Optimal Use of Antiemetics in the Outpatient Setting

In his article, Dr. Grunberg charts the history of our understanding of chemotherapy-induced nausea and vomiting, and the discovery and development of drugs for its prevention. He places appropriate emphasis on the serotonin (5-HT3) antagonists—notably, ondansetron, granisetron, and dolasetron—which have revolutionized the field over the past decade.

As detailed by Dr. Grunberg, these drugs have not only proven to be extremely effective in the prevention of acute, chemotherapy-induced emesis, but are also extremely flexible in schedule and route of administration, with remarkably few side effects. This has led to the rapid adoption of these drugs in clinical practice, and their popular use. An important problem not addressed by Dr. Grunberg in this article is how to control the cost of these agents, which can total hundreds of dollars per day.

Institutional Standards

At Memorial Sloan-Kettering Cancer Center (MSKCC), we have established an Antiemetic Subcommittee comprised of physicians, nurses, and pharmacists, to maintain institution-specific guidelines for the administration of antiemetic agents. Our recommendations are based on considerations such as the dose-response curves of various antiemetic agents. As detailed by Dr. Grunberg, the 5-HT3 antagonists have logarithmic dose-response curves, which rapidly reach a therapeutic plateau and reflect long half-lives of 5 to 10 hours. This accounts for the clinical effectiveness of a single, up-front dose of a 5-HT3 antagonist for acute emetic prophylaxis, which is our institutional standard.

We limit the automatic use of these agents to patients receiving chemotherapy likely to cause vomiting (eg, cisplatin or doxorubicin) and always administer 5-HT3 antagonists with dexamethasone to enhance the effectiveness of the regimen. We also use a 5-HT3 antagonist/dexamethasone combination for the prevention of delayed emesis. A combination of dexamethasone and metoclopramide is a good alternative regimen for delayed emesis.

As a result of our guidelines, patients at MSKCC have demonstrated excellent tolerance of emetogenic chemotherapy, accompanied by an increase in antiemetic use, yet a dramatic decrease in antiemetic drug expenditures across the institution.[1] Other groups have published similar guidelines intended to both improve patient outcomes and control resource utilization.[2]

Understanding of Mechanisms

Our understanding of the mechanism of chemotherapy-induced nausea and vomiting lags behind our ability to treat it. For example, we know that 5-HT3 antagonists work better when combined with dexamethasone, yet this phenomenon lacks a physiologic explanation. Nor do we understand why the serotonin antagonists fail to effectively prevent delayed nausea (> 24 hours after administration of chemotherapy).

A new class of drugs, the neurokinin (NK)-1-receptor antagonists, are proving to be especially suited to fill this therapeutic gap. These agents may find their way into clinical practice by improving the prevention of delayed emesis when combined with standard antiserotonergic and corticosteroid therapy following highly emetogenic chemotherapy.[3] They also appear to enhance the prevention of acute emesis achieved by the 5-HT3 antagonist/dexamethasone combinations.

Conclusions

The evolution of antiemetic therapy in oncology is an excellent illustration of how science, technology, and clinical observation can combine to promote medical progress. The field of antiemetic therapy has advanced not only through the identification of neurotransmitters and receptors, but also as the result of astute clinical observations and innovation. Dr. Grunberg’s
discussion of new findings with high-dose metoclopramide, or the development of opioids and cannabinoids for clinical use as antiemetics, are good examples of such advances. The next breakthrough in antiemetic therapy may not be the discovery of a new neurotransmitter antagonist, but rather, the use of an existing compound with a different dose or timing, or in a unique combination.

References:


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