

Guidelines for Prevention, Investigation and Treatment of Vitamin D Deficiency and Insufficiency in Children

Contents

Gu	idanc	ce algorithm for the Treatment of Vitamin D Deficiency and Insufficiency - Childrens Pathway	2			
1.	1. Background					
2.	Ide	ntification of vitamin D deficiency in children and infants	3			
	2.1.	Who to test for vitamin D deficiency	3			
	2.2.	Indications for testing Vitamin D status	3			
	2.3.	How to assess vitamin D status	3			
3. Treatment of vitamin D deficiency in children and infants						
	3.1.	Rapid correction dose	4			
	3.2.	Monitoring and follow up post rapid correction	5			
	3.3.	Routine correction of insufficiency and maintenance	5			
	3.4.	Assess need for calcium supplementation (3)	6			
4.	Тох	xicity	6			
Appendix 1 – Prevention of Vitamin D Deficiency						
Dietary sources of Vitamin D						
	Safe Sun exposure					
	Suppl	pplementation for prevention of deficiency				
Re	feren	ces	8			

Guidance for the Treatment of Vitamin D Deficiency and Insufficiency CHILDRENS PATHWAY

Routine testing of plasma 25-hydroxyvitamin(OH)D levels is not recommended for infants and children. Testing should be restricted to children and young people with a clear indication for testing vitamin D status



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1. Background

Vitamin D is a fat-soluble vitamin that regulates calcium and phosphate homeostasis, and is vital to allow for the rapid growth of infants and young children and for healthy skeletal development through childhood. (1) Nutritional vitamin D deficiency can health to health problems in children including rickets, impaired growth, muscle weakness, cardiomyopathy and seizures due to hypocalcaemia. (2)

2. Identification of vitamin D deficiency in children and infants

2.1. Who to test for vitamin D deficiency

Low levels of vitamin D are common in the UK, especially in winter. It is important to consider whether the child's symptoms or signs could be related to vitamin D deficiency before requesting measurement of vitamin D. (1)

Routine screening and measurement of Vitamin D status is not recommended (1)

2.2. Indications for testing Vitamin D status

- 1. Symptoms and signs of rickets
 - progressive bowing of legs (bowing of legs can be a normal finding in toddlers)
 - progressive knock knees
 - rachitic rosary (swelling of the costochondral junctions)
- 2. Other symptoms or conditions associated with vitamin D deficiency:
 - long-standing (> three months), unexplained bone pain
 - muscular weakness (e.g. difficulty climbing stairs, waddling gait, difficulty rising from a chair or delayed walking)

- wrist swelling
- craniotabes (skull softening with frontal bossing and delayed fontanelle closure)
- delayed tooth eruption and enamel hypoplasia
- tetany due to low plasma calcium
- seizures due to low plasma calcium (usually in infancy)
- infantile cardiomyopathy.

- 3. Abnormal investigations:
 - low plasma calcium or phosphate, high alkaline phosphatase (greater than the local age-appropriate reference range)
 - radiographs showing osteopenia, rickets or pathological fractures revealed by radiographs.
- 4. Chronic disease that may increase risk of vitamin D deficiency:
 - chronic renal disease, chronic liver disease
 - malabsorption syndromes (e.g. coeliac disease, Crohn's disease, cystic fibrosis).
- 5. Treatment with bone-targeted drugs that require vitamin D sufficiency, such as bisphosphonates.

2.3. How to assess vitamin D status

Measurement of plasma 25-hydroxyvitamin D (24(OH)D) is the best way to assess vitamin D status. There is no universal consensus on the biochemical definition of vitamin D deficiency. Current paediatric practice is to use a threshold of plasma 25(OH)D ,25nmol/l to define vitamin D deficiency. This is based on symptomatic vitamin D deficiency in children (e.g., rickets, hypocalcaemia) only usually occurring with a plasma 24(OH)D level below 25nmol/l. (1) Seasonal variation is observed with vitamin D levels with values being higher at the end of summer and lower in winter due to changes in levels of UVB exposure.

- Plasma 25(OH)D < 25nmol/l is **deficient.**
- Plasma 25(OH)D 25-50noml/l may be inadequate in some people.
- Plasma 25(OH)D >50nmol/l is sufficient for almost the whole population.

3. Treatment of vitamin D deficiency in children and infants

The Royal Osteoporosis Society (ROS) recommends that oral vitamin D3 (colecalciferol) is the treatment of choice in vitamin D deficiency (1).

There is no place for the use of 1α hydroxylate preparation (e.g. alfacalcidol or calcitriol) in the routine management of vitamin D deficiency. Their use is limited to treating significant hypocalcaemia, disorders of malasorption, renal disease, liver disease, and rare diseases of calcium and phosphate regulation. (1)

3.1. Rapid correction dose

If children are symptomatic of vitamin D deficiency, and biochemical tests have confirmed deficiency rapid correction is advised (3), followed by maintenance vitamin D therapy starting 1 month after rapid loading completed if advice to increase exposure to sunlight is not possible or insufficient.

