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Should we use weight-based vitamin D treatment in children?

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What is known on the subject:

- Vitamin D deficiency is a perennial problem in the UK in children
- Treatment of vitamin D deficiency is generally safe

What this study adds:

- Children under 18 months may be at risk of hypervitaminosis D (>240nmol/L) on current treatment guidelines
- Dose of vitamin D per kg body weight over a treatment course may need to be considered in this age group

INTRODUCTION

Vitamin D deficiency (VDD) is a perennial problem in the UK.

The Royal Osteoporosis Society (ROS) guideline for treatment of VDD, defined as 25-hydroxyvitamin D (25-OHD) <25 nmol/L, is:[1]

- 1 to 5 months - 3000 international units (IU) daily for 8-12 weeks
- 6 months to 11 years - 6000 IU/day for 8-12 weeks
- ≥12 years – 10,000 IU/day for 8-12 weeks
- Alternative ≥12 years - 300,000 IU total in single or divided dose

This is supported by the British Society of Paediatric Endocrinology and Diabetes and the RCPCH vitamin D resource page.

We planned to determine whether treatment resulted in an increase in serum 25-OHD to over 50 nmol/l and how this related to dose/kg.

METHODS

A retrospective review of consecutive patient records referred to our paediatric bone disease service between November 2010 and June 2012 with a diagnosis of VDD. Dosing guidelines equated to ROS[1].

Inclusion criteria:

- Vitamin D deficiency (<25nmol/L)
- Treatment with colecalciferol

Exclusion criteria:

- Lack of pre- and post-treatment 25-OHD levels.
- Treatment dose and duration unavailable
- Underlying bone disease unrelated to VDD

During the study period, children were referred routinely with 25OHD <25nmol to our service and pre/post 25OHD levels taken. We calculated total and per kilogram vitamin D exposure based on treatment dose and duration and measured serum 25-OHD by liquid chromatography mass spectrometry.

RESULTS

Of 66 patients referred over the study period, 37 were excluded; two on ergocalciferol, four with pre-treatment 25-OHD >25nmol/L and 31 without post-treatment levels.

In the remaining 29, dosing was concordant with guidelines , but duration was shorter (median 6, range 4-12 weeks). Total dose/kg (r^2=0.479, p= <0.0001) and increase in 25-OHD (r^2=0.142, p=0.03) were both highest at younger ages, decreasing with increasing age (Figure 1). Post-treatment change in 25-OHD was significantly associated with total dose/kg (r^2=0.195, p=0.01).

There were no adverse effects of treatment. Five children, under 18 months age, increased their 25-OHD to >200nmol/l.. Their post 25OHD levels were 215, 218, 303, 318, and 341 nmol/l with total course vitamin D 11250, 31401, 20869, 28437, and 23119 units/kg , respectively.

DISCUSSION

We demonstrated that treatment for VDD was generally effective. A small proportion of cases (5/29) had a rise in serum 25OHD to greater than 200 nmol/L; 3/5 over the toxicity threshold (250 nmol/L). These patients were under 18 months' age. None developed hypercalcaemia.

Table 1. Range of Vitamin D deficiency treatment guidelines at different ages. Max dose per kg calculated using 50th centile weight at bottom of age range. Minimum dose per kg calculated using 50th centile weight at top of

age range. Weights used- birth 3.6kg, 1 month 4.4kg, 3 month 6.3 kg, 6 month 7.7kg, 1 year 9.6kg, 2 year 12kg, 12 year 38kg, 18 year 67kg.

Age	Guideline	Daily Dose (international units)	Duration (weeks)	Total course dose/kg MIN	Total course dose/kg MAX
0-1 month	**ROS[1]**	**N/A**	**N/A**	**N/A**	**N/A**
	Misra[2]	1000	8 to 12	12,727	23,333
	Melbourne[3]	1000	12	19,090	23,333
	Munns[4]	2000	12	38,182	50,909
1-3 month	**ROS**	**3000**	**8 to 12**	**26,667**	**57,272**
	Misra	1000-5000	8 to 12	8,889	95,455
	Melbourne	1000	12	13,333	19,091
	Munns	2000	12	26,667	38,182
3-6 month	**ROS**	**3000**	**8 to 12**	**21,818**	**40,000**
	Misra	1000-5000	8 to 12	7,272	66,667
	Melbourne	1000	12	10,909	13,333
	Munns	2000	12	21,818	26,666
6-12 month	**ROS**	**6000**	**8 to 12**	**35,000**	**65,455**
	Misra	1000-5000	8 to 12	5,833	54,545
	Melbourne	1000	12	8,750	10,909
	Munns	2000	12	17,500	21,818
1-2 year	**ROS**	**6000**	**8 to 12**	**28,000**	**52,500**
	Misra	>5000	8 to 12	23,333	>43,750
	Melbourne	3000-4000	12	21,000	35,000
	Munns	3000-6000	12	21,000	52,500
2-12 year	**ROS**	**6000**	**8 to 12**	**8,842**	**42,000**
	Misra	>5000	8 to 12	7,368	>35,050
	Melbourne	3000-4000	12	6,631	28,000
	Munns	3000-6000	12	6,631	42,000
12-18years	**ROS**	**10000**	**8 to 12**	**8,358**	**22,105**
	Misra	>5000	8 to 12	4,179	>11,052
	Melbourne	3000-4000	12	3,761	8,842
	Munns	6000	12	7,522	13,263

2/29 of patients did not increase 25-OHD levels to > 50 nmol/L, however compliance with treatment was not assessed.

Numerous guidelines provide higher total course dose/kg at lower ages (Table 1). There seems to be an increased risk of raising serum 25-OHD to greater than 200 nmol/L with total doses higher than 20000 units/kg. We recognise this opportunistic retrospective study has limitations including possible selection bias with 31/66 not having post 25-OHD levels, and data lacking on calcium intake, parathyroid hormone levels and liver function. However, it may be important to consider total dose/kg, with a reduced daily dose or shorter duration of treatment, when prescribing colecalciferol to children aged less than 18 months.

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