Obstacles to the Implementation of Antiemetic Guidelines

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Abstract
Although guidelines help physicians deliver high quality clinical care, they will have minimal impact unless familiarity and adherence are achieved. Although nausea and vomiting are highly feared toxicities of chemotherapy that markedly decrease patient quality of life, modifications in physician behavior and improvements in standards of care, particularly in terms of preventing delayed emesis, have been slow. Variations in format, goals, physician education, and institutional education may all affect guideline implementation and state-of-the-art care. The relationship between these factors and the scientific basis of antiemetic guidelines must be considered to achieve optimal results and compliance. (JNCCN 2009;7:601–605)

Clinical guidelines are “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.”1 Although this definition seems to be clear and straightforward, numerous guidelines—similar, but not identical—have been developed by different organizations for the same medical conditions. Even when these guidelines are written, acceptance and implementation (the benchmarks of quality care studies) are more problematic. In oncology, this is particularly true in the area of supportive care, where the lack of “life or death” as the outcome of an incorrect decision allows more latitude to the practitioner. Chemotherapy-induced nausea and vomiting is historically the most feared toxicity of chemotherapy2,3 and has a major effect on quality of life.4 However, implementing guidelines in this area has still been difficult, with examples of significant undertreatment and overtreatment, and can serve as a model for the difficulties in providing this guidance in supportive care.

In addition to the NCCN,5 numerous organizations, including ASCO,6 the Multinational Association of Supportive Care in Cancer (MASCC),7 American Society of Health-System Pharmacists (ASHP),8 and the European Society for Medical Oncology (ESMO),9 have authored their own antiemetic guidelines. Government-authorized guidelines are also available, such as those promulgated by the National Institute for Clinical Excellence (NICE)10 in Great Britain, and numerous local guidelines. Although these guidelines are mostly similar, a better understanding of the differences can be obtained by first realizing that the final form of a set of guidelines is significantly affected by the nature of the charge given to the guidelines committee, point of view of the sponsor giving that charge, and membership of the guidelines committee itself. Guidelines from ASCO11 and MASCC,12 for example, have the stated purpose of being completely evidence-driven. Although this allows practitioners to have much faith in the validity of the content of these guidelines, it also means that numerous clinical areas and scenarios will have no guideline recommendation because no high-level evidence exists. Therefore, these guidelines may seem disjointed and be more difficult to implement and understand.

NCCN strives, by definition, to be comprehensive,11 and thus provides guidelines that can be fashioned into clinical pathways to provide advice for most clinical situations. These guidelines are intended to be...
user-friendly and are welcomed by practitioners with problems requiring immediate answers. However, to provide such a smooth pathway through numerous stages and possibilities, these guidelines must include a certain number of category 2B recommendations, which may represent best available evidence but are not always supported by high-level clinical trials or complete consensus among the experts. These guidelines may simulate a “Meet the Professor” session, for example, during which the listener receives more knowledgeable advice than otherwise available, but the line between clinical trials evidence and expert opinion may be blurred.

When financial considerations and cost-effectiveness are taken into account in guidelines creation, such as those of NICE or local guidelines, recommendations may be further modified. One particular area of concern is when individuals or groups with a significant financial stake in the outcome are allowed to control or influence the creation of guidelines. It is generally accepted that a guidelines meeting or panel organized by a pharmaceutical company might not be able to be totally objective about their own products. However, in the present economic climate, full funding of guidelines efforts by governmental agencies is unlikely and pharmaceutical house funding of guidelines meetings with unrestricted grants may become increasingly important.

Furthermore, direct financial conflicts-of-interest among guidelines committee members is also a concern. However, because the knowledge and experience of key experts in the field is valued by both academic organizations and industry, excluding experts who served as industry consultants from guidelines panels might diminish the quality of the guidelines committee and of guidelines produced. Full and transparent disclosure of financial ties, therefore, has become a significant but satisfactory substitute that allows participation by these experts (although excluding them from decisions on issues related to the subjects for which they have been consultants is a reasonable requirement).

