

Outpatient Management of Febrile Neutropenia: Is It Safe Yet?

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Commentary on "Outpatient Management of Febrile Neutropenia: Time to Revise the Present Treatment Strategy" by Carstensen and Sørensen (page 199).

Drs. Carstensen and Sørensen provide an excellent article to support the use of an outpatient treatment strategy to manage low-risk patients with chemotherapy-induced febrile neutropenia. To date, there are no large, multicenter, randomized studies to determine the efficacy and safety of inpatient versus outpatient treatment strategies, and it is unlikely that further controlled studies would change current practice. Future direction needs to minimize the misclassification of low- and high-risk patients, determine the epidemiology of infections, and build an infrastructure to ensure the delivery of best supportive care.

Further Considerations

Misclassification of individuals with febrile neutropenia can be devastating for both low- and high-risk febrile neutropenic patients. Hospitalization has social, practical, and economic ramifications.¹ Elting and colleagues² retrospectively compared the cost of outpatient and inpatient management and found that the mean cost of treatment among inpatients was twice that of outpatients (\$15,231 vs \$7,772; $P < 0.001$). Along with higher costs, low-risk patients admitted to the hospital may be exposed to superinfections with resistant bacteria and fungi. However, outpatient treatment poses its own potential risks. Patients may have a false sense of security that prevents them from seeking necessary medical intervention. High-risk patients that are misclassified as low risk may also

experience life-threatening complications, including death.

The Talcott Risk Assessment and the Multinational Association for Supportive Care in Cancer (MASCC) have successfully assisted clinicians in determining which patients are medically stable based upon the patients' presenting clinical features and an internationally validated scoring system.^{3,4} The ultimate goal for each study was to select patients who are considered low risk and might be candidates for new therapeutic treatment options, including outpatient management. Modifications to each risk-assessment strategy are needed to decrease the risk for outpatient treatment failure. Determining the severity (absolute neutrophil count [ANC] $< 100/\text{mm}^3$) and the duration of neutropenia can decrease the risk of failure. The use of granulocyte and granulocyte-macrophage colony-stimulating factors has been shown to influence the severity and duration of neutropenia and may convert some patients who would otherwise have prolonged neutropenia to the low-risk treatment group.⁵ Further studies are needed to fully understand the effect of these stimulating factors.

Prediction of mucositis and its severity will also help with the success of outpatient treatment.⁶ Identifying chemotherapeutic agents that increase the risk of severe mucositis (with a grade > 2 based on the National Cancer Institute–Common Toxicity Criteria) will allow clinicians to determine which patients can successfully take oral medications and are at a higher risk for infection. Advanced age and a decreased performance status (> 2 on the Eastern Cooperative Oncology Group measurement) are two additional considerations that may influence the success of outpatient treatment.^{6,7}

Epidemiology is another important factor to consider when treating low-risk patients in the outpatient setting. Approximately half of patients who present with febrile neutropenia will have "unexplained fever" and no clinical microbiologic docu-

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mentation of infection.⁸ Knowledge of local institutional antibiotic susceptibility patterns and organisms will enhance successful treatment. Early detection of epidemiologic changes will influence prophylactic and empiric treatment. Prophylaxis should only be considered for patients with anticipated severe or prolonged neutropenia (ANC < 100/mm³ for more than 10 to 14 days). Judicious use of antibacterial agents is extremely valuable to help minimize epidemiologic changes. Increased survival as a result of antibacterial prophylaxis has not been demonstrated.⁹

The outpatient setting is not appropriate for the treatment of every patient, and especially not for every low-risk patient. A well-established outpatient infrastructure that optimizes care and helps with early identification of potential treatment failure must be in place before instituting an outpatient program. This infrastructure must be multidisciplinary and include physicians, nurses, pharmacists, home healthcare companies, and caregivers. The validated MASCC risk-index score⁴ should be incorporated into the assessment of all patients with chemotherapy-induced febrile neutropenia, along with any necessary adjustments to prevent misclassification.

When oral medication treatment strategies are used, the patient must successfully tolerate his or her first dose before going home. Patients need to consume at least 50% of their hydration and caloric needs per day. It is imperative that there is a 24-hour caregiver available, and verbal as well as written instructions should be discussed and understood. Instructions should include a list of potential complications and an explanation of when to return to the emergency department. The patient should reside (during the time of febrile neutropenia) no farther than 30 minutes away from an emergency department and, preferably, the treating institution. Home monitoring should include, but not be limited to, oral intake (food and fluid), compliance with prescribed medications, temperature or acetaminophen consumption, diarrhea, nausea, vomiting, and urine output. Follow-up appointments or telephone calls are essential for success and should be scheduled during the first 5 to 7 days to ensure that the febrile episodes have defer-

vesced, neutropenia is resolving, and the patient is stable and lacks significant organ dysfunction.

In conclusion, Drs. Carstensen and Sørensen have identified key articles to help determine whether the outpatient setting is an appropriate option for the treatment of chemotherapy-induced febrile neutropenia. Is it safe yet? Yes, but only when clinicians follow strict criteria to ensure safety. Modifications to the classification scales currently used, close attention to the epidemiology of geographic and institutional bacterial and antibiotic factors, and, most importantly, a well-established infrastructure to care for neutropenic patients in the outpatient setting will greatly improve the chances for successful outcomes.

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