

Comment on 'Clinical impact of non-antibiotic recommendations by a multi-disciplinary antimicrobial stewardship team' (Letter)

Author

Taghizadeh-Ghehi, Maryam, Ahmadvand, Alireza, Chaibakhsh, Samira

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Title: Comments on “Clinical impact of non-antibiotic recommendations by a multidisciplinary antimicrobial stewardship team”

Authors:

Maryam Taghizadeh-Ghehi

Research Center for Rational Use of Drugs, Tehran University of Medical Sciences, Tehran, Iran

taghizadehgm@sina.tums.ac.ir

Alireza Ahmadvand

School of Clinical Sciences, Faculty of Health, Queensland University of Technology, Brisbane, Australia

E-mail: alireza.ahmadvand@hdr.qut.edu.au

Corresponding author:

Maryam Taghizadeh-Ghehi

Research Center for Rational Use of Drugs Tehran University of Medical Sciences, Tehran, Iran

Address: 4th floor, No 92, Karimkhan Zand Ave., Hafte Tir Sq., Tehran, Iran

Tel/ Fax: +982188814157

Email: taghizadehgm@sina.tums.ac.ir

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Sir,

We have read with interest the recent study by Ng TM, et al. ^[1] aimed at describing the impact of non-antibiotic recommendations on patients' outcomes. The main finding of the study was reduced 30-day mortality following acceptance of non-antibiotic recommendations.

The main purpose of antimicrobial stewardship programs (ASPs) is to achieve optimum outcomes while reducing adverse effects and the emergence of resistance. Using both process and outcome measures has been recommended to determine the impact of ASPs ^[2]. Mortality is one of the clinical outcome indicators of ASPs, and probably, one of the most objective ones. Systematic reviews with meta-analysis have revealed that ASPs and interventions to improve antibiotic use in hospitals have had beneficial effects on clinical outcomes without increasing mortality ^[3, 4]. Mortality could also be considered as a balancing measure to reassure ASP safety. However, the ASPs are not always expected to improve clinical response or reduce mortality and they might only minimize secondary damages such as the emergence of multidrug-resistant organisms ^[5]. One of the questions that arises and is relevant to the study by Ng TM, et al. is around whether mortality could also be considered as a suitable clinical outcome for 'non-antibiotic recommendations'. More specifically, since mortality as an ultimate clinical outcome is affected by multiple factors, how any reduced mortality could be related directly to the acceptance of non-antibiotic recommendations? Or, interpreted as such?

Clinical response on day seven was considered as one of the clinical outcomes following acceptance of non-antibiotic recommendations and three intentions were described for the non-antibiotic recommendations in this study: 1) to stop antibiotic or set duration, 2) to diagnose non-infectious conditions, and 3) to diagnose infection-related complications or other infections. The question raised here would be whether we could expect clinical improvement at day seven following acceptance of a recommendation aimed at stopping an antibiotic, or not. Additionally, the study showed more frequent positive clinical response at day seven in patients for whom radiological imaging/endoscopy was accepted. In many hospitals, arrangements for performing radiological imaging/endoscopy is a time- and resource-demanding process and it may take 24-48 hours to be done. Therefore, the possible delay in performing those para-clinical procedures, and any possible delay for adopting new therapeutic strategies based on the results, should be explained to support the suitability and relevance of clinical improvement at day seven after acceptance of the non-antibiotic recommendations. This aspect needs more elaboration in the article.

To overcome study design limitations, confounder adjustment using multi-variate analysis (MVA) was considered by the authors. However, some elaborations are needed about the robustness of this part of the statistical analyses. The study design and methodology of the MVA needs more clarification; more specifically, for the description of the exclusion criteria, and, the inclusion of

patients with multiple reviews during the study period. It was mentioned that only the first ASP review with non-antibiotic recommendations was included. However, limited data regarding the frequency of providing multiple reviews with non-antibiotic recommendations to patients, as well as excluded patients who had received antibiotic recommendations concurrently were provided. It would have been clearer, if the authors have notified whether the patients were excluded, subject to subsequent reviews occurred during the outcome follow-up.

The final note is about the provision of recommendations by independent healthcare professionals in a multidisciplinary team. The authors have highlighted that independent recommendations by the pharmacists have been made in 20–30% of cases, and infectious disease specialists have covered the rest in their daily clinical rounds. For explaining the optimal comparability of recommendations being made by independent observers from different disciplines, and any corresponding variability, discussing the chances of inter-observer and intra-observer variability in the recommendations given by different professionals would be informative. Even if the chances of inter-observer and intra-observer variability are low (e.g. because of standardized clinical pathways, defined procedures, clear set of guidelines, or similar), acknowledging that this variability is part of most of the recommendations given by healthcare professionals, would highlight the fact that the authors have considered the importance of increasing the reliability of their intervention.

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