Pathogenesis, diagnosis and management of osteomalacia


Abstract
Osteomalacia is a musculoskeletal condition that results in soft bones due to ineffective mineralisation. Nurses have a unique opportunity to improve awareness of osteomalacia and reduce its incidence through health education. Multidisciplinary management is important to minimise the effect of osteomalacia on activities of daily living and reduce the risk of fracture due to poor mineralisation of the bones.

Aims and intended learning outcomes
The aim of this article is to familiarise readers with the pathophysiology of osteomalacia and appropriate management strategies. After reading this article you should be able to:

■ Identify factors associated with the development of osteomalacia.
■ Discuss how osteomalacia affects activities of daily living.
■ Summarise different management strategies that may be used.
■ Discuss the role of the nurse in caring for people with or at risk of osteomalacia.

Introduction
Musculoskeletal aches and pains are a common reason for seeking medical advice, with approximately 12% of GP consultations being for musculoskeletal problems (Edwards et al 2012). It is important to establish the true cause of pain and stiffness to ensure appropriate and timely treatment, although this can be difficult in older people who may have multiple pains from other musculoskeletal pathologies such as osteoarthritis or polymyalgia rheumatica.

Osteomalacia is a condition associated with bone pain, increased bone fragility and fractures (Ralston and Mclnnes 2014). The word osteomalacia means soft bones (osteo = bone, malacia = soft). This softening of the bones occurs as a consequence of impaired bone mineralisation (deposition of hydroxyapatite), commonly due to vitamin D deficiency (Cardinal and Gregory 2009).

The deficiency may be as a result of lack of exposure to sunlight, poor nutritional intake, abnormalities in vitamin D metabolism, hypophosphataemia (low levels of phosphate) and drug-induced inhibition of bone mineralisation (Ralston and Mclnnes 2014). A brief overview of the causes of osteomalacia is shown in Box 1. In children, the same ineffective bone mineralisation is referred to as rickets.

Box 1  Common causes of osteomalacia

Usage: Vitamin D deficiency:
■ Inadequate oral intake.
■ Inadequate exposure to sunlight.
■ Intestinal malabsorption.

Abnormal vitamin D metabolism:
■ Liver disease.
■ Renal disease.
■ Medication.

Hypophosphataemia:
■ Low oral phosphate intake.
■ Excess renal phosphate loss.

Inhibition of mineralisation:
■ Bisphosphonates.
■ Aluminium.
■ Fluoride.

Hypophosphatasia (inherited autosomal disorder).
(Field et al 2014)
Vitamin D is a fat-soluble vitamin with many important roles. One of the main functions of vitamin D is to promote calcium absorption in the intestines. The absorption of calcium maintains adequate serum calcium and phosphate concentrations, which permit effective mineralisation of the bones. The majority of vitamin D comes from the skin in response to ultraviolet B radiation from exposure to sun, while less than 20% comes from dietary intake (Liberman 2014) (see Box 2).

Osteomalacia is therefore less common in geographical locations where people have sufficient exposure to sunlight, for example, countries closer to the equator. In more northern areas such as Scandinavia and Alaska, hours of daylight are shorter, and there is an increased risk of developing osteomalacia (Pearce and Cheetham 2010). As vitamin D is found only in small quantities in foods, it is unlikely that food alone can provide the body’s vitamin D requirements. As such, the Department of Health (DH) (2012) recommends that people aged 65 years and older who do not get much sun exposure should take a daily supplement containing 10µg of vitamin D.

Pathogenesis
Calcium, phosphorus and vitamin D are all required for effective bone mineralisation and skeletal health. Deficiency in calcium and vitamin D can predispose an individual to significant health risks, such as osteoporosis and osteomalacia. In osteomalacia inability to absorb or process these nutrients causes ineffective bone mineralisation, which results in weaker bones (Ralston and McInnes 2014).

Dehydrocholesterol is converted to vitamin D3 (cholecalciferol) by exposure to sunlight. Cholecalciferol is then hydroxylated in the liver by 25-hydroxylase to produce 25-hydroxy vitamin D (25OHD). This is further hydroxylated in the kidneys by the enzyme 1-alpha-hydroxylase to form 1,25-dihydroxy vitamin D (1,25 OH₂D), which is the active form of vitamin D (Hanlon et al 2014). The active form of vitamin D then binds to vitamin D receptors to promote intestinal absorption of calcium and phosphorus (Liberman 2014) (Box 3). Any abnormalities of the vitamin D pathway will affect the ability to metabolise vitamin D, and subsequently the ability to absorb calcium.