Once guidelines are created, the challenge becomes educating physicians and encouraging adherence. Most physicians believe that guidelines are educational and might improve quality of care. However, this is counterbalanced by concerns that guidelines may be too rigid, could be used to justify disciplinary actions, and are mainly driven by cost-control issues. In the case of antiemetics, use of serotonin antagonists as the mainstay of acute antiemetic therapy against highly and moderately emetogenic chemotherapy has become so widespread that guidelines are almost not necessary to encourage appropriate use. A survey of 1956 Italian patients performed in 1996 found that 99% of those undergoing highly emetogenic chemotherapy and 88% of those undergoing moderately emetogenic chemotherapy underwent acute treatment with a serotonin antagonist (with or without a corticosteroid). For delayed vomiting, for which appropriate treatment is less intuitive, guidelines might have a greater impact, but a wide variation in treatment is seen. In the same survey, 47% of patients undergoing highly emetogenic chemotherapy and 66% of patients undergoing moderately emetogenic chemotherapy had no delayed emesis prophylactic therapy although this therapy was specified by antiemetic guidelines, whereas 15% of patients undergoing low emetogenic chemotherapy had delayed emesis prophylactic therapy although this therapy was not recommended or considered necessary. In a second survey of 2393 Italian patients performed in 2002, failure to administer treatment to prevent delayed emesis decreased to 21% and 30% of patients undergoing highly and moderately emetogenic chemotherapy, respectively. However, 46% of patients undergoing low emetogenic chemotherapy also had delayed emesis prophylaxis, suggesting that these findings simply reflected an overall increase in antiemetic use.

There are several possible explanations for the lack of appropriate use of delayed emesis prophylaxis. In a comparative survey of physician/nurse perceptions and patient experience, health professionals significantly underestimated the incidence of delayed emesis, indicating that a lack of treatment may reflect a belief that no treatment is necessary because no need is unmet. In addition, Ihbe-Heffinger et al. has shown that although following antiemetic guidelines decreases the incidence of delayed emesis, up to 50% of patients will still experience this phenomenon despite antiemetic treatment.

Encouraging adherence to a guideline is more difficult if treatment with that guideline has not been clearly shown to be highly effective. Encouraging adherence, even to an effective guideline, is also more difficult if the problem addressed is not seen as a critical patient issue. Ettinger et al. presented hypo-
Implementation of Guidelines

Theoretical patient cases pairing different chemotherapy regimens and antiemetic regimens to 557 physicians. Although frequency of antiemetic use according to guidelines was consistent across scenarios, physicians were more likely to recommend aggressive chemotherapy consistent with guidelines for patients with curable tumors, but less likely to recommend chemotherapy consistent with guidelines for patients with incurable disease. Prognosis of the tumor was therefore the main driver of the level of care provided, rather than guideline recommendations.

Finally, individual physicians may or may not be familiar with specific guidelines. A survey found that ASCO guidelines were familiar to approximately 90% of 153 physicians in the United States and 404 physicians in Europe, whereas NCCN guidelines were familiar to twice as many physicians in the United States as in Europe (96% vs. 47%), and the pattern of recognition by physicians was reversed for guidelines promulgated by European organizations (23% vs. 69%). However, for each organization that published both therapeutic (tumor directed) and supportive care (antiemetic) guidelines, a greater percentage of physicians (<15%) were familiar with the therapeutic guidelines than the supportive care guidelines.

The question also remains how to best educate physicians if guideline adherence is the desired goal. Experts generally agree that passive diffusion of new information, including guidelines or consensus statements, is only minimally effective. Institutions that have been involved in antiemetic research are more likely to follow guidelines after the research is completed, suggesting either that the key opinion leaders at these institutions are influential among their colleagues or that use of antiemetics in a particular pattern had simply become ingrained within the institutions.

In an evaluation of implementation of an obstetric guideline in Ontario, Lomas et al. found that education by a local opinion leader increased guideline adherence. However, different conclusions were reached in an evaluation of the impact of different forms of education at an academic community hospital in Massachusetts that was attempting to implement antiemetic guidelines. A program of in-house education and dissemination of guidelines had only a transient effect on improving adherence. A lecture presented by a nationally known key opinion leader had no effect at all. Only when diaries of emetic response after chemotherapy were kept by a series of patients and feedback was provided to their physicians, indicating that antiemetic protection using routine measures was not as effective as expected, did adherence to the new antiemetic guidelines improve in a durable manner.

