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Title: Myelodysplastic syndromes: Update and nursing considerations

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Abstract
This article provides nurses with an update of current management approaches and care for patients with myelodysplastic syndromes (MDS), a complex group of disorders of the bone marrow. MDS has wide ranging effects on patients’ lives. Understanding the impact of a diagnosis of MDS on a patient’s quality of life (QOL) is a key nursing role and requires discussion which includes consideration of a patient’s physical, mental, emotional and social well being. Many treatment options are now available to treat MDS and nurses have an important role educating patients on recognising and managing treatment side effects. While many promising developments in the management of MDS are now available to patients, nurses need to ensure that patients and families have a realistic understanding that the treatments they are being given are for non-curative intent.

Key words: azacitidine, fatigue, myelodysplastic syndromes, supportive care, quality of life.
Aims and intended learning outcomes

The aim of this article is to provide an update for nurses on the care of patients with myelodysplastic syndromes (MDS). After reading this article and completing the time out activities, you should be able to:

- Explain what is meant by MDS.
- Understand the investigations performed to diagnose MDS.
- Summarise the treatment options for MDS.
- Summarise the side effects of treatment and appropriate interventions to manage these side effects.
- Discuss supportive care measures for MDS patients.
- Understand the psychological impact of MDS on patients and carers.

Time out 1
Pause for a moment and consider what your current understanding of MDS and what gaps in knowledge you have regarding care for patients with MDS.

Introduction

Myelodysplastic syndromes (MDS) are a complex group of blood disorders. This paper examines and explains issues that arise for patients diagnosed with MDS in order to assist nurses provide responsive and effective care to MDS patients.

MDS are a group of myeloid neoplasms characterised by dysplastic (abnormal shape, size or appearance) changes in one or more cell lineages, ineffective hematopoiesis and a variable tendency to the development of acute myeloid leukaemia (AML) (Swerdlow et al 2008). A number of physiological changes arise from MDS, including bone marrow failure which results in anaemia, thrombocytopenia and neutropenia.
MDS is predominantly a disease of the elderly, and is more prevalent among men. The incidence is approximately 4/100,000 population per year, however the incidence rises to > 30/100,000 per year in those aged over 70 years (Killick et al 2013). Considering a progressive ageing population worldwide, the number of MDS patients is destined to increase in the coming decades (Malcovati et al 2013).

It is important to point out that patients typically report that they have never heard of MDS and often do not understand the significance of their diagnosis. There is no cure for MDS and the chronic nature of the illness requires regular hospital visits for on-going treatment; this ultimately impacts on the QOL of patient and carers. Nurses should therefore provide regular opportunities for patients and carers to discuss their understanding of the illness, how they are coping and offer advice on ways to improve QOL. Referral to psychological support services should be arranged promptly if needed.

**Signs and symptoms**

MDS patients often do not have early symptoms and many patients are diagnosed following a routine blood test. Symptoms vary greatly depending on which bloods cells are affected and how low the blood counts have fallen (Barzi and Sekeres 2010). Patients’ symptoms include those related to anaemia (e.g. shortness of breath, lack of energy, pallor, weakness), symptoms related to thrombocytopenia (e.g. easy bruising, petechiae or bleeding), and symptoms related to a low white count (e.g. fever or recurrent or prolonged infections).
Diagnostic evaluation

All patients with otherwise unexplained cytopenias (i.e. reduction in the number of blood cells) or macrocytosis (i.e. enlarged erythrocytes), where MDS is suspected, should be assessed by a haematologist to rule out alternative diagnoses and reactive causes of marrow dysplasia (Killick et al 2013).

