

MyelomaAcademy™



NURSING BEST PRACTICE GUIDE

Peripheral neuropathy

This document is one of the Myeloma Academy Nursing Best Practice Guides for the Management of Myeloma series. The purpose of this Guide is to enhance knowledge and inform nursing practice of peripheral neuropathy in the care of myeloma patients.

After reading this, you should be able to:

- ★ Define myeloma-related peripheral neuropathy
- ★ Understand the causes, symptoms and consequences of peripheral neuropathy in myeloma patients
- ★ Be aware of the clinical testing and assessment tools for peripheral neuropathy
- ★ Understand the management of peripheral neuropathy
- ★ Understand the nurse's role in the assessment, intervention and management of peripheral neuropathy and in the patient education of this condition

The information contained within this Guide should be used in conjunction with local policies, protocols and best practice guidelines in oncology.

Background

Peripheral neuropathy is the term used to describe damage to the peripheral nerve cells involving sensory, motor or autonomic neurones. In myeloma, it may be a complication of the myeloma itself, or a side-effect of specific treatments^[1, 2].

Up to 14% of myeloma patients are estimated to have symptoms of peripheral neuropathy at diagnosis^[3] but approximately 80% of patients develop some degree of peripheral neuropathy as a later complication of myeloma or as a result of treatment^[4, 5].

KEY FACTS

- ★ Peripheral neuropathy is a serious and potentially debilitating condition caused by the myeloma itself or more commonly by the side-effect of certain treatments
- ★ In most cases, treatment-induced peripheral neuropathy is reversible with timely and adequate dose reduction of anti-myeloma treatment
- ★ Early detection of and intervention for peripheral neuropathy is associated with improved quality of life and outcomes for patients

In general, risk factors for peripheral neuropathy include treatment-specific characteristics such as duration and dose of specific treatments or previous exposure to other neurotoxic treatments, and patient-specific characteristics such as the presence of other comorbidities (e.g. diabetes, alcoholism, nutritional deficiency, HIV) or pre-existing neuropathy. There is evidence of genetic variation in predisposition to treatment-induced neuropathy^[6, 7].

Myeloma-related peripheral neuropathy occurs predominantly in the sensory neurones and mostly affects the hands and feet. Treatment-induced peripheral neuropathy not only affects sensory neurones but may occasionally damage motor or autonomic neurones.

The clinical consequences of sensory peripheral neuropathy include: tingling, numbness, burning or loss of sensation, sensitivity to touch (collectively referred to as paraesthesia) and neuropathic pain. If severe, it may also cause impaired muscle tone, lack of coordination and position sense. For some patients the non-painful component of neuropathy is the most disabling aspect^[8].

Symptoms of motor peripheral neuropathy include muscle cramps, tremors and weakness which may affect manual dexterity and mobility such as walking, while the consequences of autonomic peripheral neuropathy include bradycardia, orthostatic/postural hypotension, constipation and urinary bladder or sexual dysfunction.

The exact cause of myeloma-related neuropathy is not known, but may be due to the paraproteins directly damaging the nerves or as a result of the compression of the spinal cord or nerve roots by a plasmacytoma^[1]. In some patients, hyperviscosity caused by excessive paraprotein levels in the blood may also lead to symptoms of peripheral neuropathy.

Treatment of the myeloma can reduce the symptoms of myeloma-associated neuropathy and improve the neuropathy to varying degrees.

However, as described before, for many myeloma patients treatment for myeloma is the main cause of peripheral neuropathy and is a common side-effect of key anti-myeloma treatments such as thalidomide and Velcade[®]^[9, 10] and certain chemotherapy drugs such as vincristine^[11]. Revlimid[®] has been shown to carry a low risk of neurotoxicity even in patients with pre-existing chemotherapy induced peripheral neuropathy (CIPN)^[12].

