

Guideline for the Diagnosis and Management of Vitamin D Deficiency

As the symptoms and treatment doses can be different for adults and children, this guideline will separate the two groups.

ADULTS and vitamin D

Measurement: –

There are over 40 identified metabolites of vitamin D. Vitamin D status is best estimated by measurement of serum 25 hydroxyvitamin D.

Measurement of vitamin D can be considered for patients with bone diseases where correcting vitamin D deficiency is appropriate.

Interpretation of results: –

< 30 nmol per litre is deficient,

30 – 50 nmol may be inadequate in some people*,

> 50 nmol is sufficient for almost the whole population.

Note some guidelines also quote >80 as “replete”. This mostly refers to patients with severely impaired bone health where higher levels of vitamin D might be sought.

Deficient vitamin D is associated with osteomalacia and osteoporosis.

For optimal bone health it is important to optimise vitamin D levels.

* For example all pregnant and breastfeeding women, older people over 65 years, people who have little or no exposure to the sun for example the housebound or those covered due to cultural reasons, those with darker skin who require greater intensity of sunlight to synthesise equivalent amounts of vitamin D, those with osteoporosis, those taking anti-epileptic medication, those with raised PTH, those taking oral steroids, those with malabsorption.

Treatment: –

This is with oral vitamin D3 i.e. cholecalciferol.

This is an inactive form. It is activated by being hydroxylated by the liver to become 25 hydroxyvitamin D and then hydroxylated by the kidney to become 1 – 25 dihydroxyvitamin D. Patients with renal failure therefore will not be able to make this final hydroxylation step. Therefore they are given (one) alfacidol and these guidelines are not meant to cover the management or treatment of vitamin D deficiency in renal failure. Similarly activated vitamin D preparations such as alfacalcidol should not be used for the treatment of simple vitamin D deficiency.

Loading Doses & Maintenance doses:-

A loading dose of 280,000 IU or 300,000 IU is recommended. This can be achieved by taking 40,000 IU (i.e. 20,000 x2) each week for seven weeks. This is then followed by the maintenance dose.

The maintenance dose is 800–2000 IU daily. Due to the wide therapeutic window this can be

given as an alternate weekly ie. fortnightly dose comprising 20,000 IU of vitamin D.

Patients who take calcium and vitamin D may therefore obtain sufficient vitamin D for maintenance if their daily intake is 800 IU. A number of products are included on the formulary which would be suitable for use in these circumstances. There are some patients with osteoporosis who continue to have low levels of corrected calcium and Vitamin D despite supplementation. Some of these patients may have hypoparathyroidism. Here additional Vitamin D can be given as an adjunct to specific therapy for osteoporosis.

Monitoring vitamin D status: –

This is generally unnecessary. Occasionally vitamin D3 unmasks primary hyperparathyroidism and measurement of calcium and phosphate (not vitamin D) could be considered one month after commencement of treatment. Similarly measurement might be requested in patients with malabsorption or when poor adherence is suspected. To achieve a steady state of vitamin D, at least three months and preferably six months treatment is required. Therefore re-measuring vitamin D within this time is a waste of resources.

Conversion factors

10 µg of vitamin D = 400IU of vitamin D

At Colchester the laboratory reports the 25 hydroxyvitamin D result in nanomoles per litre. Some American literature refers to nanograms per ml.

2.5 nmol per litre = 1 ng per ml of 25 hydroxyvitamin D. e.g 30 nmol/l = 12 ng/ml

Difference between ergocalciferol and cholecalciferol

Ergocalciferol alias vitamin D2 is derived from plants. Cholecalciferol alias vitamin D3 is derived from animals and is more bioavailable. The laboratory will often quote levels of D2 and D3. If a patient is taking only D3 then the D2 level will naturally be low or undetectable. This does not matter.

All pregnant and breastfeeding women should take a daily supplement containing 10 µg (400 IU vitamin D). This can be purchased over-the-counter or obtained via the healthy start program for patients who qualify.

There is no strong evidence that correcting vitamin D might increase the risk of renal stones. Patients who have osteoporosis and have had calcified kidney stones should avoid combination preparations of calcium and Vitamin D, and instead take Vitamin D alone.

Preparations: –

There are many! In general it is good practice to use licensed preparations, thereby guaranteeing good quality control. Similarly licensed preparations are subject to proper pricing regulation. When prescribing licensed products it should be done at the dose recommended by the SPC. Occasionally the doses show slight variance to the recommended guidelines from authoritative bodies. This reflects the wide therapeutic window of vitamin D and the different doses used during trials. *Named patient liquid specials of vitamin D (unlicensed) for adults in primary care should not be routinely prescribed. There is an*

Author Responsible Dr Paul Byrne*

Consultant Rheumatologist Colchester General Hospital December 2015

Review date December 2017

exorbitant cost of some of these preparations for example up to £500 for 30 ml. If prescribing a liquid form, it is best to prescribe a licensed preparation for example Thorens. Patients may choose to buy vitamin D preparations for maintenance therapy (following initial treatment) over-the-counter, as part of self-care. Such preparations are often cheap, and at the right dose, probably satisfactory.

Vitamin D is an oily subject substance usually contained within a gelatin capsule. The gelatin is derived from beef and this is usually kosher and Halal guaranteed. However Hindus may take objection. Some vitamin D compounds contain peanut oil and are best avoided with a history in patients with a history of peanut allergy.

Adults: –

Fultium D3 - 20,000IU capsules

Loading dose: Two 20,000 IU capsules/ week for 7 weeks then

Maintenance dose: 1x 20,000 IU capsule / fortnight thereafter.