The approach to diagnosing MDS should begin with the exclusion of non-malignant causes of cytopenias. All patients require a detailed medical history with particular focus on medications, alcohol, smoking, infections and bleeding/bruising episodes. In addition, a patient history of prior chemotherapy, radiotherapy, radioiodine, and occupational or hobby exposure to benzene is obtained. It is estimated that approximately 10% of MDS cases are secondary, most usually from radiation or chemotherapy given for a cancer diagnosis in the previous five years (Ma et al 2007). A small number of MDS cases are as a result of occupational exposure to radiation or benzene (Barzi and Sekeres 2010). It is important to reassure patients and families that while the causes of MDS are multifactorial, previous exposure to other treatments or occupational exposure to chemicals are possible causes of their illness. Hearing that their treatment for a previous cancer may have caused their new diagnosis of MDS can be very distressing for some patients, and nurses need to be ready to respond with appropriate psychological support. Moreover, nurses should ensure that sufficient time is set aside to facilitate answering patients’ questions about their diagnosis and clarifying the difference between MDS and other blood cancers. Finally, in younger patients, it is important to determine if there is a
family history of inherited bone marrow failure disorders e.g. Fanconi anaemia and telomere disorders (Holme et al 2012).

<table>
<thead>
<tr>
<th>Time out 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pause for a moment and make a list of investigations that you think would be undertaken in a diagnostic evaluation of MDS</td>
</tr>
</tbody>
</table>

All patients with suspected MDS should have blood tests performed (Table 1). In addition, a bone marrow aspirate, biopsy and cytogentics should be performed to confirm a diagnosis of MDS, provide information on disease sub-type, inform management options and provide prognostic information whilst also excluding other haematological conditions e.g. Acute Myeloid Leukaemia or Aplastic Anaemia (Malcovati et al 2013, Killick et al 2013).

MDS can mimic the signs and symptoms of other haematological malignancies such as myeloma or acute leukaemia so the tests outlined in Table 1 assist health care professionals to rule out other causes of cytopenias. The range of tests also facilitates cytogenetic testing to be carried out which can be an important prognostic tool. By identifying a patient’s prognosis early, appropriate treatment choices can be made early in the disease trajectory (Figures 1 & 2).

All patients should have a physical examination to determine spleen size; although splenomegaly in MDS is rare, its presence can indicate an overactive bone marrow disorder (myeloproliferative disorder) e.g. myelofibrosis (Barzia and Sekeres 2010).
<table>
<thead>
<tr>
<th>Investigation Type</th>
<th>Investigations Undertaken</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haematology</strong></td>
<td>Full blood count</td>
</tr>
<tr>
<td></td>
<td>Blood Film</td>
</tr>
<tr>
<td></td>
<td>Reticulocyte count</td>
</tr>
<tr>
<td></td>
<td>Crossmatch</td>
</tr>
<tr>
<td></td>
<td>Hb electrophoresis</td>
</tr>
<tr>
<td></td>
<td>Direct coombs test</td>
</tr>
<tr>
<td><strong>Biochemistry</strong></td>
<td>Full biochemistry including LDH, Bilirubin</td>
</tr>
<tr>
<td></td>
<td>Ferritin</td>
</tr>
<tr>
<td></td>
<td>Iron stores</td>
</tr>
<tr>
<td></td>
<td>Haptoglobin</td>
</tr>
<tr>
<td></td>
<td>C-reactive protein</td>
</tr>
<tr>
<td></td>
<td>TFT's</td>
</tr>
<tr>
<td></td>
<td>Uric acid</td>
</tr>
<tr>
<td></td>
<td>Serum Protein Electrophoresis</td>
</tr>
<tr>
<td></td>
<td>Beta 2 Microglobulin</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>Anti-HIV</td>
</tr>
<tr>
<td></td>
<td>Anti-parvovirus B19</td>
</tr>
<tr>
<td></td>
<td>CMV</td>
</tr>
<tr>
<td></td>
<td>Hepatitis B &amp; C</td>
</tr>
<tr>
<td><strong>Bone Marrow</strong></td>
<td>Aspirate</td>
</tr>
<tr>
<td></td>
<td>Biopsy</td>
</tr>
<tr>
<td></td>
<td>Cytogenetics</td>
</tr>
<tr>
<td></td>
<td>FISH</td>
</tr>
<tr>
<td></td>
<td>Flow cytometry</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Paroxysmal Nocturnal Haemoglobinuria</td>
</tr>
<tr>
<td></td>
<td>Specific genetic analyses (in patients in whom a suspicion about inherited bone marrow failure has been raised).</td>
</tr>
</tbody>
</table>
Classification of MDS

MDS includes an extremely heterogenous (varied or mixed) group of disorders, ranging from indolent conditions with a near to normal life expectancy, to forms approaching acute myeloid leukaemia (AML) (Malcovati et al 2013). Classification is based on bone marrow examination and cytogenetic information which will assist in determining patient treatment plan e.g. patients with 5q-may benefit from lenalidomide treatment.