Evidence indicates that treatment-induced peripheral neuropathy is dose-related^[13]. Therefore, reducing the dose, changing the schedule or temporarily halting treatment can, in most cases, significantly reduce symptoms and reverse damage if implemented early^[3]. However, these treatment changes may have an impact on the response to and outcome of the anti-myeloma treatment.

For Velcade, changing the route of administration from intravenous infusion to subcutaneous injection significantly reduces the incidence and severity of peripheral neuropathy without affecting efficacy^[14, 15].

Peripheral neuropathy is without doubt a serious and potentially debilitating complication which if not managed correctly, can lead to a significant decrease in patients' quality of life and interruption of their treatment. Prevention of peripheral neuropathy wherever possible and early detection is therefore a priority.

The following describes the medical approach to the treatment of peripheral neuropathy and provides guidance on nursing interventions and nursing management of myeloma patients with peripheral neuropathy^[4].

Recently published guidelines offer advice on peripheral neuropathy prevention and management^[14, 16, 17].

GENERAL RECOMMENDATIONS:

- ★ All newly diagnosed myeloma patients should undergo a neurological assessment before starting treatment
- ★ Patients should be assessed for signs of neurotoxicity before the start of each treatment cycle particularly if they are on Velcade or thalidomide
- ★ Specific management strategies for peripheral neuropathy should be based on the grade of severity and on signs and symptoms, and should include dose and schedule modification if neuropathy is treatment-induced
- ★ Both pharmacological interventions and non-pharmacological approaches should be considered to relieve symptoms of peripheral neuropathy

NURSING RECOMMENDATIONS:

- ★ Patient education is fundamental and the importance of patients reporting the earliest signs of peripheral neuropathy should be clearly communicated
- ★ Patients should be evaluated at every visit for signs and symptoms of peripheral neuropathy
- ★ The ability of the patient to perform activities of daily living should be assessed on a regular basis
- ★ Patients should be provided with self-care measures to increase environmental safety and to avoid injury



Medical Approach

Peripheral neuropathy is one of the most challenging complications of myeloma, and side-effects of treatment, to assess and manage and relies on patients reporting symptoms.

There is no treatment as such for peripheral neuropathy, however, appropriate timely management, together with treatment of symptoms, are crucial to maintain quality of life and to reduce the risk of permanent neurological damage.

This section describes the general medical approaches taken in the management of peripheral neuropathy in myeloma patients which may involve referral to pain specialists, neurologists and other allied healthcare professionals.

Assessment

Neurological assessment

Prior to the start of treatment, patients should undergo an accurate neurological assessment (see Appendix I) including patient history, patient reporting and general clinical examination.

The initial assessment should identify patients at an increased risk of, or who already have pre-existing neuropathy caused by the myeloma itself or other comorbidities (e.g. vitamin B12 deficiency, diabetes). Further neurotoxicity assessments should then be repeated preferably before the start of each new treatment cycle, so that any emergent symptoms or worsening neuropathy can be detected as early as possible.

Assessments should continue even after treatment has stopped, particularly if the patient has been on thalidomide.

Although several general neurotoxicity assessment tools are available, no standardised reliable measure of peripheral neuropathy exists.

Grading the severity of symptoms is perhaps the most important criteria for any neurotoxicity assessment tool so that an objective assessment of peripheral neuropathy can be made allowing different members of the multidisciplinary team to assess the same patient accurately.

Examples of some of the neurotoxicity assessment tools used include the following:

World Health Organisation (WHO) Criteria

Sensory Grade	Neuropathy
0	None or no change
1	Mild paraesthesia, loss of deep tendon reflexes
2	Mild or moderate objective sensory loss, moderate paraesthesia
3	Severe objective sensory loss or paraesthesia interfering with function

National Cancer Institute (NCI) Common Toxicity Criteria (CTC) Sensory Guide^[18]

Sensory Grade	Neuropathy
1	Asymptomatic; loss of deep tendon reflexes or paresthesia
2	Moderate symptoms; limiting instrumental ADL
3	Severe symptoms; limiting self care ADL
4	Life-threatening consequences; urgent intervention indicated
5	Death



