Classification of Cilio-Inhibiting Effects of Nasal Drugs

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Objective/Hypothesis: Nasal drug formulations are widely used for a local therapeutic effect, but are also used for systemic drug delivery. In the development of new nasal drugs, the toxic effects on the mucociliary clearance and therefore on the ciliated tissue is of importance. In this study, the effect of nasal drugs and their excipients on the ciliary beat frequency (CBF) is investigated. Study Design: Experimental, in vitro. Methods: CBF is measured by a photograph–electric registration method. Excised ciliated chicken trachea tissue is incubated for 15 minutes in the formulation, followed by a reversibility test. To estimate the ciliostatic potential, a classification is given of all tested formulations. According to the CBF, after 60 minutes every drug or excipient could be classified as follows: cilio-friendly: after 60 minutes the CBF has regained 75% or more of its initial frequency; cilio-inhibiting: after 60 minutes the CBF has regained between 25% and 75% of its initial frequency; or ciliostatic: after 60 minutes the CBF has regained 25% or less of its initial frequency. Results: Most formulations used are cilio-friendly or cilioinhibiting. Only some are ciliostatic. Preservatives have a major role in the cilio-inhibiting effect of the drug. Also, other additives can contribute to the toxicity profile of nasal drug formulations. Conclusion: This classification of the cilio-inhibiting potential of nasal drug formulations is a valuable tool in the design of safe nasal drugs. The number of animal studies in vivo can be reduced substantially by using this in vitro screening technique. This study demonstrates that the effect on ciliary movement of most drug formulations is due to the preservatives and/or additives and mostly not to the drug itself. Key Words: Nasal drug, preservatives, ciliary beat frequency, ciliostatic, cilio-inhibiting, cilio-friendly.

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