The diagnosis and classification of MDS should be based on the widely accepted World Health Organisation (WHO) classification system, revised in 2008 (Vardiman et al 2009) (Table 2). Adults patients with > 20% blasts are now classified as having AML (Swerdlow et al 2008).
### Table 2. WHO classification of MDS (Swerdlow et al 2008)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractory cytopenia with unilineage dysplasia</td>
<td>The patient has too few of one type of blood cell and have 10% change in one of more of the other blood cells. Patients have less than 5% blasts in bone marrow and less than 1 % in peripheral blood.</td>
</tr>
<tr>
<td>Refractory anaemia (RA)</td>
<td>Patients have a normal platelet and white cell count, however are anaemic. They have &lt;5% blasts.</td>
</tr>
<tr>
<td>Refractory neutropenia (RN)</td>
<td>Patients’ neutrophils are reduced.</td>
</tr>
<tr>
<td>Refractory Thrombocytopenia (RT)</td>
<td>Patients have reduced thrombocytes</td>
</tr>
<tr>
<td>RA with ringed sideroblasts (RARS)</td>
<td>Patients have normal platelet and white cell count however they are anaemic and their red cells have too much iron inside the cell.</td>
</tr>
<tr>
<td>Refractory cytopenia with multi lineage dysplasia (RCMD) + ringed sideroblasts (RCMD-RS)</td>
<td>Patients have two or more changes in myeloid lineage and less than 5% blasts.</td>
</tr>
<tr>
<td>RA with excess blasts -1 (RAEB-1)</td>
<td>The patient is anaemic and has between 5-9% blast cells in their bone marrow. White cell count and platelets may also be low. Patients with RAEB-1 may progress to acute myeloid leukaemia</td>
</tr>
<tr>
<td>RA with excess blasts-2 (RAEB-2)</td>
<td>As per RAEB-1 however blast counts are between 10-19%.</td>
</tr>
<tr>
<td>Unclassified MDS</td>
<td>The number of blasts in the bone marrow and blood are normal and the disease is not one of the other MDS syndromes.</td>
</tr>
<tr>
<td>MDS associated with an isolated del(5q) chromosome abnormality.</td>
<td>Patients are anaemic with less than 5% blasts cells in blood or bone marrow, however patients have a single chromosomal abnormality deletion of chromosome 5q.</td>
</tr>
</tbody>
</table>
Prognosis with MDS

Prognostic factors for patients with MDS may be subdivided into **patient related characteristics** such as general health, co-morbidities, performance status, frailty, nutritional status and cognition, and **disease related factors** based on the MDS clone (Malcovati et al 2013). Moreover, increasing age is an independent adverse prognostic factor in MDS (Morel et al 1996). The assessment of individual risk is important because it enables the identification of fit patients with poor prognosis who are candidates for chemotherapy followed by transplantation and those where therapeutic intervention is aimed at preventing cytopenia-related morbidity and preserving quality of life (QOL).

It is imperative that the nursing response to patients deemed to have a poor prognosis is both compassionate and educational. These patients and their carers need to be aware of risks such as pyrexia and bleeding, and supports such as home care that are available when needed.