Functional Assessment of Cancer Therapy/ Gynaecology Oncology Group Neurotoxicity Questionnaire (FACT/ GOG-Ntx)

Patients grade each of the following statements as follows:	
0	Not at all
1	A little bit
2	Somewhat
3	Quite a bit
4	Very much
NTX1:	I have numbness or tingling in my hands
NTX2:	I have numbness or tingling in my feet
NTX3:	I feel discomfort in my hands
NTX4:	I feel discomfort in my feet
NTX5:	I have joint pain or muscle cramps
HI12:	I feel weak all over
NTX6:	I have trouble hearing
NTX7:	I get ringing or buzzing in my ears
NTX8:	I have trouble doing up buttons
NTX9:	I have trouble feeling the shape of small objects when they are in my hand
An6:	I have trouble walking

In addition, it is helpful to assess the pain intensity caused by the neuropathy and the effect it has on normal day to day function for example, using the 'Worst pain in past week' item (score 0 - 10) of the Brief Pain Inventory^[19].

Psychological assessment

An initial psychological assessment should be considered for certain patients to determine if any underlying problem, such as depression, may affect their response to, and ability to cope with pain.

Treatment

Peripheral neuropathy

Symptoms related to myeloma-associated neuropathy should improve with ongoing conventional anti-myeloma drug treatment or with radiotherapy (for a plasmacytoma).

If the neuropathy is caused by anti-myeloma treatment then prompt action is essential.

If neuropathy is a result of Velcade treatment, the severity based on the NCI CTC grading (see Appendix II) should be established and one of the following carried out:

- ★ Dose reduction
- ★ Schedule modification from twice-weekly to once-weekly administration
- ★ Temporary suspension of treatment

A change to a subcutaneous route of administration may also be considered.

If treatment has been suspended, it may resume when neuropathy has returned to baseline or is less than a Grade 1 severity.

Although there are no validated guidelines for thalidomide, dose reduction or temporary suspension of treatment should also be carried out based on the graded severity of neuropathy. See Appendix III for general recommendations.

Pain

It is generally recognised that neuropathic pain responds poorly to standard analgesics. Opioids can be effective but given at high doses, are associated with significant side-effects. Therefore, other pain modulating treatments such as calcium channel blockers (gabapentin, pregabalin), sodium channel blockers (oxcarbazepine) or certain anti-depressants (amitryptiline, duloxetine) should be considered for neuropathic pain relief^[20].

As response to analgesia varies substantially from patient to patient, a trial and error approach with type and dose of analgesia is often necessary.

Topical treatment may also be used for painful skin areas (e.g. lidocaine cream, capsaicin - or menthol-based preparations).

Patients who do not respond well to their prescribed pain management should be referred to the pain specialist team.

Nursing interventions and management

Nurses play a key role in the prevention, treatment and overall management of myeloma patients with peripheral neuropathy.

The following provides best practice recommendations for nursing interventions related to the assessment, treatment and monitoring of myeloma patients with peripheral neuropathy, and for nursing management related to the provision of knowledge, education and a more holistic approach to caring for myeloma patients with peripheral neuropathy.