Education of institutions presents problems unique from those of educating individuals. Challenges in introducing antiemetic guidelines have been addressed in different ways by several different institutions. From the viewpoint of institutional goals and priorities, excellent antiemetic efficacy according to present knowledge is still a primary goal. However, in these cases, interdisciplinary teams consisting of physicians, nurses, and pharmacists are often constituted to design guidelines that assign equal importance to advancement of the institution’s economic goals.

Berard and Mahoney reported a program at Rhode Island Hospital that emphasized lower ondansetron doses, increased use of oral formulations, and decreased use of serotonin antagonists for preventing delayed emesis, which resulted in a cost avoidance of $205,000 per year. Engstrom et al. used a standard antiemetic form at the VA Maryland Health Care System to institute a new oral antiemetic regimen with potential savings of $20,000 per year. Mutnick and Szymusiak-Mutnick used decision analysis techniques and a decision tree to determine that granisetron would be more cost-effective than ondansetron in patients undergoing highly emetogenic chemotherapy and incorporated this concept into the antiemetic guidelines for the University of Iowa Hospitals and Clinics.

More detailed descriptions have been given of the antiemetic guideline design and implementation projects at Mayo Clinic and Memorial Sloan-Kettering Cancer Center, both of which involved several iterations of in-house guidelines. Loprinzi et al. reported establishment of initial antiemetic guidelines at the Mayo Clinic and then 3 revisions between September 1995 and December 1998, with a gradual shift from intravenous to oral antiemetics and the elimination of ondansetron for preventing delayed emesis, resulting in marked cost savings.

Rather than requiring physicians to keep track of these changes in the guidelines, a standard chemotherapy order form allows physicians to request...
standard antiemetics, with an in-house algorithm then assigning the antiemetic regimen. Nolte et al.\textsuperscript{33} described the generation of initial antiemetic guidelines at Memorial Sloan-Kettering Cancer Center, followed by 2 revisions between 1993 and 1995. Cost savings of $1,500,000 resulted from switching from ondansetron to granisetron and from the intravenous to oral route for highly emetogenic chemotherapy. Efficacy was not compromised, but the authors acknowledged that education efforts were necessary to convince practitioners to first change from the familiar serotonin antagonist (ondansetron) to a new agent and then to believe that an oral agent could be as potent as an intravenous one. In this case, a preprinted form with a check box for “Antiemetics as per Guidelines” was not sufficient to induce adherence (the box was often not checked) and was replaced with a preprinted form with the check box already checked so that physicians would have to make an extra effort not to follow the guidelines.

This experience confirms that guidelines reflecting changes in existing routine will be more difficult to implement,\textsuperscript{19} but also shows (with the prechecked order form) that, faced with peer or institutional pressure, physicians will follow the path of least resistance in an area that may not be considered of primary importance. Ironically, although a primary purpose of the guideline process is education, implementation on an institutional level seems to be more effective when personal knowledge and active decision making are removed from the process and replaced with a general order for standard antiemetics that relies on institutional knowledge and policies instead.

Implementing antiemetic guidelines is therefore associated with all of the basic challenges of implementing guidelines along with obstacles specific to supportive care guidelines as opposed to therapeutic guidelines. However, pausing to consider the optimal goal of guideline implementation is not unreasonable. In measuring quality of care according to guideline adherence, a higher adherence rate is assumed to imply better quality of care, with the ultimate goal of excellent care being 100% compliance.

Perhaps a more reasoned approach is described in the 2003 movie “Pirates of the Caribbean: The Curse of the Black Pearl,”\textsuperscript{35} when the pirate captain states that “the code is more what you’d call ‘guidelines’ than actual rules.” After acknowledging the general guidance of the code, he takes the action deemed most appropriate for the situation. Similarly, the surgical community accepts that a finding of acute appendicitis in 100% of appendectomies without any false positives would imply that the level of clinical suspicion was too low and that a certain number of cases with significant pathology were also being missed.\textsuperscript{36} By the same token, recognizing the many factors that go into the creation and implementation of antiemetic guidelines, a high but not perfect level of compliance might provide reassurance that the knowledge base of the guidelines was being used to establish clinical direction, but that clinical judgment regarding benefits and toxicities of treatment was also being used to attempt to deliver optimal patient care.

References


