Vitamin D

Fact Sheet

Multiple Sclerosis Trust

MS

Information | Education | Research | Support

Vitamin D

Date of issue: February 2010
Review date: February 2011

Contents

1. Introduction

For many years, vitamin D has been known to have an important role in maintaining bone structure by controlling the flow of calcium into and out of bones from the blood. In the early 1800s, cod liver oil and the exposure of skin to sunlight were found to be effective treatments for rickets, a severe bone-deforming disease which is seen mostly in children. In 1922, the common element in exposed skin and cod liver oil was identified and named as vitamin D.

In more recent years, studies of vitamin D have broadened. Research has shown that vitamin D has important effects throughout the body. It has been found to serve as a significant regulator of immune system responses. Many of these non-skeletal functions are maximized when vitamin D is present in the blood at levels considerably higher than those found in many populations. These findings, together with studies linking low vitamin D levels to disease, have raised concern that widespread vitamin D deficiency is contributing to a number of serious illnesses [1].

Recent reviews have concluded that there is increasing evidence that vitamin D may influence MS susceptibility and may also be of use for treating MS

itself. However, further research is needed to establish appropriate doses of vitamin D, who is most likely to benefit, and when treatment will be most effective [2, 3].

The Shine on Scotland campaign fronted by schoolboy Ryan McLaughlin has raised interest in the role of vitamin D. In November 2009, the campaign persuaded the Scottish Parliament to provide information about vitamin D to pregnant women, reflecting advice issued by NICE in England and Wales in 2008 [4].

2. Vitamin D

The term 'vitamin D' generally refers to two very similar molecules. Vitamin D3, also known as cholecalciferol, is created by skin cells in response to ultraviolet B light. Vitamin D2, or ergocalciferol, occurs naturally in some mushrooms and yeast.

Neither version has any biological activity in the body. Both must be modified to first generate 25-hydroxyvitamin D (25D). 25D is the main form of vitamin D circulating in the blood. Tests to assess vitamin D status measure levels of 25D in the blood.

A further conversion of 25D takes place to produce the biologically active form 1,25-dihydroxyvitamin D, also known as calcitriol.

3. Sources of vitamin D

Sunlight

The major natural source of vitamin D is exposure of the skin to ultraviolet B wavelengths in sunlight. In a fair skinned person, 20 to 30 minutes of sunlight exposure on the face and forearms at midday repeated two or three times a week is estimated to generate sufficient vitamin D in the summer in the UK. However, there are risks of skin cancer associated with extended exposure to sunlight.

The amount of vitamin D synthesised in the skin is reduced with darker skin pigmentation and in older or obese people. For six months of the year (October to April) the sunlight for most of the UK does not have adequate ultraviolet B rays for vitamin D synthesis [5].

Food

Only a relatively small number of foods contain substantial amounts of vitamin D. Oily fish, including salmon, mackerel and trout contain the highest amounts of vitamin D3. Smaller amounts are found in eggs. Cod liver oil is a rich source of vitamin D3 [5].

Vitamin D2 occurs naturally in some mushrooms (for example shiitake and chanterelle) and yeast. The amount in most vegetables is negligible.

Some foods such as breakfast cereals and margarine have vitamin D added during manufacture.

Supplements

There are two types of vitamin D supplements: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). For a number of reasons, it is generally considered that vitamin D3 is the most effective form for supplements [6].

The best approach for supplementing in people with lower levels of vitamin D has not been established and varies depending on the individual. Short courses of high doses can be used to adjust levels. Prolonged supplementation with very high doses can lead to loss of calcium from the skeleton causing problems such as weakening of bones, high blood pressure and kidney problems. For this reason, high doses of vitamin D are often combined with calcium supplements.

The current recommended daily intake of vitamin D in the UK for people with MS is the same as for the general population [5]:

- 400 IU* (10 micrograms) per day for an adult
- 280 IU (7 micrograms) for children aged 6 months to 3 years
- 340 IU (8.5 micrograms) for infants under 6 months

The Food Standards Agency recommends [7]: Most people should be able to get all the vitamin D they need from their diet and by getting a little sun. However, if you are pregnant or breastfeeding you should take 10 micrograms (0.01 mg) of vitamin D each day.

