

Antiemetic Guidelines-Are They Being Used?

Rolf Kaiser, MD

Objectives

1. Understand how important therapeutical guidelines for the improvement of the drug treatment in general are
2. Get an impression that the implementation of the antiemetic guidelines has to be improved
3. Understand that the successful implementation of such guidelines depends on multiple factors e.g. structural problems, patient factors as well as other quite strong barriers, such as the individual acceptance of guidelines and education of physicians and nurses.

Today clinical practice guidelines are still regarded as therapeutical standards for different medical therapies. These evidence-based recommendations are designed to improve and to harmonize the individual drug therapy. However, from the data available at the moment, the successful implementation of all these recommendations seems to be rather difficult. In 1997 an international antiemetic guideline for the treatment of patients undergoing a chemotherapy was issued by the Multinational Association of Supportive Care in Cancer, and has been in use ever since. But for multiple reasons, these guidelines especially for delayed emesis have not been pursued completely, although it has been known for a long time that when using the antiemetics properly their antiemetic efficiency is similar to that observed in randomized controlled trials. Besides, structural problems and patient factors as well as other quite strong barriers, such as the individual acceptance of guidelines and the education of the physicians and nurses, may represent a crucial factor for a successful implementation of the respective guideline. Furthermore, a lack of agreement with specific guidelines or guidelines in general may also be one underlying reason. In conclusion, the aim of a better acceptance and use of the antiemetic guidelines can only be achieved through a complex and long-term process. Thus, an efficient education and training of all persons involved in the patient's treatment is necessary. Besides the educational process the individual compliance of the guidelines should be monitored independently to assure that these recommendations are being implemented.

Nausea and vomiting are still among those side effects of a cytostatic therapy that patients fear to suffer from. It was the full comprehension of the pathophysiological processes that result in chemotherapy-induced nausea and vomiting (CINV) which finally gave way to a new form of antiemetic therapy introducing 5-HT₃- and NK1-receptor antagonists in combination with glucocorticoids. An optimized antiemetic therapy not only improves the overall condition of the patients and their quality of life, but may also influence their response to the chemotherapy. In 1997 guidelines for the antiemetic therapy were published by the Multinational Association of Supportive Care in Cancer¹. These guidelines were modified in a meeting, which was held recently in Perugia. According to these guidelines patients that undergo a therapy with high-emetogenic cytostatics shall be treated with a combination of 5-HT₃-receptor antagonists, a NK1-receptor antagonist and a glucocorticoid. Unfortunately, the findings of the controlled clinical trials on this issue will remain rather ineffective, if they are not applied to everyday routine in the hospitals.

Thus, based on a large, prospective, observational study on drug utilization and effectiveness of antiemetics carried out in 1996 the Italian Group for Antiemetic Research was able to show that 23% of the patients that underwent a high-emetogenic cytostatic therapy were not being treated with a combination of a glucocorticoid and a 5-HT₃ receptor antagonists to prevent acute vomiting. These patients suffered from acute vomiting to a much larger extent than those that were treated according to the respective guidelines (37% versus 21.6%)². More than 47% of the former patients were not even treated to prevent delayed vomiting. Similar observations were made after the publication of the MASCC-guidelines: between 49% and 53% of all patients did not have a treatment according to the guidelines to prevent delayed vomiting, and as much as 26% up to 48% of all patients did not have prophylactic treatment for acute vomiting^{3,4}. These data clearly show how important an improvement of the introduction of guidelines is for this field of therapy.

The phenomenon of guidelines not being followed is not only found in the field of antiemetic therapy, but sadly enough is widely spread in the various fields of medicine. But given the large number of medical guidelines, which nowadays add up to more than several hundreds, it is quite evident that there are problems implementing them into the clinical routine. The reasons are manifold: They may be due to the patient, the physician, the health care team or the respective health care organization in charge. To a certain extent the problems result in the guidelines themselves. Whenever they are based on scientific evidence, they are precise, set out clearly, and refer to acute diseases, they are easily accepted and followed. Whenever they are vague, unspecific or controversial or not compatible with current values, related to chronic diseases or will provoke negative reactions in patients, there is a lower rate of acceptance⁵⁻⁸. Thus, for guidelines to be implemented better, various changes need to be made. Of course, the physician plays a crucial role here, but different barriers may influence his behaviour to guideline adherence. Thus, external barriers

(social and organisational context) such as patients', structural and guideline factors and internal barriers (knowledge and attitudes), like lack of awareness, lack of familiarity or lack of agreement with specific guidelines may influence the physicians' behaviour and his adherence to guidelines^{7,9}. Besides the individual factor of the respective physician the way in which guidelines are being introduced is quite important. The passive dissemination of educational materials are generally ineffective to improve health professional performance, whereas multifaceted interventions composed of audit, feedback, reminders, outreach visits or patient mediated interventions have proved to be more successful^{7,10,11}. But also computerized decision support can be effective for drug dosing and preventive care^{12,13}.