The revised international prognostic staging system (IPSS-R) (Table 3) uses the same parameters as IPSS (i.e. cytogenic groups, marrow blasts % and cytopenias); however it is able to refine these further by categorising more cytogenetic subgroups, refinement of blast counts < 5% and depth of cytopenias (Greenberg et al 2012).
Table 3. IPSS-R prognostic risk categories/scores and clinical outcomes

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Risk score</th>
<th>Survival (median- years)</th>
<th>25% AML evolution (median- years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>&lt;= 1.5</td>
<td>8.8</td>
<td>NR</td>
</tr>
<tr>
<td>Low</td>
<td>&gt; 1.5-3</td>
<td>5.3</td>
<td>10.8</td>
</tr>
<tr>
<td>Intermediate</td>
<td>&gt;3-4.5</td>
<td>3.0</td>
<td>3.2</td>
</tr>
<tr>
<td>High</td>
<td>&gt;4.5-6</td>
<td>1.6</td>
<td>1.4</td>
</tr>
<tr>
<td>Very High</td>
<td>&gt;6</td>
<td>0.8</td>
<td>0.73</td>
</tr>
</tbody>
</table>

A recent multicentre validation study reported the IPSS-R to be a very effective tool in the prediction of survival as well as progression to AML (Neukirchen et al 2014). The IPSS-R provides prognostic scoring at diagnosis, however the WHO based classification prognostic system (WPSS) provides prognostic details at any point during the disease course. The WPSS includes WHO diagnosis, IPSS-R cytogenetic criteria, transfusion need and Hb concentration and provides a more accurate definition of prognosis (Killick et al 2014). The WPSS is particularly useful in those with low or inter-1 IPSS (Malcovati et al 2013).
Figure 1. Treatment algorithm for higher risk myelodysplastic syndromes (Fenaux et al 2014) (Permission granted from Oxford Journals to reproduce)

Figure 2. Treatment algorithm for lower risk myelodysplastic syndromes (Fenaux et al 2014). (Permission granted from Oxford Journals to reproduce).
Treatment overview in MDS

Several factors influence treatment decisions in MDS. These include age, symptoms, MDS classification, co-morbidities, performance status, IPSS Risk category and QOL (Killick et al 2013). The goals of MDS treatment are to prolong survival and improve patients’ QOL by treating symptoms and minimising complications from cytopenias. In addition, in high-risk patients the goal is to delay transformation to AML and prolong survival.

Patients classified as lower or higher risk are provided supportive care concurrently with treatment (Table 3). For patients with low risk disease initial treatment broadly includes management of cytopenias, watchful waiting, immunosuppressive agents and immunodulatory drugs. Median survival in low risk MDS can be measured in a number of years. Conversely high risk patients’ median survival is less than 2 years, therefore, they are given disease modifying therapy at diagnosis including hypomethyaling agents, combination chemotherapy and allogenic haematopoietic stem cell transplant (HSCT) (Fenaux et al 2014) (Figures 1 & 2).

Where available, patients should be entered on registry programmes to maximise information about the natural history and treatment of MDS to benefit future patients. In addition, where available, patients should be entered into clinical trials (Killick et al, 2013).
MDS patients should undergo regular follow-up. The frequency of hospital visits are individualised depending on the disease risk and therapeutic choice. Many patients, particularly the elderly and those with co morbidities, receive only palliative care or best supportive care (Santini et al, 2010). As highlighted earlier, nurses need to place compassionate care at the centre of their response to these patients and provide adequate time to allow discussion of available care options and supports.

**Supportive care**

<table>
<thead>
<tr>
<th>Time out 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflect for a few moments and consider what forms of supportive care MDS patients need while on treatment</td>
</tr>
</tbody>
</table>

MDS is a chronic disease and this illness places significant burden on patients and carers. Supportive care is therefore an important component of the overall management of MDS and is provided concurrently with treatment. The goals of supportive care are to manage patients’ symptoms, increase blood counts, treat infections and treat iron overload. Supportive care interventions include red cell and platelet transfusion, growth factors, antibiotics and iron chelation therapy.

Central to supportive care is observation, clinical monitoring, psychological support and QOL assessment (NCCN, 2014). Managing signs and symptoms of MDS requires detailed assessment of a patient’s symptoms and early intervention. As previously outlined the severity of symptoms is individual and influenced by the reduced levels in blood counts.
The regular visits to the haematology centre and follow-up telephone conversations when required, facilitates the development of relationships between specialist haematology nurses and patients and their carers. These relationships promote opportunities to involve patients and carers in decision-making and helps build up trust. This in turn offers opportunities for nurses to empower patients to stick with their treatment and know when they need to contact the hospital in order to manage and control symptoms.

