MANAGEMENT OF PATIENTS WITH LOW-RISK FEBRILE NEUTROPENIA

Matt Fowler looks at how new tools to assess the possibility of septic complications can guide future care options

Abstract
The National Institute for Health and Care Excellence in the UK advocates that patients with neutropenia who are at low risk of developing septic complications should be considered for management in the community rather than in hospital. The Multinational Association of Supportive Care in Cancer (MASCC) risk index is widely used to identify patients who are deemed to be at low risk of developing septic complications as a result of febrile neutropenia (FN), but it has limitations. A newer tool, the Clinical Index of Stable Febrile Neutropenia (CISNE), further stratifies patients who may be suitable for management in the community. This article uses a case study to explore the management of a patient who presented with suspected FN. It examines the use of the MASCC risk index and the CISNE to make recommendations for the future management of patients with low-risk FN in the community.

Keywords
Chemotherapy, low-risk febrile neutropenia, management, risk, treatment complications

CHEMOTHERAPY IS well documented to cause a plethora of toxicities, however, febrile neutropenia (FN) is one of the most serious complications (Innes et al 2003), with a mortality rate of 5% (de Naurois et al 2010). FN is defined by de Naurois et al (2010) as ‘an oral temperature >38.5°C or two consecutive readings of >38.0°C for two hours and an absolute neutrophil count <0.5 × 10⁹/L, or expected to fall below 0.5 × 10⁹/L’.

In the nurse-led chemotherapy unit where I work as an advanced nurse practitioner (ANP) many of the decisions traditionally made by oncologists and haematologists are made by the nurse consultant and me. All patients who present as emergency admissions with suspected FN are initially managed by the senior nursing team during office hours.

As an autonomous ANP, it is crucial that my decisions about patient management are backed up by robust evidence to safeguard the patient and the practitioner. Greenhalgh et al (2014) advocated the use of evidence-based clinical guidelines, however, they stressed that care should still remain individualised. Glasziou et al (2013) cautioned against over-reliance on pathways/templates for managing patients as this can result in ‘over-treatment’ because of fear of litigation. Management of patients with FN is a classic example of protocol/pathway-driven care. However, the variations in practice identified in the National Institute for Health and Care Excellence (NICE) (2012) guideline on managing patients with neutropenic sepsis suggest there is justification for examination of the initial diagnostic and management plan.

Case study
Julie (pseudonym) was a 38-year-old woman receiving adjuvant chemotherapy post-mastectomy for breast cancer who presented to the ambulatory
chemotherapy unit ten days post-chemotherapy with a pyrexia of 38.0°C. Julie was at the nadir point in her chemotherapy cycle. She was cannulated on arrival, bloods taken for full blood count, urea and electrolytes, C-reactive protein (CRP), liver function tests as well as lactate and blood cultures. In accordance with local guidelines she received an immediate dose of intravenous (IV) tazocin and gentamicin empirically while blood results were processed. This practice was in accordance with local policy and the NICE (2012) guideline (Figure 1), as well as the surviving sepsis campaign (Dellinger et al 2013).

Table 1 outlines the initial examination findings and investigations requested.

As can be seen from Table 1, Julie had a temperature of 38.0°C and a neutrophil count of 0.2, which confirmed a diagnosis of neutropenic sepsis (NICE 2012). The National Cancer Institute (1999) classified neutropenia as follows:

- Grade 1 ≥1.5–<2.0.
- Grade 2 >1.0–<1.5.
- Grade 3 >0.5–<1.0.
- Grade 4 <0.5.

Although FN carries a mortality rate of 5% (de Naurois et al 2010), Julie had grade 4 neutropenia, which can carry a mortality rate as high as 9% (Lalami et al 2006).

**Alternative options**

I have worked in haematology for more than 15 years and cared for many neutropenic patients. Julie's care appeared to represent the 'gold standard': safe care in accordance with best available evidence. She received antibiotics within 30 minutes of arrival at hospital, had an uneventful stay with successful neutrophil recovery and a five-day stay that is in accordance with national averages (Parish et al 2013).

On deeper reflection, however, I considered whether her care could have been delivered differently.

The NICE (2012) guideline advocated that patients with low-risk FN should be considered for management in the community, which has potential benefits for patients and healthcare economies.

Worth et al (2011) identified savings of up to 30% for patients with low-risk FN managed as outpatients compared with the traditional method of receiving antibiotics as inpatients. Nonetheless, 25% of all deaths within 30 days of receiving chemotherapy have been attributed to FN (Yoong et al 2012).

A literature search revealed a large amount of research on the subject of low-risk FN. Table 2 identifies the databases searched and the number of hits broken down into adult and paediatric settings. Search terms used were 'low risk', 'febrile' and 'neutropenia'.

Although there appeared to be a large amount of research available on the adult population with low-risk FN, there did not appear to be any published evidence of centres in the UK implementing the NICE (2012) recommendations for managing patients with low-risk FN. This notion was supported by Slavin and Thursky (2013) who, in a survey of oncologists in Australia and the UK, found an overwhelming reluctance by clinicians to manage patients with low-risk FN in the community. This was not the case in the paediatric setting as there was clear evidence of children with low-risk FN being managed at home (Manji et al 2012, Orme et al 2014). Of further significance is that children are often at greater risk of developing
complications as a result of FN than adults because their immune systems are not as well developed, they often receive intensive chemotherapy regimens and often have central venous access devices in situ (Sung et al 2011).