Common reasons for calcium and vitamin D deficiency include poor nutritional intake, poor absorption from the digestive tract, limited exposure to sunlight, and renal failure or liver failure (Liberman 2014). Abnormalities in vitamin D metabolism may be inherited or acquired, for example, patients with chronic renal failure may not be able to synthesise the active metabolite of vitamin D. However, routine measurement of vitamin D levels in people with stage 1, 2, 3A or 3B chronic kidney disease is not recommended (National Institute for Health and Care Excellence (NICE) 2008). Liver disease can impede the hydroxylation process in the liver and consequently affect conversion of vitamin D to its active form.

Medications such as carbamazepine, phenytoin and sodium valproate or rifampicin can also affect vitamin D metabolism and increased clearance of vitamin D (Medicines and Healthcare products Regulatory Agency 2009, Pearce and Cheetham 2010). Patients taking these medications long term require regular review to ensure they are not at increased risk of mineralisation deficits.

Older people are at increased risk of vitamin D deficiency due to the reduced ability of the skin to synthesise vitamin D, and reduced synthesis in the kidney as a result of declining kidney function (Kinyamu et al 1997).

The parathyroid hormone (PTH) is a polypeptide that is secreted in response to falling serum calcium levels. A rise in PTH levels increases reabsorption of calcium from bone by increasing osteoclast (cells that resorb bone) activity and promotes reabsorption of calcium by the renal tubules (Strachan and Newell-Price 2014). As vitamin D deficiency causes reduced absorption of calcium from the intestines, this results in low serum

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**Box 2** Sources of vitamin D
- Ultraviolet B radiation from exposure to sun.
- Oily fish, such as trout, salmon, mackerel, herring and sardines.
- Cod liver oil and other fish oils.
- Egg yolk.
- Mushrooms.
- Fortified breakfast cereal.
- Margarine (statutory supplementation in the UK).
(Pearce and Cheetham 2010)

**Box 3** Vitamin D synthesis
- Exposure to ultraviolet radiation from the sun and dietary intake
  - Hydroxylation in the liver to form 25-hydroxy vitamin D
  - Hydroxylation in the kidney to form 1,25-dihydroxy vitamin D (active form)
  - Activation of vitamin D receptors

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Causes

Risk factors

There are at-risk populations in every geographical region, such as older people living in long-term care settings who do not get adequate exposure to sunlight or people with restricted mobility who are unable or lack the confidence to venture outside. Exposure to sunlight and ultraviolet radiation can also be restricted by other methods, for example, the use of clothes to keep skin covered for religious or cultural reasons (Arthritis Research UK (ARUK) 2013).

The use of sunscreen with a protection factor of 15 or more can block more than 99% of dermal vitamin D synthesis by preventing exposure to ultraviolet rays (Pearce and Cheetham 2010). This lack of exposure to sunlight and ultraviolet rays consequently affects the production of vitamin D, and continued deficits in vitamin D synthesis can affect the mineralisation process and bone strength. Nutritional deficits of calcium, vitamin D or phosphorus also predispose people to developing osteomalacia. These nutritional deficits could be due to poor nutritional intake or vegan and lacto-vegetarian diets in which calcium or vitamin D may be lacking. Other common causes include malabsorption in the intestines as a result of conditions such as lactose intolerance, coeliac disease or inflammatory bowel disease (Pearce and Cheetham 2010, ARUK 2013).

Incidence

The onset of osteomalacia often goes unnoticed, because many people are unaware of vitamin D or calcium deficiencies, which may predispose to developing the condition. As symptoms are often mild during the early stages of the pathology, many people remain unaware of the condition. Hyppönen and Power (2007) noted that more than half of the adult UK population did not have sufficient levels of vitamin D and that 16% had severe deficiency during winter and spring. The National Diet and Nutrition Survey (DH 2012) has more recently shown that up to one quarter of people in the UK have low levels of vitamin D in their blood.

Vitamin D deficiency is a common problem and particularly prevalent in the older population (Cardinal and Gregory 2009). There is also a higher incidence in people with darker skin pigmentation, for example, those of African or south Asian origin who live in a milder climate (Pearce and Cheetham 2010), because darker pigmented skin requires more sun exposure to produce sufficient levels of vitamin D (Holick 2004). Vitamin D deficiency is also more prevalent in people who are obese (Cardinal and Gregory 2009) or who have had stomach surgery (Cardinal and Gregory 2009, ARUK 2013).