Older people should also consider taking 10 micrograms (0.01 mg) of vitamin D each day.

You might be particularly short of vitamin D, and so might want to think about taking 10 micrograms (0.01 mg) of vitamin D each day, if you:

- are of Asian origin
- always cover up all your skin when you're outside
- rarely get outdoors
- eat no meat or oily fish

Taking 25 micrograms (0.025 mg, 1000 IU) or less of vitamin D supplements a day is unlikely to cause any harm.

*40 IU (International Unit) is equivalent to 1 microgram (µg) of D2 or D3.

The (England and Wales) National Institute for Health and Clinical Evidence (NICE) [4] recommends that pregnant women "should be informed about the importance for their own and their baby's health of maintaining adequate vitamin D stores during pregnancy and whilst breastfeeding. In order to achieve this, women may choose to take 10 micrograms of vitamin D per day, as found in the Healthy Start multivitamin supplement."
The recommended daily intake provides only sufficient vitamin D to prevent rickets and osteomalacia (a condition similar to rickets seen in adults) and this intake alone will not provide blood levels of 25D now considered sufficient for optimal health. Consequently, there have been calls for national and international agencies to increase dietary recommendations and to increase the amount of vitamin D in supplements [8]. Current clinical trials are investigating the safety of very high doses of vitamin D, up to 40,000 IU/day in people with MS. If you are concerned about your vitamin D levels, speak to your doctor.

4. Vitamin D levels in the general population

Vitamin D status is generally defined by measuring the concentration of 25D in the blood. The following categories for blood levels of 25D have been proposed:

Optimal	greater than 75 nmol/l
Sufficient	50-75 nmol/l
Insufficient	25-50 nmol/l
Deficient	less than 25 nmol/l

Prolonged deficient levels of vitamin D will lead to rickets and other conditions affecting the bones.

Vitamin D insufficiency, although not enough to cause bone disease, is associated with an increased risk of a number of conditions including heart disease, diabetes, cancer and multiple sclerosis. Optimal levels are required to ensure best possible health [1].

A recent survey in the UK showed that more than 50% of the adult population have insufficient levels of vitamin D and that 16% have severe deficiency during winter and spring [9].

Vitamin D deficiency is more likely to develop in the following groups of people:

- Pregnant or breastfeeding women.
- Breastfed babies whose mothers are lacking in vitamin D, or with prolonged breastfeeding. (These babies do not need to stop breastfeeding, they can have breast milk plus vitamin drops).
- People who get very little sunlight on their skin such as those who are stay indoors a lot, or cover up when outside, for example, if wearing a veil.
- People with conditions that affect the way the body handles vitamin D such as coeliac disease, Crohn's disease, and some types of liver and kidney disease.
- People taking certain medicines: carbamezepine, phenytoin, primidone or barbiturates.
- People with dark skins or of South Asian origin, elderly people, and those with a family history of vitamin D deficiency.

5. Vitamin D deficiency as a trigger for MS

The causes of MS still remain a mystery. It is generally agreed that one or more environmental factors cause some people with a particular genetic make up to go on to develop MS. Studies have suggested that environmental factors may act during pregnancy and/or the early years.

The environmental factors have not been identified, but studies have looked at infections like glandular fever (caused by the Epstein Barr virus) or chickenpox. No particular virus or other infection has so far been found consistently linked with MS.

While the evidence to support an involvement of vitamin D as a trigger for MS is still not conclusive, a number of studies have suggested that there may be a connection.

Geographical distribution of MS

Many studies have shown that the prevalence of MS increases with distance from the equator. In the UK, a higher prevalence of MS is found in Scotland than in England [10]. The reverse is seen for blood levels of vitamin D, with higher levels being found in people living closer to the equator and lower levels found with distance from the equator. A north-south gradient has been reported for vitamin D levels in the UK [9]. This has led to the hypothesis that low sunlight exposure and consequent low vitamin D production increases the risk of developing MS for those people with a pre-existing genetic predisposition.

