

Febrile Neutropenia and Compliance with NCCN Guidelines

By Sarah Jones, RN, MS, ACNS-BC, AOCNS, CRNI

It has long been known that cancer chemotherapy has associated complications, and that chemotherapy induced neutropenia (CIN) is one of the most severe, often resulting in serious morbidity and mortality (Nirenberg et al, 2006). Despite improvements in



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therapy and supportive care, early identification and treatment of febrile neutropenia continues to be a problem.

Febrile neutropenia (FN) can be defined as a single temperature of 38.3°C (100.9°F) or more orally or 38.0°C (100.4°F) or more over one hour and an absolute neutrophil count (ANC) of less than 500 neutrophils/mm³ or less than 1,000 neutrophils/

mm³ and a predicted decline to less than 500 mm³ over the next 48 hours (NCCN, 2011). CIN predisposes patients with cancer to life threatening infections by suppression of neutrophil production. Neutrophils comprise the first line of defense against infection and contribute to innate immunity. Since CIN blunts the body's inflammatory response, classic signs and symptoms of infection may not be present, and patients often present with a fever as the only indication of infection (Friese, 2006). In the first of a series of articles on neutropenia, Nirenber et. al, (2006) discussed how Bodey, Buckley, Sathe, and Freireich were the first to demonstrate in their 2006 article that the severity, depth, and duration of neutropenia correspond with the risk of infection and death.

While the introduction of colony stimulating factors (CSF) has been identified as the most useful pharmacologic tool to reduce overall adverse events associated with neutropenia, the appropriate use of administration has often been unclear. Due to the cost of CSF and unclear clinical benefit, a 'wait and see' attitude has often been utilized, despite that researchers have identified that in certain types of cancers, a significant proportion of FN events occur in

the first treatment cycle (Friese, 2006). The National Comprehensive Cancer Network (NCCN) clinical practice guidelines outline the use of CSF for first line therapy and targets patients with a 20% or greater risk of FN. It also identifies important clinical factors, independent of the planned therapeutic regimen, that place patients at risk for FN.

Utilizing the NCCN guidelines, a retrospective chart review was done to identify the compliance with the guidelines at Upper Valley Medical Center. This review was done in two parts. The first review involved a two year period from 2007-2008 to get baseline data in regards to volume of CIN patients admitted with FN incidents, as well as compliance to NCCN guidelines. The second review involved patents admitted in 2010 to review compliance with the NCCN guidelines as well as the Surviving Sepsis guidelines utilizing the Sepsis Resuscitation Bundle (Table 3). The criteria used to identify patients in both reviews were a) diagnosis of cancer currently receiving myeloablative chemotherapy and/or radiation therapy, b) Admission to the hospital with diagnosis of neutropenia, drug induced neutropenia, or fever, and c) UVMC managing physician. Coded data was used to help identify patients.

Table 1. ICD-9 Codes to identify patients

METHOD

- Retrospective review of charts of patients admitted to the hospital with one of the following diagnosis codes:

288.00	Neutropenia NOS
288.03	Driu Ind Neutropenia
288.09	Neutropenia NEC
780.6	Fever

Table 2. Patient related Clinical Risk Factors

IDENTIFIED CLINICAL RISK FACTORS

- Age >65
- Previous chemotherapy and/or XRT
- Pre-existing neutropenia or bone marrow involvement
- Pre-existing conditions
 - Neutropenia
 - Infection/open wounds
 - Recent surgery
- Poor performance status
- Poor renal function
- Liver dysfunction/elevated bilirubin

The first review identified 27 patients with 31 evaluable admissions. Twenty nine of the admissions (29/31 = 94%) had documented clinical risk factors for developing FN, while only two (2/31=6%) had been covered prophylactically with a CSF. Average Length of Stay (LOS) was 6.8 days with a range of 1-20 days. Twelve of 31 (39%) had a grade 3 neutropenia, and 17/31 (55%) had a grade 4 neutropenia. There was an overall 9.6% mortality rate (3/31=9.6%). These results were shared with the UVMC Cancer Committee and its practicing physician members in the fall of 2009.

During the second review conducted in 2010, 14 evaluable admissions were identified using the previously identified methods, coded data, and clinical risk factors. In this clinical review, 0/14 episodes occurred on the initial chemotherapy cycle. 1 (1/14=7%) episode occurred on a second cycle. 7 of 14 were prophylactically covered with Neulasta (50%), a 44% improvement over the previous study. The average LOS was 5.3 days (range 2-13 days), a decrease of 1.7 days from previous study.

Table 3. Components of Surviving Sepsis Bundle

SEPSIS RESUSCITATION BUNDLE

- Measure serum lactate
- Obtain blood cultures prior to antibiotic administration
- Administer broad-spectrum antibiotic within
 - 3 hrs. of ED admission
 - 1 hr. of non-ED admission
- In hypotension and/or s. lactate >4mmol/L
 - Deliver 20 ml/kg of crystalloid or equivalent
 - Vasopressors for nonresponse to fluid resuscitation

In regards to compliance to Surviving Sepsis guidelines (Denlinger et al., 2008), 0% (0/14) of admissions had serum lactate measured. 100% (14/14) of patients had blood cultures drawn prior to start of antibiotics. Of the 3 patients who were direct admits to the hospital, 0 out of the 3 received their first dose within the 1 hour time frame (range 2-5hrs) as outlined in the guidelines. Six of the eleven (55%) patients admitted through the Emergency Department (ED) received their first dose of antibiotic within the recommended 3 hour timeframe (range 1-6 hours). Six of eleven patients demonstrated signs of hypotension and 100% (6/6) received appropriate fluid resuscitation and vasopressor support as indicated. There were no mortalities during the course of the second study.

In review, there was moderate improvement in regards to compliance with NCCN guidelines between the intervals of the two reviews. Overall patient risk assessments and coverage with CSF improved by 44%. Hospital LOS decreased by 1.7 days. There remain many opportunities for improvement in regard to time to first dose of antibiotic from education directed at both nurses and physicians in the ED, as well as opportunities for collaboration of care between the ED and Oncology Services.

References:

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