



Stoss Therapy (Single High-Dose Cholecalciferol) in Childhood Vitamin D Deficiency



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Introduction

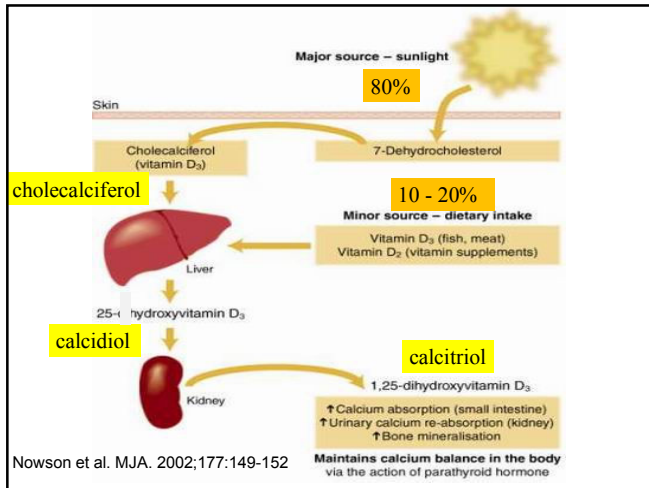
- Vitamin D - Multiple roles:
 - Bone health
 - Immune function
 - Cardiovascular disease
 - Cancer
 - Type 2 diabetes
- Vitamin D deficiency causes significant morbidity and mortality

Prevalence D-deficiency

- Vitamin D deficiency in Australia
(25(OH)-D level <50nmol/L)
 - 80% dark skinned, veiled woman during pregnancy (*Grover Et al*)
 - 76% elderly people in institutions (*Nowson Et al*)
 - 23% – 43% younger adults (*MacGrath Et al & Pascoe Et al*)
- New Zealand Children Aged 5 -14 y
(*Rockell Et al. J Nutr. 2005;135:2602-2608.*)
 - 4% <17.5 nmol/L
 - 31% <37.5 nmol/L
 - >31% of NZ school children are Vitamin D deficient
- These figures mirror those across the world

Vitamin D

- 80-90% from sunlight
 - Recommendations for limited sun exposure
 - Lifestyle changes
- 10-20% from diet



Vitamin D deficiency

- Defined by 25-Hydroxy Vitamin D level < 50 nmol/L
- Recent literature suggests deficient if 25(OH)-D < 80 - 90 nmol/L
(Heaney Et.al, J Am Coll Nutr, 2003, 22:142-146)

Vitamin D Deficiency in Children and its Management: Review of Current Knowledge and Recommendations

(Misra, et al. *Pediatrics*. 2008;122(2):398-417.)

- **Treatment: 1,000 – 5,000IU daily for 1 month, then 400IU maintenance daily**
- BUT Poor compliance with daily dosing common
- **Alternative = STOSS THERAPY**

Aim

Determine safety and efficacy of stoss therapy

SCH STOSS therapy protocol

- **Bloods:**
 - Vitamin D Bloods: 25(OH) Vitamin D, Ca, PO₄, Albumin, ALP, PTH
 - FBC, Iron studies (Fe deficiency associated with Vit D deficiency)
- **X-ray:**
 - Knee for radiological evidence
(presence of two big metaphases makes it more sensitive for detection of radiological rickets)

SCH STOSS therapy protocol

- **STOSS therapy:** Calciferol Strong 50,000IU (1.25mg)
 - Age <3 years 150,000IU 3 tablets
 - Age 3-12 years 300,000IU 6 tablets
 - Age >12 years 600,000IU 12 tablets
- Ensure Dietary Calcium adequate:
 - On going supplementation:
 - Caltrate Plus (600mg elemental Ca + 200IU cholecalciferol)
 - <8 years = 1 tablet daily, >8 years = 2 tablets daily
 - Pentavite - infants (1 drop = 333IU)

SCH STOSS therapy protocol

- **4 weeks post treatment:**
 - Repeat Vitamin D bloods
 - If 25 (OH) Vit D, PTH and ALP normalised – repeat Vit D bloods in **6 months**
 - If **not** normalised – **repeat STOSS Therapy**, with repeat bloods in **4 weeks**.
- **6 months post treatment:**
 - Repeat Vitamin D bloods **6 monthly basis**
 - Repeat X-ray knee if rickets on initial X-ray

Methods

- Reviewed Medical Records of children with Vitamin D deficiency treated with STOSS from Jan 2006 – May 2008
- Children with malabsorption excluded

Results

- 40 Children (25 male) - median age 3.7 yrs (range 0.1 – 17.5yrs)
 - 55% darker pigmented skin
 - 15% on anticonvulsants
 - 37.5% on glucocorticoids