Studies on the implementation of antiemetic therapy guidelines demonstrated that a multifaceted intervention program can promote the use of the guidelines in a clinically appropriate manner. However, physicians' participation in guideline development and evidence of poor compliance alone did not improve the implementation of guidelines in the clinical practice. It was more a self-reflecting process of the physicians through the antiemetic failure of the patients, and an external control of the physician compliance to the antiemetic guidelines that improved the antiemetic results¹⁴⁻¹⁶. But even if the guidelines are being followed a 100% it is known from a large number of controlled clinical trials that still 20 up to 30% of the patients do not respond enough to an antiemetic therapy that is carried out according to the therapy guidelines. The reasons may be individual, patient-specific factors that have an impact on the pharmacokinetics and the pharmacodynamics of the antiemetics. If further clinical studies prove these correlations, it will be necessary to add such individual risk factors to therapy guidelines in the future. Furthermore, cultural differences may hinder the implementation of therapy guidelines too.

So far, none of the approaches to implement change in patient's care is superior for all changes in all situations, but the mere introduction of therapy guidelines that is not supported by additional measures to change the physicians' behaviour is rather ineffective or even useless. It seems that only a complex approach including the patients, the physicians, the health care team as well as a structural change of the health care system may ultimately improve antiemetic therapy. This will be a challenge for all of us in the near future.

References

1. Antiemetic Subcommittee of the Multinational Association of Supportive Care in Cancer (MASCC). Prevention of chemotherapy- and radiotherapy-induced emesis: results of Perugia Consensus Conference. *Ann Oncol*. 1998;9:811-819.
2. The Italian Group of Antiemetic Research. Transferability to clinical practice of the results of controlled clinical trials: the case of antiemetic prophylactic treatment for cancer chemotherapy-induced nausea and vomiting. *Ann Oncol*. 1998;9:759-65.
3. Drug Utilization Review Team in Oncology (DURTO). Antiemetic prescription in Italian breast cancer patients submitted to adjuvant chemotherapy. *Support Care Cancer*. 2003;11:785-9.
4. Fabi A, Barduagni M, Lauro S, et al. Is delayed chemotherapy-induced emesis well managed in oncological clinical practice? An observational study. *Support Care Cancer*. 2003;11:156-61.
5. Grilli R, Lomas J. Evaluating the message: the relationship between compliance rate and the subject of a practice guideline. *Med Care*. 1994;32:202-13.
6. Grol R, Dalhuijsen J, Thomas S, et al. Attributes of clinical guidelines that influence use of guidelines in general practice: observational study. *BMJ*. 1998;317:858-61.
7. Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. *Lancet*. 2003;362:1225-30.
8. Michie S, Johnston M. Changing clinical behaviour by making guidelines specific. *BMJ*. 2004;328:343-5.
9. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA*. 1999;282:1458-65.
10. Oxman AD, Thomson MA, Davis DA, et al. No magic bullets: a systematic review of 102 trials of interventions to improve professional practice. *CMAJ*. 1995;153:1423-31.
11. Bero LA, Grilli R, Grimshaw JM, et al. Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. The Cochrane Effective Practice and Organization of Care Review Group. *BMJ*. 1998;317:465-8.
12. Hunt DL, Haynes RB, Hanna SE, et al. Effects of computer-based clinical decision support systems on physician performance and patient outcomes: a systematic review. *JAMA*. 1998;280:1339-46.
13. Walton R, Dovey S, Harvey E, et al. Computer support for determining drug dose: systematic review and meta-analysis. *BMJ*. 1999;318:984-90.
14. Nolte MJ, Berkery R, Pizzo B, et al. Assuring the optimal use of serotonin antagonist antiemetics: the process for development and implementation of institutional antiemetic guidelines at Memorial Sloan-Kettering Cancer Center. *J Clin Oncol*. 1998;16:771-8.
15. Dranitsaris G, Leung P, Warr D. Implementing evidence based antiemetic guidelines in the oncology setting: results of a 4-month prospective intervention study. *Support Care Cancer*. 2001;9:611-8.
16. Mertens WC, Higby DJ, Brown D, et al. Improving the care of patients with regard to chemotherapy-induced nausea and emesis: the effect of feedback to clinicians on adherence to antiemetic prescribing guidelines. *J Clin Oncol*. 2003;21:1373-8.