Sun exposure and risk of MS

Past exposure to sunlight, particularly during childhood, has been linked to the risk of developing MS. A study of 79 pairs of identical twins (who therefore have the same genetic makeup), where only one of the twins had MS, found that the twin who developed MS had significantly lower exposure to the sun during childhood, assessed on the basis of nine different activities implying sun exposure [11]. In another study, when a group of people with MS were compared to another group without MS, the risk of MS was found to be lower in those who in their childhood had been exposed to sunlight during their

holidays and weekends, a finding that was confirmed by skin changes indicating cumulative sun exposure [12].

Effect of vitamin D levels on the risk of MS

A review of blood samples taken from US military personnel when they enlisted found that levels of vitamin D in those who subsequently developed MS were lower than levels in those without the condition [13].

Birth month

A number of studies have drawn a connection between vitamin D levels in mothers and subsequent risk of developing MS in their children. Studies have found that more people with MS than would be expected are born in May than in November [14, 15]. In a recent study conducted in Scotland researchers looked at records of 1,300 people with MS born in the west of Scotland between 1922 and 1992. A much higher than expected proportion was born in March, April or May. In contrast, a lower proportion of those born in the autumn, particularly in November went on to develop MS [16]. For children born in April, the later stages of the pregnancy will have coincided with the darkest months of the year. It has been suggested that decreased exposure to the sun during winter pregnancies results in low vitamin D levels which in some way increases the risk of developing MS later in life for children who are genetically susceptible.

Laboratory studies

In laboratory experiments, researchers have demonstrated a direct link between a particular genetic variant and vitamin D which can determine an individual's risk of developing MS. The study found that an important gene implicated in susceptibility to MS, the variant gene HLA-DRB1*1501, can be switched on by vitamin D in laboratory experiments. The study authors suggested that a lack of vitamin D during pregnancy and the early years of life could increase the risk of developing MS later in life [17].

6. Vitamin D for people with MS

Levels of vitamin D in people with MS

Some studies have looked at vitamin D levels in people who already have MS.

- A study of samples from 267 people found that higher levels of vitamin D were associated with a lower relapse rate. Low levels were associated with higher disability scores. People with progressive forms of MS had lower levels than those with relapsing remitting MS [18].
- Another study of 132 people found significantly lower levels of vitamin D in people experiencing a relapse than in people who were in remission [19].
- A study in Tasmania found a high prevalence of vitamin D deficiency in both people with MS and in a matched group without MS; however people with MS with higher disability (EDSS - a disability scale - greater than 3) were more likely to have insufficient levels of vitamin D, perhaps as a result of lower sun exposure [20].

Effect of vitamin D treatment in MS

Despite the accumulating evidence which suggests its importance in MS, there have so far been only a limited number of studies on treatment with vitamin D:

- In a small study, a two year course of treatment with vitamin D (5000 IU/d in the form of cod liver oil) in ten people with MS found a 60% reduction in the predicted number of relapses [21].
- In another small uncontrolled study, 15 people with MS who received 100 IU/d for 48 weeks experienced a 50% reduction in relapses [22].
- High doses of vitamin D3 (cholecalciferol, 14,000 IU/d) over a period of 6-12 months increased blood levels of vitamin D to nearly 400 nmol/l and did not lead to hypercalcaemia (excessively high levels of calcium in the blood) or other significant side effects [23]. After 12 months, a 41% reduction in the number of relapses and a significant improvement in EDSS was reported for the 25 people receiving vitamin D3 compared to the 24 who were untreated [24].

- 39 people were treated with 1000 IU/d vitamin D3 for six months compared to 22 untreated controls. There was a significant increase in certain cytokines, mediators of the immune response [25].

7. Further studies into the role of vitamin D in MS

Research to date has provided circumstantial evidence to support a role for vitamin D in the risk of developing MS as well as for treating MS.

Studies are currently underway or in the planning stages to look more closely at the prevalence of vitamin D deficiency in people with MS, to establish the safety of high doses (up to 40,000 IU/day) of vitamin D in MS and to assess the effects of supplementation on the immune system and on the skeleton.