Vitamin D is a fat-soluble vitamin, and when deficiency has been identified, this means that stores have been depleted. The purpose of the rapid correction dose is to replenish the vitamin D stores in the liver, so that maintenance doses can be lower to maintain effective calcium (and magnesium) homeostasis.

For all age ranges the British National Formualry for Children (BNFC) states that loading doseing may be given daily, or the equivalent dose given intermittently e.g. weekly or fortnightly. Recommended treatment doses (loading doses) for correction of Vitamin D deficiency from ROS (1) PrescQIPP (4) and BNFC (5) are:

Infant 1-5 months of age:	3,000units daily for 8-12 weeks
Child 6 months to 11 years of age:	6,000units daily for 8-12 weeks
Child 12-17 years of age:	10,000units daily for 8-12 weeks (A single or dividing loading dose totalling 300,000units can be considered if there are concerns about compliance)

Vitamin D rapid correction courses should be prescribed as a whole course acute prescription

Weekly Dosing								
Liquid - Colecalciferol 25,000units/1ml oral solution 1ml ampoule (InVita D3 1ml ampoule)								
Age	Dose	Course length	Total dose (units)					
Below 6 months	25,000units (1x25,000unit ampoule) as a single dose once a week	7 weeks	175000					
6 months-11 years	50,000units (2x25,000unit ampoule) as a single dose once a week	7 weeks	350000					
12 years-18 years	75,000units (3x25,000unit ampoule) as a single dose once a week	8 weeks	600000					
Solid dose - Over 12 years old treatment by solid dose is the preferred option.								
6 years-11 years	50,000unit capsule as a single dose once a week*	7 weeks	350000					
12 years-18 years	50,000unit capsule as a single dose once a week*	12 weeks	600000					
Daily Dosing								
Colecalciferol 10,000units/ml oral drops (Thorens 10,000/ml oral drops - 50 drops/ml)								
Age	Dose	Course	Total dose					
		length	(units)					
Below 6 months	3,000units daily (15 drops)	8 weeks	168000					
6 months-11 years	6,000units daily (30 drops)	8 weeks	336000					
12-18 years old –	10,000units daily (1ml, 50 drops)	8 weeks	560000					
liquid preparation								
Solid dose - Over 12 years old treatment by solid dose is the preferred option								
6 years – 11 years	4000unit tablet daily	12 weeks	336000					
12 years-18 years	2 x 4000unit tablets daily	10 weeks	560000					

* 2 x 25,000unit colecalciferol tablets weekly may be given in acute trusts in place of 50,000unit capsules with the whole course provided to the patient by the acute trust.

InVita D3 1ml ampoule, Thorens 10,000/ml oral drops are suitable for vegetarians and those following Halal or Kosher diets. See the Specialist Pharmacy Service advice on <u>Choosing an oral vitamin D preparation for vegetarians</u> or vegans for advice on suitable solid dose products (6)

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3.2. Monitoring and follow up post rapid correction

Bone profile and vitamin D tests (with PTH if patient has rickets or hypocalcaemia) should be repeated at the end of a rapid correction course of treatment. (1)

If the 25(OH)D level is >50nmol/ml and bone profile is normal:

• Advice multivitamin supplement containing 400-600units per day. Continue unless there is a significant lifestyle change to improve vitamin D status.

If 25(OH)D is below 50nmol/ml:

- Consider poor compliance, drug interactions and underlying disease such as renal disease, liver disease and malabsorption.
- Specialist advice should be sought for children with malabsorption or reduced storage capacity (e.g., liver disease)
- If poor compliance is suspected a high dose treatment may be considered if the patient is aged 12-18 years (e.g. 300,000units as a single or divided dose) (1) (5)

If a child's symptoms/signs have not improved despite a satisfactory 25(OH)D concentration, they are unlikely to be related to vitamin D deficiency and other causes should be investigated. (1)

3.3. Routine correction of insufficiency and maintenance

If correction of vitamin D insufficiency is needed, or after completion of rapid correction regime above, advise on the need for long term maintenance via supplements. (3) (4) Advise that supplements should be purchased (3) unless patient meets one of the nationally defined exception criteria:

3.3.1 Nationally defined exceptions:

- Medically diagnosed deficiency, including those patients who may have a lifelong or chronic condition or have undergone surgery that results in malabsorption. Continuing need should be reviewed on a regular basis.
- To treat side effects of a prescription medicine i.e., patients on long-term primidone, carbamazepine, phenytoin, phenobarbitone and sodium valproate (MHRA recommendation)
- Patients who prescriber considers cannot treat themselves, for example with learning disabilities, severe social vulnerability or mental health problems.
- Patients who have undergone 2 or more rapid treatment courses
- Patients suitable to receive Healthy Start vitamins accessed via Healthy start route (7)

Child 1 month to 11 years of age:	400-600units daily, maintenance to be started one month after loading dose completed, or if correction of vitamin D deficiency is less urgent, maintenance may be started without the use of loading doses.
	Some infants and children under 4 years of age may be eligible for free vitamins via the <u>Healthy Start Scheme</u>
Child 12 years to 17 years of age:	400-600units daily, maintenance dosing may be given daily, or the equivalent dose given intermittently. Maintenance to be started one month after loading dose completed, or if correction of vitamin D deficiency is less urgent, maintenance may be started without the use of loading doses. Higher maintenance doses may be necessary in those at high risk of vitamin D deficiency; maximum 4000units per day.

