CORRESPONDENCE

The Effects of Theophylline on Hospital Admissions and Exacerbations in COPD Patients: Audit Data From the Bavarian Disease Management Program

by Johannes Fexer, Ewan Donnachie, Prof. Dr. med. Antonius Schneider, Prof. Dr. oec. publ. Stefan Wagenpfeil, Dr. rer. nat. Manfred Keller, Dr. rer. nat. Frank Hofmann, Dr. med. Michael Mehring in issue 17/2014

No new Insights

Introducing, the authors explain that based on evidence from studies, theophylline is of little benefit in COPD and associated with risks. At the same time, they state that the interesting question cannot be clarified "conclusively" with their study so that "further ... studies of routine data are needed". Even if one does not follow the obvious conclusion that the interesting question was already answered before this study, this analysis has at least not helped to resolve the uncertainty. One wonders why this analysis was performed at all. It does no produce any new insights and, according to the authors, has significant limitations. Therefore, the "causal interpretation … is limited" and the "effectiveness ... und adverse effects ... could only be conclusively assessed in RCTs". Consequently, further studies with the same known limitations will not clarify the matter. These are a waste of resources (1–3) and ethically problematic as they attempt to answer an apparently relevant question with insufficient means, according to the authors' evaluation, and thus delay the answering of the question. Why "it is hard to imagine" that ethics committees would approve RCTs is hard to understand. Either the question is open and can only be answered "conclusively" by means of RCTs—in which case ethics committees would certainly be sensible enough to realize this—or the question is no longer open. In that case, the question of ethics would not even arise and further studies would not be required.

RCTs are certainly not needed to answer each and every question, but where they are needed they should be conducted. We certainly do not need analyses where it is foreseeable that the results will not add to our knowledge – even if they make use of routine data.

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Conflict of interest statement
The author declares that no conflict of interest exists.

In Reply

We would like to respond to this letter to the editor. We have not written in our introduction that theophylline is of little benefit in COPD and associated with risks. We stated that it presently is regarded a third-line treatment (1). The studies conducted so far were generally not aimed at evaluating side effects of theophylline as a primary outcome measure. The one exception is the cohort study of Cyr et al. with 36 492 COPD patients (2). This study, however, did not use a causal method to identify theophylline effects and it found no evidence of severe side effects. Other than that, RCTs have so far been rather small, as stated already in the Discussion section. Therefore, the observed effects could also have occurred randomly, or only the inferiority of theophylline compared with other drugs was demonstrated without evidence of a definitive potential for harm (3). In this respect, we consider our routine data analysis to be an important and complementary contribution, also from an ethical perspective, as we were the first to decidedly demonstrate these effects with regard to exacerbations and hospitalizations. Furthermore, our analysis reveals that theophylline is still a commonly used drug. After all, 5.6% of the patients observed by us received theophylline. Since any matching or adjustments can only be performed with observed or accessible measures, we wrote that the pharmacological efficacy or the side effects can ultimately only be demonstrated in RCTs. Maybe we went too far with our assumption that ethics committees will not approve such studies. We would therefore welcome any suggestions on how such a study could get approved and be realized. Finally, it should be noted that reproducible analyses of routine data represent a valuable addition to evidence from RCTs.

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