Management of Anaemia

Haemoglobin level is reported to be most important independent predictor of QOL among patients with MDS (Olivia et al 2012). Managing anaemia therefore requires careful assessment of a patient’s symptoms including palpitations, chest pain, fatigue, dyspnoea, dizziness and headaches. Treatment is indicated in patients with symptomatic anaemia. Furthermore, although many of the MDS treatments can initially worsen a patient’s blood counts and it is important not to discontinue therapy before it may achieve a benefit.

Treatment options for anaemia in MDS include red cell transfusion or administration of erythropoietin agents. The threshold Hb concentration for transfusion will vary from patient to patient due to co-morbidities including chronic pulmonary disease and heart failure; therefore no single recommendation for a transfusion trigger can be made (Killick

Time out 4

Make a list of the symptoms of anaemia, thrombocytopenia and neutropenia and how these symptoms are managed.
et al 2013). The objective of red cell transfusion is to improve QOL and avoid anaemia related symptoms and ischemic organ damage. MDS patients with underlying cardiac disease are at an increased risk for chronic heart failure exacerbation and may require diuresis with transfusions. CMV negative blood products are recommended wherever possible. In the absence of CMV negative blood, leukodepleted blood may be used (NCCN, 2014).

It is important to reassess patient symptoms following transfusion to measure its benefits in relieving symptoms. Benefits from transfusion are temporary thus patients often require regular transfusion. The onset of regular transfusion requirement in MDS patients is associated with a poorer prognosis (Killick et al 2014).

Patients receiving regular transfusions invariably develop iron overload. Iron chelation is recommended for patients with ferritin levels above 2500ng/ml (Greenberg et al 2013). A number of studies have reported better overall survival among low-risk MDS patients who received iron chelation therapy when compared to those who did not receive iron chelation (Rose et al 2010, Lyons et al 2011). However, the British Committee for Standards in Haematology recommend that iron chelation cannot be routinely recommended for MDS patients with transfusional overload but may be considered in specified circumstances including a serum ferritin >1000 μg/l in patients for whom continuing red cell transfusion is predicted (Killick et al 2014).

Patients receiving iron chelation therapy, such as desferrioxamine, need education and support and may need training on self administration and subcutaneous site management.
as well as treatment related side effect management. Furthermore, MDS patients who are potentially candidates for allo-HSCT can be considered for appropriate iron chelation therapy prior to the conditioning regime for transplantation (Malcovati et al 2013).

Erythropoiesis stimulating agents (ESAs) including erythropoietin alfa and beta (EPO) have been used to manage anaemia over many years. EPO therapy should be considered in anaemic MDS patients with an IPSS score of low or INT-1 (Killick et al 2013). EPO therapy is commenced for a minimum of 8 weeks and where no response is seen the dose of the EPO is doubled; however if there is no response after 16 weeks treatment should be discontinued. However, it is important to highlight that caution is needed with the use of EPO in some MDS patients, in particular those patients at risk of thrombosis (e.g. patients with vascular risk factors including previous stroke, diabetes and hypertension). Thrombotic risk increases when the patient’s Hb goes above 12.0 g/l and therefore close monitoring of Hb levels is indicated. It is recommended where the Hb goes above 12.0 g/l, EPO is temporarily discontinued and the dose reduced on recommencement (Barzi and Sekeres 2010). Finally, in patients with RARS and RCMD (see Table 2), the addition of Granulocyte Colony Stimulating Factor (G-CSF) to EPO is synergistic and therefore recommended at the outset.

Management of Thrombocytopenia

Thrombocytopenia is common among MDS patients and their carers are often concerned of their bleeding risk. Carers need to be reassured that bleeding is unlikely despite very low platelet levels. Prophylactic platelet transfusion is recommended in patients with a count lower than 10 x 10^9/L or in those with any risk factor for bleeding (fever, infections, rapid platelet decrease, invasive procedure), provided the thrombocytopenia is...
transient. Routine platelet transfusion is not indicated in patients who have long standing stable thrombocytopenia with no symptoms of bleeding and not receiving intensive chemotherapy (Killick et al 2013). It is important to carefully assess patients on an individual basis for bleeding risk and establish each patient's threshold bleeding platelet level. Moreover, patients' QOL needs to be considered if attending for platelet transfusion becomes a huge burden for them.