3.4. Assess need for calcium supplementation (3)

All children who require supplementation with vitamin D should have their dietary calcium intake assessed. Consider using an online calcium calculator, such as the UK Centre for Genomic and Experimental Medicine (CGEM) calcium calculator.

The recommended daily calcium intake for children to prevent rickets is:

- Birth to 6 months: 200mg/day
- 6-12 months: 260mg/day •
- Over 12 months: more than 500mg a day

If calcium intake is sufficient vitamin D alone should be supplemented as per clinical indications described in sections 4.2 and 4.3.

If the child has an inadequate calcium intake, advise parents/carers to increase dietary calcium intake.

- The British Dietetic Association (BDA) Calcium: food fact sheet may be helpful.
- The Royal Osteoporosis Society (ROS) Calcium-rich food chooser may be helpful.

If the child is unable or unwilling to increase dietary calcium intake, consider the need for calcium supplements. Seek specialist advice if there is any uncertainty regarding which calcium preparation to recommend. See NICE CKS on Available preparations for more information. The ROS leaflet Calcium includes a factsheet on calcium supplements and tests that may be helpful.

Note: combination calcium and vitamin D preparations (such as Calcichew D3[®]) are *not* recommended for people needing high-dose vitamin D treatment, as they contain very low levels of vitamin D (200–400units per tablet) and may increase the risk of hypercalcaemia. See the CKS topic on Hypercalcaemia for more information.

4. Toxicity

Vitamin D toxicity is defined as hypercalcaemia with a 25(OH)D >250nmol/l with hypercalciuria and supressed PTH. (8) There is no widespread agreement on the threshold concentration or amount of vitamin D that results in toxicity. Acute vitamin D intoxication is rare and usually results from vitamin D doses much higher than 10,000 units per day. (1)

Caution is required in children or young people with a granulomatous disease (e.g., tuberculosis or sarcoidosis) (1)

Infants under 12 months should not have more than 25micrograms (1,000units) vitamin D a day (other than for rapid correction).

Children aged 1-10 years should not have more than 50micrograms (2,000units) vitamin D a day (other than for rapid correction).

Appendix 1 – Prevention of Vitamin D Deficiency

Dietary sources of Vitamin D

Dietary sources of vitamin D are limited and only 10-20-% of vitamin D is derived from dietary sources, with oily fish being the only significant source. Small amounts are provided by egg yolk, red meat and fortified foods. The major natural source (80-90%) is from skin synthesis following exposure to sunlight (9). However, in the UK from October to the beginning of April there is no ambient ultraviolet sunlight of the appropriate wavelength for skin synthesis of vitamin D. During this time, the population relies on both body stores from sun exposure in the summer, dietary sources or supplementation to maintain vitamin D status.

Safe Sun exposure

In the UK between April to September recommended children spend short periods outside around midday, exposing minimum of face/hands/forearms WITHOUT sunscreen. The time should be less than the time taken to redden or burn (in Caucasian children approx. 10-15 minutes but the exact time will depend on skin pigmentation, pollution, age). If children have sun-sensitive conditions or are using medication which may predispose this, exposure should be restricted as per dermatologist advice. (10)

You cannot overdose on vitamin D through exposure to sunlight. Parents and carers should be reminded to ensure infants, children and young people cover up or protect their skin with sun cream if out in the sun for long periods to reduce the risk of skin damage and skin cancer. (11)

Between October and early March in the UK we do not get enough vitamin D from sunlight and it is difficult to get the recommended daily intake from diet alone, so supplementation is advised.

Supplementation for prevention of deficiency

The government recommends all children aged 6 months to 5 years are given vitamin supplements containing vitamins A, C and D every day. Recommended for Vitamin D supplementation is: (3) (11) (12)

- All babies from birth to 1 year of age should consume 8.5-10micrograms (340-400units) vitamin D per day.
- Babies receiving infant formula do not require additional supplements if they are receiving more than 500mls of formula per day (as infant formula is already fortified with vitamin D).
- Children aged 1-4 should be given a daily supplement containing 10micrograms (400units) vitamin D per day throughout the year.
- A supplement containing 10micrograms (400units) vitamin D per day should be considered for children aged 4-11 years of age during autumn and winter.
- Children over 4 years of age should take a supplement containing 10micrograms (400units) Vitamin D all year round if they:
 - \circ $\;$ Usually wear clothes that cover up most of their skin when outdoors.
 - Are not often outdoors.
- A supplement containing 10micrograms (400units) vitamin D should also be considered throughout the year for children with dark skin for example Africa, African-Caribbean or south Asian backgrounds as not enough vitamin D may be made from sunlight exposure.
- Young people aged 12-17 years should take a supplement containing 10-25micrograms (400-1000units) vitamin D per day.

Children aged 1-4 who qualify for the <u>Health Start Scheme</u> can get free supplements containing vitamin D. For other children supplements or drops containing vitamin D can be purchased at most supermarkets and pharmacies.

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