Now do time out 2.

Signs and symptoms

As the symptoms of osteomalacia are not specific it can be some time before the condition is diagnosed. In some cases the condition can be present for several years before diagnosis (ARUK 2013). Early symptoms often have a gradual onset and may be non-specific, such as persistent fatigue, bone and joint pain and tenderness. Muscular weakness is one of the later signs of osteomalacia. It is characteristically proximal weakness that affects the
shoulders, thighs and main trunk (ARUK 2013). Bony
tenderness and skeletal deformity may also be apparent
as the condition progresses, particularly in the long bones
and pelvis (Cardinal and Gregory 2009). Bone pain
classically affects the legs, groin, knees and feet initially,
although it can be felt all over as the condition progresses
and simple movements might become painful (ARUK
2013). Muscles may become weak and stiff, which can
make many activities difficult. Unfortunately, diffuse
muscular aches can be misdiagnosed as fibromyalgia or
somatisation of depression (Sievenpiper et al. 2008).

Red flags are warning signs that should prompt
consideration of a different underlying pathology such as
cancer or infection. Red flag signs include weight loss,
fever or other systemic signs of infection such as night
sweats or chills, night pain, neurological signs and
symptoms (Edwards et al. 2012). As generalised bone
pain is one of the main symptoms of osteomalacia, it is
essential that any new pains or persistent localised pains
are investigated because this could indicate a fracture
or metastatic bone lesions.

As a result of muscle weakness and stiffness common
problems for people with osteomalacia include climbing
stairs, getting out of chairs and, in severe cases, getting
out of bed (ARUK 2013). These activities can already
be difficult for many older people so it is important
that thorough assessments are made of function and
daily living activities. It is also important to ensure that
any risks as a result of reduced strength and mobility
caused by osteomalacia are identified, for example, falls,
difficulties with shopping and self-care activities.

Changes in function may have a significant effect
on social and daily activities, and should be considered
as part of a patient-centred approach. Due to the
complexities of decreasing levels of function in the older
person, it is important that assessment and management
plans are multidisciplinary.

Investigations and diagnosis
Patients who are suspected of having osteomalacia
should have blood tests to assess biochemical markers.
The following are of particular interest (Ralston and
McInnes 2014):

- Renal function to assess for underlying signs of
renal failure.
- Serum calcium.
- Phosphate.
- Alkaline phosphatase, an enzyme produced
by osteoclasts.
- Serum 25-hydroxy vitamin D.
- PTH levels.

Measuring serum 25-hydroxy vitamin D is the best
way to assess someone’s vitamin D status (Holick
2007). However, this will not provide a good indicator
of total vitamin D in patients with renal insufficiency
who are unable to convert vitamin D to its active form,
1,25-dihydroxy vitamin D.

Laboratory abnormalities in osteomalacia might
include low serum calcium and/or phosphorus, reduced
serum 25-hydroxy vitamin D levels, elevated serum
alkaline phosphatase and elevated PTH levels (Liberman
2014). More than 80% of adults with osteomalacia have
a high concentration of serum alkaline phosphatase and
elevation of plasma PTH is also found in approximately
80% (Pearce and Cheetham 2010).

Radiography is of limited use to make an initial
diagnosis, because there are often little defects to visualise
on plain X-ray, although pathological changes are often
present in more advanced stages (Ralston and McInnes
2014). Osteopaenia or reduced bone density is the most

![Looser's zone](Wellcome Images)
common finding on radiography, although in advanced cases of osteomalacia there can be Looser’s zones (Ralston and McInnes 2014). Looser’s zones are radiographically lucent areas in the cortical bone, which represent areas of demineralised bone (Figure 1, page 35). These areas may be seen in the ribs, pelvis and long bones, and are often referred to as pseudo fractures or milkman’s fractures. Diagnosis can also be confirmed by bone biopsy.

Demineralised areas predispose to complete fractures (ARUK 2013). As standard radiographs do not provide an accurate assessment of bone mass, dual-energy X-ray absorptiometry scans can be used identify bone mineral density. Differential diagnoses to be considered include other pathologies such as Paget’s disease, osteoporosis and myeloma.