Results

- Presentation
 - 25/40 asymptomatic – screened – chronic disease
 - 4/40 FHx Vitamin D deficiency
 - 1/40 incidental finding rickets on CXR
 - 4/40 investigation raised ALP or low Ca
 - 5/40 symptomatic (3/40 fracture, 2/40 seizure)
 - (younger, lower 25(OH)-D, lower Ca, higher ALP and higher PTH – see table)

	SYMPTOMATIC n=5	ASSYMPTOMATIC n=35
AGE (yrs) (p=0.002)	0.8 (0.2 - 0.9)	6.5 (0.1 – 17.5)
25(OH) D (nmol/L) (p=0.008)	0 (0 -14)	29 (0-49)
ALP (U/L) (p=0.006)	689 (459 – 1262)	247 (64 – 1341)
Cr Calcium (mmol/L) (p=0.009)	1.94 (1.57 – 2.31)	2.38 (1.51 – 2.64)
PTH (pmol/L) (p=0.006)	23.4 (7.6 – 56.3)	4.0 (0.4 – 56.3)

Post Stoss therapy

- Median increase in 25(OH)-D level **70.5 nmol/L** (range 14 – 319)
 - Single dose corrected **87.5%** “normal range”

	Pre-Treatment	Post-Treatment
25(OH)Vit-D (nmol/L)	26.5 (0-49)	93 (24-319)
Cr Calcium (mmol/L)	2.35 (1.51 – 2.64)	2.4 (2.26-2.71)
PTH (pmol/L)	4.4 (0.4 – 56.3)	4.0 (0.7 – 8.2)
ALP (U/L)	273.5 (64-1341)	274 (55-817)

Post Stoss therapy

- **12.5%** required second dose
 - Lower baseline 25(OH)-D
 - Higher ALP
 - Higher PTH

single vs multiple doses		
	Single dose (n=35)	Multiple dose (n=5)
Age (yrs) p = 0.08	6.5 (0.1 - 17.5)	1.4 (0.8 – 4.1)
25(OH)-D pre (nmol/L) p = 0.016	29 (0-49)	0 (0-22)
ALP pre (U/L) p = 0.012	247 (64 – 1310)	924 (267 – 1341)
Cr Ca pre (mmol/L)	2.37 (1.61 – 2.64)	2.13 (1.51 – 2.52)
PTH pre (pmol/L) p = 0.06	4.3 (0.4 – 56.3)	25 (3.1 – 56.3)

Results - Safety

- **No** Side Effects Documented
- **No** Hypercalcaemia
- 2 neonates - **supra-physiological levels** 25(OH)-D 319 and 269nmol/L
 - normal corrected Ca levels and asymptomatic
- Recommended **decreased dose** 25(OH) Vit D in **<3 months → 100,000IU**
- Life savers levels >250 nmol/L without intoxication (Misera Et al)

Results – Long Term Follow Up

- 11/40 data present
- **7.5 months** (3-25 months) Post Stoss →
25(OH)-D level **48 nmol/L** (25 – 94nmol/L)
- **55%** Vitamin D deficient
- Maintenance therapy recommended – could not verify taken

Results – x-ray's

- 27/40 had imaging
 - 9/40 radiological rickets
 - **Younger age** 1.4yrs (0.2 – 2.4yrs)
 - 8/9 had **undetectable 25(OH)-D** levels
 - 9/9 had **raised ALP** 768U/L (1341-457)
 - 9/9 had **raised PTH** 25pmol/L (7.6-56.3)
 - 8/9 had **decreased Cr Ca** for age

Future

Randomised Control Trial:

- Compare daily Vitamin D to Stoss therapy
- Determine optimal timing - monitoring (25(OH)vit-D) and re-treatment

Conclusion

- Age based protocol
 - single high dose oral Cholecalciferol (Vitamin D3) is:

simple, safe and effective
- Stoss therapy allows:
 - rapid treatment
 - addresses issue poor compliance

ACKNOWLEDGMENTS

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Dr Kristen Neville

Dr Jan Walker

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Excessive Vitamin D

- Maximum RDI

- 0-12 mths 25mcg = 1000IU
- 1-8 yrs 50mcg = 2000IU
- 9-50 yrs 50mcg = 2000IU

Daily reference intake reports of the food and nutrition board, institute of medicine. July 24th 2007.

- Can get intoxication with symptoms of

- » Hypercalcinuria – renal stones
- » Confusion
- » Polyuria
- » Polydipsia
- » Anorexia
- » Vomiting
- » Muscle weakness
- » Bone demineralisation with pain