Vidal et al (2013) conducted a systematic review comparing oral versus IV antibiotics for the management of patients with FN and found no significant difference in mortality or morbidity for those who were identified as low risk. However, they recommended that further research was required to stratify low-risk FN patients.

**MASCC risk index**

The Multinational Association of Supportive Care in Cancer (MASCC) risk index is the tool most widely used to identify low-risk FN patients (Klastersky et al 2000) (Table 3).

<table>
<thead>
<tr>
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<th>Blood pressure</th>
<th>Urine</th>
<th>Systemic inflammatory response syndrome</th>
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<tbody>
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**Respiratory rate** 15

**Oxygen saturation** 99% on room air

**Blood glucose level** 5.2

**Glasgow Coma Scale** 15

**Modified Early Warning Score** 1

**Past medical history**

- Mastectomy for breast cancer
- Caesarean section

**Medications**

- Omeprazole 20mg daily
- No known drug allergies

**Diagnosis**

Probable neutropenic sepsis

**Plan**

- Full blood count (including differential)
- Liver function tests
- Lactate
- Urine dipstick
- 4.5g intravenous (IV) tazocin immediately and 320mg IV gentamicin
- 1,000ml 0.9% sodium chloride over eight hours

**Blood results**

- Haemoglobin 118
- White cell count 0.8
- Neutrophils 0.2
- Platelets 148
- Sodium 136
- Potassium 4.2
- Urea 5.6
- Creatinine 58
- Bilirubin 12
- Alkaline phosphatase 48
- Alanine transaminase 40
- CRP 5
- Lactate 0.8
- Blood cultures negative after five days

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Using the MASCC risk index, Julie would have scored 25 as follows: burden of illness 5; no hypotension 4; no chronic obstructive pulmonary disease 4; solid tumour 4; no dehydration 3; outpatient status 3; and age <60 2.

Julie’s score classified her as having low-risk FN. Although Klastersky et al (2000) suggested that low-risk FN patients can be managed in the community thus avoiding hospital admission, Talcott et al (2011) advocated the admission of low-risk FN patients for a period of 24 hours observation before discharge into the community.

In view of the current perceived reluctance of clinicians to manage low-risk FN patients in the community, this option would appear to be feasible. Teuffel et al (2010) also identified a cohort of low-risk FN patients who go on to develop complications necessitating hospital admission; this further substantiates the case for initial admission to hospital for observation.

In response to some of the concerns raised about the MASCC risk index including that it is not specific to solid tumours, Carmona-Bayonas et al (2011) devised the Clinical Index of Stable Febrile Neutropenia (CISNE) tool to identify patients who are at low risk of developing complications of FN and can be discharged home after 24 hours if their CISNE score is 0.

Table 4 demonstrates the CISNE score as well as how Julie’s FN would have been classified.

The fact that Julie had a MASCC risk index score of 25 and a CISNE score of 0 further supports the notion that she could have been managed in the community after an initial 24-hour inpatient admission. Although monocytes are recorded on the differential full blood count they are not routinely checked, hence I had to examine the results retrospectively and discovered that Julie had a monocyte count of 0.42.

A new way of scoring
There is evidence to support early discharge of low-risk FN patients as long as they fulfil criteria in accordance with a locally agreed tool. Although widely used in practice in the US, the MASCC risk index has limitations and in light of this the CISNE tool can be used to further stratify patients identified as low risk by the MASCC risk index (Carmona-Bayonas et al 2011).

I propose that a combination of Systemic Inflammatory Response Syndrome (SIRS) score and CISNE score should be adopted in routine practice to identify low-risk FN patients who could be discharged home on oral antibiotics after a 24-hour hospital admission. NICE (2012)
advocated that low-risk FN patients could be managed in the community, which also supports this recommended change in practice from a clinical governance perspective.

More robust trials are advocated for management of low-risk FN patients in the UK (Phillips et al 2012), although this should not be seen as a barrier to implementing changes in practice. I intend to conduct a retrospective audit of notes of patients who have been admitted with FN over the past six months, an average of six patients a month, to identify how many would have been classified as low risk.

As with any change in practice, the management of change process is important. Liaising with interested parties in the acute trust as well as primary care is fundamental, especially considering how such a change in practice could have far-reaching implications for both settings.

**Conclusion**

Although most chemotherapy can be administered in outpatient settings, it is time to start evaluating which further elements of the cancer patient pathway can be delivered in the ambulatory/home setting. Use of diagnostic tools including SIRS and the Modified Early Warning Score as well as the CISNE tool has the potential to revolutionise the care of patients with low-risk FN. In the case of Julie their use would have meant she could have been discharged home after 24 hours with oral antibiotics and robust education. This has fundamental and far-reaching implications for the healthcare economy and most importantly for patients.