**Management of neutropenia and infections**

Early diagnosis and prompt intervention for MDS patients with symptomatic neutropenia is important. Early reporting of signs and symptoms including fever, cough, dysuria, recurrent or refractory infections is essential. Close monitoring of blood counts is also required and some patients receiving active therapies may require withholding of treatment or dose adjustment.

It is argued that MDS patients with neutropenia are not exposed to significant infection risk and therefore do not warrant the use of given prophylactic antibiotics (Garcia-Manero 2014). In addition, prophylactic antibiotics are also not routinely advised because of the risk of resistance (Wells et al 2014). Moreover, the routine use G-CSF with patients being treated with the hypomethlating agent, azacitidine (discussed later) is not recommended by some because of the increased risk of blast growth (Wells et al 2014). However, the use of G-CSF may be considered in patients with recurrent infections who have low risk disease (Killick et al, 2014).
**Watchful waiting.**

A watchful waiting approach should be adopted for patients with low IPSS risk MDS and asymptomatic from cytopenias. In addition, patients with intermediate-1 IPSS risk, asymptomatic cytopenia, no excess blasts and no poor risk cytogenetic abnormality require no immediate treatment (Malcovati et al, 2013).

**Time out 5**

Pause for a few moments and consider what you think the psychological impact of watchful waiting would have on patients and their carers.

The psychological burden on MDS patients can be huge (Thomas et al 2012). These patients must live with uncertainty on their disease trajectory and often live in fear of disease progression to AML. However, it is essential that a clear explanation is provided to patients and carers of their prognosis and the likely clinical outcomes (Table 3). Moreover, nurses must educate these patients on the importance of reporting any symptoms and attending scheduled clinic reviews. The goal of follow-up is to identify early worsening cytopenias, increasing blast counts and karyotic evolution (Malcovati et al, 2013). A repeat bone marrow is required where deterioration in cytopenias is observed.

**Immunosuppression**

Immunosuppressive therapy, with antithymocyte globulin (ATG) and cyclosporine is recommended for patients with a hypoplastic bone marrow (Malcovati et al 2013). ATG is administered as an in-patient and patients are monitored closely for bleeding, cardiac
events, serum sickness, thrombosis and severe infection. Cyclosporine is administered following ATG and continued for a minimum of 6 months. Patients require monitoring of cyclosporine levels with the aim to keep the trough level between 100-200 ug/L (Killick et al, 2014). Nurses play an important role in educating patients on these agents and the importance of timing of medication, monitoring levels and dietary advice, for instance, the importance of avoiding grapefruit juice when taking cyclosporine. In addition, close monitoring of blood pressure, renal function and liver function is essential to avoid drug related toxicity.

**Immunomodulatory drugs.**
The use of thalidomide has been shown to beneficial in reducing or abolishing transfusion dependence, however is limited by its neurotoxicity profile (Malcovati et al, 2013). Lenalidomide is licensed in Europe for patients with transfusion dependent anaemia due to low or INT-1 risk MDS associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate (Killick et al, 2013). Adverse effects of lenalidomide include neutropenia, thrombocytopenia and deep vein thrombosis. Nurses play a central role in education of patients on side effects and the importance of prompt management to minimise morbidity. In additions MDS patients receiving thalidomide or lenalidomide should be assessed for thrombosis risk and where benefit outweighs risk, thromboprophylaxis should be prescribed.
Hypomethylating agents

Until recently active treatments for MDS patients were limited to allogeneic HSCT and chemotherapy. However new therapeutic strategies e.g. hypomethylating agents (HMAs) have been developed and shown significant benefit for patients. However, these agents are not curative and therefore ongoing development of new agents is required.