Stexerol D3 tablets

Loading dose: Two 25,000 IU tablets per week for six weeks then

Maintenance dose: One 25,000 IU tablet per month.

Alternatively the maintenance dose can be achieved with the lower strength tablet i.e. Stexerol D3 1000 IU one per day.

Liquid formulations

Thorens

Thorens is licensed both for adults and children. It is a liquid containing a concentration of vitamin D at 10,000 units per mL. It is supplied in larger bottles of 10 mL (i.e 100,000 units total) or smaller bottles of 2.5 mL (i.e 25,000 units total).

The larger bottle comes with a dropper applicator cap. This allows individual drops to be applied directly into the mouth or on food. It tastes of olive oil and so is quite palatable. Each drop contains 200 international units of vitamin D. This is more suitable therefore in the younger paediatric patients, especially those receiving daily doses. Each bottle therefore has enough for 500 drops.

The small bottle is meant for a single dose. It does not come with a dropper applicator cap, and instead can be drunk down in one go or placed on food. Alternatively use of a syringe might facilitate oral administration.

For Adults:-

Loading dose: 50000 IU/week (two single dose bottles/week) for 6-8 weeks followed by

Maintenance dose: 25,000 IU (one single dose bottle) per month.

CHILDREN and vitamin D

Prevention

The Department of Health and the Chief Medical Officer recommend a dose of approximately 300 IU for all children from six months to 5 years of age. This is the dose that the NHS healthy start vitamin drops provide. The Healthy Start Programme aims to provide vitamins free to people on income support. The British Paediatric and Adolescent Bone Group recommends that exclusively breastfed infants receive vitamin D supplements from soon after birth.

Adverse effects of vitamin D overdose are rare but care should be taken with multivitamin preparations as vitamin A toxicity is a concern. Multivitamin preparations often contain a surprisingly low dose of vitamin D.

In paediatric patients RCPCH guidance suggests testing those patients with risk factors and symptoms of Vitamin D deficiency.

Symptoms in children are age dependent

Age	Symptoms
Infants	Seizures, tetany, cardiomyopathy
Children	Myopathy leading to delayed motor development, poor growth, rickets, muscle weakness, aches and pains
Adolescents	Aches and pains ,muscle weakness

Children who have had treatment for deficiency with symptoms, should then be maintained on a prevention dose until their growth is complete.

Children with risk factors and no symptoms, can be given lifestyle advice AND prevention doses of Vitamin D

Risk factors in paediatric patients

Increased need	< 1 year, twins/triplets etc, adolescents, obesity
Reduced sun exposure	Immobility e.g. children with cerebral palsy, excessive use of sun block
Limited diet	Prolonged breastfeeding, exclusion diets, malabsorption, liver disease, renal disease, drugs (e.g. anticonvulsants)

Interpretation of results

* In paediatric patients (up to 18 years of age)

< 25nmol/l is defined as deficiency

25-50 is defined as insufficiency

Paediatric Dosages

Thorens

This is a liquid preparation and as above is provided at a concentration of 10,000 IU per ml, provided as either a single dose bottle of 2.5 ml i.e. 25,000 IU total or a 10 ml dropper bottle.

Use of the bottles

Loading dose alias “treatment of deficiency” 0-18 years 25,000 IU (1 bottle) once every 2 weeks for 6 weeks

Maintenance dose : alias “prevention of deficiency”

0-1 years 25,000 IU (1 single dose bottle) every 8 weeks

1-18 years 25,000 IU (1 single dose bottle) every 6 weeks

An alternative maintenance therapy of 1,000 IU/day can be achieved by **Stexerol D3** 1000 IU /day which is licensed for those 12 years and older

Use of the dropper bottles

1 drop contains 200 IU cholecalciferol (vitamin D₃)

Loading dose alias “treatment of deficiency”

0-18 years 2000 IU/day (10 drops) for 6 weeks, followed by

Maintenance dose: alias “prevention of deficiency”

0-1 years 400 IU/day (2 drops)

1-18 years 600 IU/day (3 drops)

NB doses of up to 1000 IU/day (5 drops) may be required to prevent deficiency in some children

Non pharmacological Treatment

Only a few natural foods such as oily fish and eggs (20 – 40 IU per egg) contain significant amounts of vitamin D. All formula milks are fortified but plain cows milk is not fortified in the UK. Breast milk generally contains little vitamin D. Sunshine is the main source allowing the skin to synthesise vitamin D. There is only sufficient intensity in sunlight for six – eight months of the year to synthesise any vitamin D. Levels in the serum in the summer are inevitably higher than levels in the winter. The time required by the skin to make sufficient vitamin D varies according to intensity of sunlight and darkness of the skin but it is typically short often around 15 minutes, less than the amount of time needed for skin to redden and burn. Therefore enjoying the sun safely enables appropriate levels of vitamin D without increasing the risk of skin cancer.

Reference:- National Osteoporosis Society Guidelines Vitamin D and Bone Health: a Practical Clinical Guideline Patient Management 2013

Reference: – guide for vitamin D in childhood Royal College of Paediatrics and Child Health October 2013

Author Responsible Dr Paul Byrne*

Consultant Rheumatologist Colchester General Hospital December 2015

Review date December 2017

Acknowledgements

Special thanks to Carol Sampson, Sheila Baldwin, Vicky Saliba, Charles Bodmer, Ravi Menon, Nicola Cackett, Andrea Turner Catherine Speed, for their help with preparation.