Further studies are needed to evaluate the role of vitamin D during pregnancy and early years for reducing the risk of children developing MS later in life.

8. References

1. Holick MF. Vitamin D deficiency. New England Journal of Medicine 2007;357:266-281.
2. Pierrot-Deseilligny C. Clinical implications of a possible role of vitamin D in multiple sclerosis. Journal of Neurology 2009;256:1468-1479.
3. Myhr K. Vitamin D treatment in multiple sclerosis. Journal of Neurological Sciences 2009;286:104-108.
4. National Institute for Health and Clinical Experience.Antenatal care: routine care for the health pregnant woman (clinical guideline 62).London:NICE;2008.
5. Pearce SHS, Cheetham TD. Diagnosis and management of vitamin D deficiency. British Medical Journal 2010;340:142-147.
6. Wolpowitz D, Gilchrest BA. The vitamin D questions: how much do you need and how should you get it? Journal of the American Academy of Dermatology 2006;54:301-307.
7. Food Standards Agency. Eat well, be well – Vitamin D [cited 2010 16 Feb] Available from: www.eatwell.gov.uk/healthydiet/nutritionessentials/vitaminsandminerals/vitamind
8. Vieth R et al. The urgent need to recommend an intake of vitamin D that is effective. American Journal of Clinical Nutrition 2007;85;649-650.
9. Hypponen E, Power C. Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors. American Journal of Clinical Nutrition 2007;85:860-868.
10. Compston A et al. McAlpine's multiple sclerosis.4th ed.London:Churchill Livingstone;2006.
11. Islam T et al. Childhood sun exposure influences risk of multiple sclerosis in monozygotic twins. Neurology 2007;69:381-388.
12. Van der Mei IA et al. Past exposure to sun, skin phenotype, and risk of multiple sclerosis: case-control study. British Medical Journal 2003;327:1-6.
13. Munger KL, et al. Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. Journal of the American Medical Association 2006;296:2832-2838.
14. Willer CJ et al. Timing of birth and risk of multiple sclerosis: population based study. British Medical Journal 2005;330:120.
15. Salzer J et al. Season of birth and multiple sclerosis in Sweden. Acta Neurologica Scandinavica 2010:121;20-23.
16. Bayes HK et al. Timing of birth and risk of multiple sclerosis in the Scottish population. European Neurology 2010;63:36-40.
17. Ramagopalan SV et al. Expression of the multiple sclerosis-associated MHC class II Allele HLA-DRB1*1501 is regulated by vitamin D. PLoS Genetics 2009;5(2):e1000369.
18. Smolders J et al. Association of vitamin D metabolite levels with relapse rate and disability in multiple sclerosis. Multiple Sclerosis 2008;14:1220-1224.
19. Correale J et al. Immunomodulatory effects of vitamin D in multiple sclerosis. Brain 2009;132:1146-1160.
20. Van der Mei IA et al. Vitamin D levels in people with multiple sclerosis and community controls in Tasmania, Australia. Journal of Neurology 2007;254:581-590.
21. Goldberg P et al. Multiple sclerosis: decreased relapse rate through dietary supplementation with calcium, magnesium and vitamin D. Medical Hypotheses 1986;21:193-200.
22. Wingerchuck DM et al. A pilot study of oral calcitriol (1,25-dihydroxyvitamin D3) for relapsing-remitting multiple sclerosis. Journal of Neurology Neurosurgery and Psychiatry 2005;76:1294-1296.
23. Kimball SM et al. Safety of vitamin D3 in adults with multiple sclerosis. American Journal of Clinical Nutrition 2007;86:645-651.
24. Burton JM et al. A phase I/II dose-escalation trial of oral vitamin D3 with calcium supplementation in patients with multiple sclerosis. Multiple Sclerosis 2008;14(Suppl 1);S34.
25. Mahon BD et al. Cytokine profile in patients with multiple sclerosis following vitamin D supplementation. Journal of Neuroimmunology 2003;134:128-132.