition by using the "eflow" device. Masks which are not close-fitting, crying during nebulisation and using bigger droplets have in the past all been shown to result in insufficient deposition. As visualised by gamma camera picture the finding in one child of a significantly improved deposition does however not generally imply, that the used device is four times better than the conventional nebulisers, as the reported deposition rates of 8% versus 36% might suggest.

Second, the specifications and quality of the nebuliser used, which generated higher deposition, are not described in the paper and also not referenced. Significant basic information about the nebuliser system – as it is generally requested – such as nebuliser type and function, fill volume, nebulisation time, residual solute volume etc. are lacking in the "methods" section, despite the fact that the "eflow" device and its actions have been presented at several meetings on poster presentations [3–5]. It was shown, that in vitro this device had a high respirable drug delivery rate and short inhalation time when customised solutions and suspensions were used; in vitro studies however were lacking so far.

Third, the paper does not take into account, that the figure with the significantly favourable deposition pattern could be exploited by prescribers as final proof of in vivo efficacy of this new device. Therefore, the report also creates potential problems regarding responsibilities of manufacturers and prescribers.

Why then was this report published? Does it bridge the gap between in vitro and in vivo research results? The authors of the study are in fact very fair in weighting their results and indicate that complementary combinations of delivery device and drug formulations are necessary for determining optimal drug deposition in the lungs of children. They also call for more results by way of verifying their observations and do therefore admit, that the shortage of clinical trials and quality of reporting of published trials is genuine. The dataset is unique and studies like the one here are difficult to perform. It is understandable that larger numbers of subjects can not be included in such study protocols. Nevertheless, the study has to be considered rather as an observational, interesting and putatively promising report and not as an established comparative research trial. More evidence is required in order to make definitive statements about the effectiveness of the new nebuliser. The authors' contribution to closing the gap between in vitro nebuliser research and in vivo efficacy testing in this first mini-step is well acknowledged. However, it is the wish and hope of the author, that the pleasing gamma picture from a single patient is not misused (by manufacturer and prescriber) as "proof" of high deposition with the new electronic nebuliser device.

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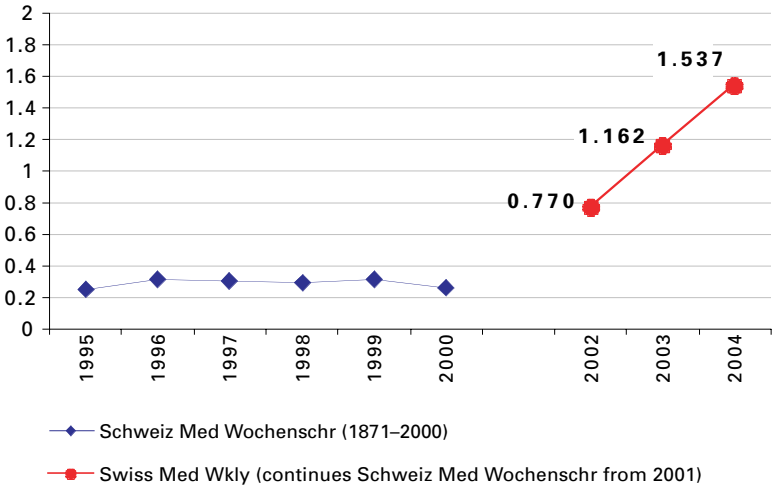

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