Hypomethylating agents inhibit DNA methylation, a biochemical cell process. These new agents include the drugs azacitidine and decitabine. Azacitidine improves overall survival rate and also improves QOL when compared to supportive care only (Kornkblith et al 2002). Azacitidine is recommended as a treatment option for patients not eligible for HSCT, with MDS (Ipss Int-2 or high), Chronic Myelomonocytic Leukaemia (CMML-2) and AML (NICE, 2011).

Stopping treatment with azacitidine is not recommended because it ultimately leads to loss of response; however it may be necessary to interrupt treatment in exceptional circumstances, such as severe infection (Wells et al 2014). In addition dose reduction or duration between treatments may be prolonged based on patients’ blood counts. To date the standard of care is to continue azacitidine as long as a response persists.

Time out number 6
Make a list of side effects of azacitidine and the nursing management of patients on this agent.

Nurses have a key role in management of adverse events in order to prevent early discontinuation of treatment (Götze et al 2010). Adverse effects from azacitidine usually
occur in the first two cycles. Therefore it is important that patients are closely monitored to minimise risks of the treatment being stopped (Götze et al 2010).

Azacitidine results in myelosuppression and it important that patients’ blood counts are tracked over time to identify patients most at risk (Murray et al 2012). Patients need to be advised about how to prevent infection and bleeding and to report any signs and symptoms, especially a raised temperature. Azacitidine also causes common gastrointestinal side effects (i.e. nausea, vomiting, diarrhoea, constipation and anorexia). Pre-medication with anti-emetics are advised before each injection (Murray et al 2012). Constipation occurs in about 50% of patients requiring ongoing nursing assessment and intervention.

Azacitidine can be given intravenously or subcutaneously. When given subcutaneously, the injection site should be rotated (Götze et al 2010). Azacitidine often results in painful inflammation at the injection site. Evening primrose oil has been found effective in eliminating inflammatory skin reactions among a small group of patients in Germany (Platzbecker et al 2010). Moreover, anecdotal evidence suggests that some MDS patients report relief if they take over-the-counter anti-histamines before or after their injection (Murray et al 2012). While severe skin infections are rare, any patient with severe or persistent pain or erythema at the injection site should be assessed for signs of a developing secondary cellulitis (Wells et al 2014).

**Allogeneic HSCT**

Allogenic HSCT is the only potentially curative option in MDS (Koenecke et al 2014). However, it is not an option for the majority of patients due to advanced age, significant
co-morbidities and lack of suitable donor (Kurtin, 2011), even if they are young (Garcio-Manero 2014). Age at transplantation was identified as one of the most important prognostic factors for MDS patients undergoing HSCT. The older the age the shorter the overall survival and disease free survival (Sierra et al, 2002). In addition, disease stage is a significant factor affecting outcome after transplantation. Therefore appropriate selection of MDS patients for transplant is an important determinant of outcome. The decision to transplant involves balancing risk of disease progression, chances of success and risk of transplant related mortality (Killick et al 2014). Although many patients are ineligible for transplantation, all newly diagnosed patients should be assessed and the role of transplantation considered.

To date no specific recommendations can be given on the best myeloablative conditioning regime (Malcovati et al 2013). For some patients eligible for HSCT treatment who require a reduction in tumour burden, the use of azacitidine or decitabine may be used as a bridge to transplant by significantly reducing the marrow blast count (NCCN, 2014). In addition, reduced intensity regimes (RIC) have been studied in patients with MDS with positive outcomes and should be considered in patients where a standard myeloablative preparation regime is contraindicated. Regardless of the induction regime used prior to transplant it is essential that the patient is involved in the decision making process and receives ongoing support.

**Managing MDS at end of life.**

Treatment failure in patients with MDS is associated with a poor prognosis. Median survival after hypomethlyating agent failure is estimated at < 6 months for high risk MDS
patients and less < 18 months for low risk MDS. Nurses have an important role in providing support for patients and their carers and identifying their wishes and fears. It is well documented that haematology patients do not receive appropriate end-of-life care (McGrath and Holewa 2006, McGrath 2013). But nurses are ideally placed to raise the need for end-of-life care for MDS patients, in order to optimise a shift from active treatment to palliative care co-ordinated by the MDT.

**Nursing role**

Patients living with MDS are confronted with a myriad of quality of life issues.