Interventions

- ★ Before the start of each treatment cycle, screen patients for baseline peripheral neuropathy. This may involve asking questions such as:
 - ★ Do you have numbness and tingling in the tips of your fingers or toes?
 - ★ Did you have this with any other previous treatment?
 - ★ Is this getting worse?
 - ★ Do you have any pain in your fingers and toes?
 - ★ Does it affect your daily life at all?
 - ★ Can you still manage to walk and is your balance affected?
 - ★ Do you have trouble picking up small objects and carrying out fine movements with your fingers, such as doing up buttons?
- ★ Monitor patients on a regular basis for symptoms that may indicate signs of peripheral neuropathy
- ★ Question patients about other symptoms that may indicate autonomic peripheral neuropathy
- ★ Test patients for their gross and fine motor skills by getting them to perform relevant tasks
- ★ Ensure you are proficient in assessing patients for peripheral neuropathy
- ★ Refer to a neurologist to determine if peripheral neuropathy is treatment-emergent or myeloma-related by administering an electromyogram
- ★ Report any relevant information related to any aspect of peripheral neuropathy the patient has discussed with you to the haematologist
- ★ Explain to patients the reasons for any changes to their anti-myeloma treatment (for example, any dose reductions) and that they must comply with their treatment
- ★ Continually assess patients for their pain. If necessary, coordinate referral to the pain specialist team (see Myeloma UK Nursing Best Practice Guide on Pain)
- ★ Establish whether patients are able to perform activities of daily living (dressing, feeding and washing). Inform the haematologist and make referrals to physiotherapy and occupational therapy teams where appropriate or to other members of the multidisciplinary team

Management

- ★ Educate patients and their families about the possible causes of peripheral neuropathy, the signs and symptoms and the importance of early reporting. Ensure that patients know how, when and to whom the symptoms should be reported
- ★ Inform patients who drive that they need to tell the Driver and Vehicle Licensing Agency (DVLA) they have peripheral neuropathy



- ★ Provide patients with written information to help them understand about myeloma-related peripheral neuropathy
- ★ Encourage patients to describe the symptoms of their peripheral neuropathy as accurately as possible and to speak up about how much pain they have and the impact it has on their quality of life
- ★ Counsel patients if their treatment has temporarily stopped.
- ★ If treatment is to be discontinued, discuss alternative treatment options as sometimes patients find this difficult to accept especially if it is working well against their myeloma
- ★ Help identify potential safety hazards to minimise the possibility of accidents and injuries and suggest measures for managing personal safety. For example:
 - ★ Using aids to help with everyday tasks, such as getting hand-rails fitted
 - ★ Being cautious when taking a bath or shower such as checking the water temperature first
 - ★ Looking after the feet by inspecting them regularly and wearing properly fitted comfortable shoes
 - ★ Protecting hands and feet from extremes of temperature to reduce the risk of ischaemic and thermal injuries
 - ★ Adopting a good posture and avoid sitting cross-legged for long periods of time to avoid extra pressure on the nerves
 - ★ Rising to standing position slowly
- ★ Explore non-pharmacological approaches for the relief of symptoms of peripheral neuropathy such as:
 - ★ Daily vitamin and nutritional supplements e.g. multi-B complex vitamins, folic acid, vitamin E, α -lipoic acid, acetyl-carnitine
 - ★ Emollient creams e.g. cocoa butter, eucalyptus-based creams
 - ★ Quinine tablets or drinking tonic water to help with cramps
 - ★ Transcutaneous electrical nerve stimulation (TENS) machines to help reduce pain
 - ★ Complementary therapies such as acupuncture, reflexology and gentle massage
 - ★ Magnesium supplements which may alleviate muscle cramps
- ★ Encourage patients to take regular gentle exercise to help keep muscles toned and improve circulation and to maintain a healthy balanced diet. Coordinate referral to a physiotherapist or dietician if necessary
- ★ Encourage patients who smoke to stop, provide them with tips and information on any local support groups
- ★ Educate patients and their families about signs and symptoms of depression and anxiety and coordinate referral to a counsellor or clinical psychologist if necessary
- ★ Promote interdisciplinary communication between colleagues to ensure successful management of each patient
- ★ Stay current with developments in the management of peripheral neuropathy

Summary

Peripheral neuropathy is a frequent and potentially debilitating complication of myeloma which can adversely affect quality of life and compromise optimal anti-myeloma treatment.

Identifying patients at risk or those with signs of neuropathy as early as possible allows for prompt intervention to limit the clinical consequences and to relieve symptoms.

Nurses play an important role in the initial and ongoing assessment of peripheral neuropathy and in providing effective management strategies for their patients to help alleviate symptoms and promote safety.