Prevention and treatment
Prognosis and recovery are usually good if the underlying causes of osteomalacia and vitamin D deficiency are identified and managed appropriately. These can be simple measures such as encouraging the person to eat an adequate diet and ensuring that they have enough exposure to the sun. It can take months for bones to recover and muscles to regain strength with the appropriate treatment (ARUK 2013). Late diagnosis will require a longer recovery period, especially if fractures have occurred. It is important to identify the cause of osteomalacia to ensure effective treatment, for example, the cause of vitamin D deficiency or direct inhibition of mineralisation. It is also important to assess the effect of osteomalacia on activities of daily living, and tailor a plan of care to meet needs.

Diet Encouraging a diet rich in vitamin D and calcium will help to maintain nutritional levels required for effective mineralisation of the bones. Discussing dietary requirements and highlighting foods that are rich in calcium and vitamin D will help raise awareness of important food sources. Referral to a dietitian can also be helpful in assessing and planning nutritional support, especially where people have specific dietary requirements, for example, in coeliac disease. In many countries some food sources are fortified with vitamin D such as margarine and cereals to improve nutritional intake.

Now do time out 4.

The recommended daily intake of vitamin D for an adult in the UK is 10µg (400 international units) (DH 1998), however, this level is only sufficient to prevent osteomalacia, rather than provide optimal levels (Pearce and Cheetham 2010).

Cardinal and Gregory (2009) and ARUK (2013), however, recommend supplementation with 20µg vitamin D, as well as consideration of calcium supplements. Osteomalacia that occurs secondary to chronic renal failure may require treatment with active vitamin D metabolites because these will bypass the metabolic defect (Ralston and McInnes 2014).

Exposure to sunlight Where possible, people should be encouraged to go outside and expose their arms and face to the sun to increase vitamin D levels (ARUK 2013). Approximately 15 minutes exposure will increase levels, although care should be taken not to allow the skin to burn in strong sunshine (ARUK 2013). Adequate exposure may be difficult to achieve in people who are housebound or who may be confined indoors for long periods, therefore the DH (2012) recommendation that people aged over 65 years should take a daily supplement of 10µg of vitamin D will have a substantial effect on bone health in the older population.

Now do time out 5.

Dietary and lifestyle strategies

Write a list of dietary and lifestyle advice that you may consider giving to a patient with or at risk of developing osteomalacia.

Exercise As stiffness and weakness increase with advanced osteomalacia, it can become difficult to perform a variety of activities. Physiotherapy is useful to help strengthen muscles and improve physical function. Weight-bearing exercise such as walking can help to strengthen muscles and bones, although high impact and intensive exercise should be avoided until Looser’s zones or fractures have healed. Analgesics can be taken for pain to help manage exercise and daily activities, especially if fractures have occurred (ARUK 2013).

As mobility becomes more difficult with advanced osteomalacia it is important to assess the risk of falling, because it may increase with reduced muscle strength and increased pain and stiffness. Osteoporosis often co-exists with osteomalacia (Cardinal and Gregory 2009), and this further increases the risk of fracture in the event of falls. Falls assessments should be a
comprehensive multidisciplinary effort and can include assessment by physiotherapists, home assessment by occupational therapists, and an overview of drug therapies by the medical or pharmacy team.

Now do time out 6.

6 Exercise

Characterise some simple exercises that an older person might do to help strengthen musculoskeletal function. These should be low impact. Can some of the exercises be done even if the person is sitting down?

Occupational therapy services can help with coping strategies, or aids and equipment that will make activities of daily living easier and safer to perform. Pacing activities may also be useful when planning daily activities to try to optimise function. Nurses can identify patients who are at risk of developing osteomalacia and support them through diagnosis and treatment. Simple health advice can be important in preventing the onset of osteomalacia and is central to the nursing role.

Recent NICE draft recommendations for consultation (NICE 2013) include additional training and raising awareness of vitamin D deficiency and making supplements containing the recommended amount of vitamin D more widely available.

Conclusion

Vitamin D deficiency is important in the development of osteomalacia, which may not be diagnosed until there is significant demineralisation of the skeleton. Nurses have a unique opportunity to improve awareness of osteomalacia and reduce incidence through health education. Nurses can enhance the multidisciplinary management of patients with osteomalacia through appropriate and timely assessment and referral to multidisciplinary team members. Nurses are also ideally placed to become involved in the early recognition and assessment of patients at risk of developing osteomalacia and can provide important support for the older person with or at risk of developing the condition.

7 Practice profile

Now that you have completed the article you might like to write a practice profile. Guidelines to help you are on page 38. http://rcnpublishing.com/r/nop-practice-profile

References


Department of Health (2012) Vitamin D - Advice on Supplements for At Risk Groups. tinyurl.com/qys5fa (Last accessed: June 16 2014.)


