Review Article

A Review on "Risk Factors of Febrile Neutropenia in Cancer Patients"

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ABSTRACT

Febrile neutropenia (FN) often causes serious side effects in cancer patients during chemotherapy. Factors such as patient's nutritional condition, health problems, illness and the treatment approach all have an impact on how severe FN becomes. This review includes information from Indian and international studies about the occurrence, risk factors, clinical effects of FN. The reported rate of FN varies from 10% to 60%, depending on the type of cancer and the treatment given. Risk factors for FN include older age, poor general health, malnutrition, medical comorbidity, and poor performance status. FN can lead to hospitalization, halted treatment or lowered chemotherapy dosage, and all while reducing treatment effectiveness. To stop this, understanding the various contributing factors is crucial to being able to tailor relevant preventive or curative support. FN is related to higher medical costs, early death, and less adherence to chemotherapy. Granulocyte colony-stimulating factors (G-CSF) play a major role in managing and preventing FN they are generally safe but can have slight side effects. This review highlights the importance of personalized risk assessment for FN.

Keywords: Febrile Neutropenia, Chemotherapy, Risk Factors, G-CSF.

INTRODUCTION

Febrile neutropenia (FN) is a clinical condition which is characterized by the presence of fever and it is defined as an oral temperature of at least 38.3 °C or a continuous temperature of at least 38.0 °C for at least one hour, along with neutropenia, or is defined as an absolute neutrophil count (ANC) of less than 500 cells/µL. It develops bone marrow suppression, especially after chemotherapy. Decreased bone marrow activity leads to decreased neutrophil production, which reduces the host immune system and makes the body at risk for serious infections.

Although myelosuppression, especially neutropenia and febrile neutropenia (FN), is a common side effect of cancer chemotherapy, it increases the survival rates. Along with increasing hospitalization and delaying chemotherapy, that can raise treatment-related deaths.[1,6,8] Even with preventive guidelines. [10,11] FN remains common, especially in areas with less resources. [12,19] The aim of this review is to provide guidance for clinical practice by summarizing current information on FN occurrence and risk factors of FN.

RISK FACTORS FOR FN

Several factors including the patient's medical history, the type or stage of the cancer, and the chemotherapy treatment, can affect the development of febrile neutropenia. It is important to understand these risk factors in order to identify risks, direct the use of preventative measures such granulocyte colony-stimulating factors (G-CSFs) and promote clinical monitoring.

Patient-related factors:

Patient factors such as older age, poor performance status, comorbidity, malnutrition, and baseline low blood count.[2,5,9,12,20]

Advanced Age: With the presence of comorbid conditions weakened immune defenses and reduced bone marrow cell numbers advancing age results, in a higher likelihood of FN.

Low body. Poor nutrition: Nourishment impacts immune system functionality and blood cell formation which extends neutropenia duration and raises infection susceptibility.

Medical Comorbidities: Long-term conditions like diabetes mellitus, osteoporosis/osteoarthritis and renal insufficiency can impair both immunity and the ability to withstand chemotherapy; predisposing towards an increased risk to infection.

Treatment related factors:

Treatment factors like prolonged treatment cycles, dose intensity (R-CHOP, anthracycline, and taxanes, and discontinuation of peg-filgrastim prophylaxis), are also important risks. [7,13,15]

Long-Term or Dose-Dense Chemotherapy Cycles: Bone marrow cells are depleted by repeated myelosuppressive cycles without sufficient regeneration periods.

High Dose Intensity: Risk of FN is greatly magnified in increased doses regimens although, FN is a dose limiting toxicity in the treatment of cancer.

Specific Regimen: R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin and Vincristine) is used in the treatment of lymphomas and strongly associates with FN (febrile neutropenia), particularly in the older age population.

Myelotoxic, high (>1.5g/m^2)-dose anthracyclines (doxorubicin, epirubicin) and taxanes (paclitaxel, docetaxel) prolonged and severe neutropenia.

Discontinuation of Peg-filgrastim Prophylaxis: Patients who did not receive or had G-CSF support had a much higher incidence of FN, emphasizing the importance of growth factors in prophylaxis.

Disease factors like lung cancer, blood-related cancers, advanced stages of cancer, and poor general condition contribute to the risk. [6,8,11,16,17]

Hematological cancers associated with febrile neutropenia: FN is more prevalent with the existence of leukemias, lymphomas, or multiple myeloma, which often necessitates invasive techniques of myelosuppressive therapy.

Lung Cancer: Patients with small and non-small cell lung cancer lung on platinum and dose-intense regimens are more commonly found to be at risk.

Advanced Stages of Cancer: There is increased risk of infection with febrile neutropenia in patients with metastatic disease who are receiving high-dose chemotherapy.

Other risk factors:

Absence of prophylactic: G-CSF (Granulocyte Colony-Stimulating Factor) in high-risk patients

Mucosal barrier injury (oral mucositis, GI mucosal damage)

Role of G-CSF:

The G-CSF drug stimulates the bone marrow to increase its production of certain types of white blood cells and, specifically, neutrophils. After chemotherapy, the white blood cells (WBC) decrease, and the chance of infection increases. G-CSF decreases the risk of infection by speeding up WBC replenishment. G-CSF is recommended to be used as a preventive measure when the risk of FN is more than 20%. [10,11] In the case of Indian patients, common side effects are bone pain and gastrointestinal symptoms of mild intensity and no severe reactions [3.] There are still gaps in the guidelines, such as the overuse in instances where the risk is low as well as the underuse when the risk is high.[10,17] Involvement of clinical pharmacists have shown to reduce the rate of FN complications and mortality.[4] Also, the length of time covered by G-CSF or filgrastim prophylaxis is important. Complications have been more common in patients with shorter prophylactic periods.[18] G-CSF drugs include, but are not limited to, Filgrastim and Peg-filgrastim.

Implications of Neutropenia Risk Factors:

Identification of risk factors for febrile neutropenia has important clinical and hospital implications. From a clinical point of view, it allows patients at risk and provides a way to intervention with G-CSF prophylaxis or anti-microbial therapy or nutritional support to decrease mortality. Integrating such risks into the practice of clinical oncology might help to guide treatment decision-making to strike a balance between chemotherapy dose intensity and patient safety while avoiding unnecessary dose reductions or delays. On the side of clinical practice, appropriate risk assessment decreases hospitalization and saves cost in treatment and more effective resources utilization. In addition, knowledge about these risk factors allows for adherence to therapy, improves survival and is associated with quality of life in patients with cancer. More broadly, risk factor evaluation serves as a basis for development of predictive models and regional guidelines in order to better tailor and deliver effective supportive care proceeding transplant.

CONCLUSION

The data shows changes in FN rates across different populations, cancer types, and treatment regimes. Comorbidities, age, and malnutrition are normally related to worse outcomes. Asian studies, specifically from Thailand and India, focus to issues such as poor nutrition, misuse of traditional treatments, and low-protein diets that increase the risk of FN Even though G-CSF is effective, actual practice often doesn't follow recommended guidelines, leading to preventable health issues and deaths. Historical and current data in elderly patients may improve early identification of high-risk individuals, though more testing is needed across different populations. One serious side effect of chemotherapy is that it elevates illness, mortality and delays treatment in FN. Early risk assessment, individualized G-CSF prophylaxis, nutritional support, and continuous clinical monitoring can greatly reduce the burden of FN. Upcoming research should focus on predictive risk models, patient specific therapy and guidelines specific to different regions to improve supportive care in cancer patients.

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