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<thead>
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<th>Time out number 7</th>
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<tr>
<td>Pause for a moment and think about the range of quality of life issues that arise with a diagnosis of MDS</td>
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Hepinstall (2008) examined QOL in MDS patients and highlighted both positive and negative impacts on patients’ QOL and psychological health (Table 4). The physical and functional restrictions are caused by the illness and its treatment but also other issues associated with ageing (Thomas et al 2012).
Table 4. QOL and psychological aspects (Hepinstall, 2008).

<table>
<thead>
<tr>
<th>Negative effects</th>
<th>Positive effects</th>
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<tr>
<td>Diminished physical and mental capacity</td>
<td>Reassessing priorities</td>
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<tr>
<td>Loss of independence</td>
<td>Improved family relationships</td>
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<tr>
<td>Symptoms caused by MDS and toxicity with treatment</td>
<td>Adoption of positive health behaviours</td>
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<td>Diminished role with the family</td>
<td>Deeper more spiritual meaning</td>
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<td>Emotional toll</td>
<td>Feelings of hope when positive results of treatment</td>
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<td>Increase time on health related care</td>
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<td>Employment and economic challenges</td>
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Nursing management of patients with MDS not only requires attention to disease related factors but also specific focus on QOL assessment using validated tools e.g. European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 (version 3) (Aaronson et al 1993). In addition nurses play a significant advocacy role in ensuring patients’ concerns are addressed at MDT discussions and early referral to supportive services (e.g. social worker) is initiated. Moreover, due to the chronic nature of the disease patients needs require continual assessment and reassessment.

Fatigue is very common among MDS patients and many factors are believed to be involved, not just low Hb levels. It is multidimensional in nature with physical, cognitive and affective dimensions (Thomas et al 2012). Fatigue has been reported as the symptom which impacts most on MDS patients’ QOL (Steeesma et al 2008). Knowing that fatigue has a huge impact on all MDS patients’ lives can be a first step for patients to explore
with nurses some practical interventions that could be introduced to minimise the effects. However, it is also important for nurses to set realistic expectations with patients about living with their fatigue (Thomas et al 2012).

Patients with MDS are older aged and require careful assessment of functional ability and ability to undertake activities of daily living (Kurtin and Demakos 2010). Furthermore, nurses need to remain cognisant of the additional stressors placed on those caring for their older relatives with MDS and advise them to where they can get support. Nurses should also be aware of supportive organisations that some patients may find helpful. These include the UK MDS Patient Forum (www.mdspatientsupport.org.uk) and international supportive organisations include MDS Beacon (www.mdsbeacon.com) and MDS Foundation (www.mds-foundation.org).

Specialist haematology nurses play a key role in educating patients and nursing colleagues on MDS and its disease trajectory. For instance, a recent US survey reported that only 10% of the patients who responded (n=477) agreed that MDS was a 'cancer'. A majority of patients surveyed responded that MDS was 'bone marrow failure' (60%), a blood disease (38%) or a pre-leukaemia condition (17%) (the answers sum to >100% because patients were given multiple options) (Steensma et al 2014). Furthermore, patients in the survey perceived the treatments for MDS more positively than physicians and non-physicians (nurses and social workers) (Steensma et al 2014). A very interesting finding in this survey was that the nurse responses were more similar to the patient
responses than the physician responses, highlighting the need for more education for nurses on MDS (Steensma et al 2014).

**Time out 8**

Now that you have almost finished reading this paper, consider what new knowledge you have gained about MDS. What three pieces of new information will help you effectively support MDS patients living with their disease?

**Conclusion**

Significant advances in our understanding and management of MDS have evolved in the past decade. Progress in disease management includes improved treatment options for cytopenias with improved overall survival benefit. However, to date, MDS remains incurable without HSCT. Treatment in MDS is aimed at preventing cytopenia related (usually anaemia) morbidity and preserving QOL. In the context of treatments being given with non-curative intent, it is vital that nurses place QOL issues for these patients to the forefront of care. However, this involves difficult discussions with patients and carers on prognosis which must be based on a sound understanding of MDS.
References