Abbreviations

★ ACE	Angiotensin converting enzyme	★ ENA	Extractable nuclear antigen
★ ANA	Anti-nuclear antibody	★ FBC	Full blood count
★ ANCA	Antineutrophil cytoplasmic antibody	★ LFT	Liver function tests
★ Ca	Serum calcium	★ mg/ml²	milligram per square millimetre
★ CIPN	Chemotherapy induced peripheral neuropathy	★ MRI	Magnetic resonance imaging
★ CSF	Cerebrospinal fluid	★ NCI	National Cancer Institute
★ CTC	Common toxicity criteria	★ NTX	Neurotoxicity
★ DVLA	Driver and Vehicle Licensing Agency	★ SAP	Serum amyloid P
		★ ThFT	Thyroid function tests
		★ U&E	Urea and electrolytes

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ABOUT THE NURSING BEST PRACTICE GUIDES

The Nursing Best Practice Guides have been developed by Myeloma UK and an expert nursing advisory group, with input from relevant specialist healthcare professionals. They have been developed to enhance nurse knowledge, inform nursing practice and support nurses in the delivery of high quality treatment and care to myeloma patients and families.

Nursing Best Practice Guide series:

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ABOUT THE MYELOMA ACADEMY

The Myeloma Academy provides healthcare professionals involved in the treatment and care of myeloma patients with access to comprehensive accredited learning resources and tools in an innovative online environment and through educational events.

It supports the education and continual professional development of myeloma healthcare professionals so they can provide optimum patient-centred treatment and care within the current UK health and policy environment.

For more information visit:

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ABOUT MYELOMA UK

Myeloma UK is the only organisation in the UK dealing exclusively with myeloma.

Our mission is to provide information and support to people affected by myeloma and to improve standards of treatment and care through research, education, campaigning and raising awareness.

For more information about Myeloma UK and what we do, please visit **www.myeloma.org.uk** or contact us at **myelomauk@myeloma.org.uk** or **+44 (0)131 557 3332**.

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Appendix I

Example of initial assessment of peripheral neuropathy

Routine	Additional	Consider	Specialist tests
FBC	Serum B12	MRI of spine and plexuses (if radicular compression is suspected)	Nerve conduction studies
U&E	Lipids	Oral glucose tolerance test	Lumbar puncture and CSF protein
LFT	Fasting glucose	SAP scan	Anti-neuronal antibodies
Ca	ANA		Nerve biopsy
ThFT	ENA ANCA		
	Serum ACE		

Appendix II

Recommended dose modifications of Velcade for myeloma patients with Velcade-induced peripheral neuropathy

Severity of peripheral neuropathy	Modification
Grade 1: Paraesthesia and/or loss of reflexes, no pain or loss of function	No action
Grade 1 with pain <i>or</i>	Reduce Velcade to 1mg/m ² or consider weekly administration
Grade 2: Interfering with function but not with activities of daily living	
Grade 2: with pain <i>or</i>	Discontinue Velcade until toxicity resolves. Then restart with a reduced dose of 0.7mg/m ² and change the treatment schedule to once per week
Grade 3: Interfering with activities of daily living	
Grade 4: Permanent sensory loss that interferes with function	Discontinue Velcade

Appendix III

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Recommended dose modifications of thalidomide for myeloma patients with thalidomide-induced peripheral neuropathy

Severity of peripheral neuropathy	Modification
Grade 1: Paraesthesia and/or loss of reflexes, no pain or loss of function	No action
Grade 1 with pain <i>or</i>	Reduce dose by 50%
Grade 2: Interfering with function but not with activities of daily living	
Grade 2: with pain <i>or</i>	Discontinue thalidomide treatment until toxicity resolves to Grade 1 or better. Restart with a 50% reduced dose only if the benefit/risk is favourable
Grade 3: Interfering with activities of daily living	
Grade 4: Permanent sensory loss that interferes with function	Discontinue thalidomide treatment



Notes



Notes



Notes



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