352 A new water-soluble oral vitamin E formulation in cystic fibrosis (CF) children

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Objectives: To investigate efficacy and safety of long-term daily oral administration of a water-soluble new chemical entity of vitamin E (vE)-tocofersolan (d-α-tocopherol-polyethyleneglycol-1000) in pediatric CF patients.
Methods: A multicentre open-label study. Patients were supplemented with vE at a mean (SD) dose of 10.4 (4.3) mg/kg/d and switched to tocofersolan at a dose of 6.7 mg/kg/d (d-α-tocopherol being 1.5 times more potent). Efficacy was monitored by tocopherolemia (T), ratio of vE/lipids (T/L) at baseline, months 3 and 6. Safety analysis combined adverse events (AE), vital signs, laboratory data.
Results: 32 children were included (18 M, 14 F, median age: 65.7 months) and 29 completed the study. Compliance was excellent. At 3 and 6 months, T, T/L did not change significantly from baseline (under liposoluble or water-miscible preparations of dl-alpha-tocopherol) and remained within respective normal ranges (12–35 μmol/L and >0.6 mg/g). Five serious AE (SAE) were recorded (bronchitis (2), hypotrophy, moderate hair loss, behaviour disorders). The relationship between tocofersolan and hair loss, which completely recovered after cessation of the drug, is unknown, yet all other SAE were unrelated to the study drug.
Conclusion: Efficacy of tocofersolan was consistently maintained over time with normal indices of T. This is in accordance with pharmacokinetics in CF demonstrating similar oral absorption of water-miscible **vE** and tocofersolan (Jacquemin E. et al., J Clin Pharm & Ther 2009). Tocofersolan was well tolerated and represents a liquid preparation of vE adapted to younger CF patients, with growing interest due to generalisation of neonatal screening.

353 Vitamin D status in Stockholm cystic fibrosis patients in 2007–2009

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Background: Majority of cystic fibrosis (CF) patients are vitamin D insufficient. No evidence of benefit or harm of vitamin D supplementation exists in the CF population. Intervention trials are necessary, which require baseline data on vitamin D status at the respective latitude.
Objective: To assess the vitamin D status in all CF patients living in Stockholm region (n = 133; 59° 20′ North latitude), its development over 2007–2009 and seasonal variation.
Methods: Descriptive statistics, independent t-test and univariate linear regression were used to determine and compare serum 25-hydroxyvitamin D (s25OHD) levels, seasonal variation (summer: May-Oct; winter: Nov-Apr) and vitamin D insufficiency (s25OHD <75 nmol/L) prevalence.
Results: Over the years 2007–2009, the number of measurements of s25OHD increased, whereas mean measured s25OHD remained stable (52.5; 52.7 and 51.3 nmol/L). Each year, 78–80% measured values were below the lower sufficiency level. In 2009, more measurements were done in winter (61.5 vs. 44.6 and 44.1%; $p = 0.017$ and $p = 0.009$). Mean s25OHD from measurements done in summer (n = 150; 60.2 nmol/L) was higher than those from winter (n = 157; 44.3 nmol/L), $p < 0.001$. Vitamin D insufficiency prevalence was lower during summer season (68.0% vs. 89.8%; $p < 0.001$). Summer season explained 9% and 7% of variation in s25OHD and vitamin D insufficiency.
Conclusion: Without coordinated intervention, vitamin D status of CF patients does not change. Summer season is associated with better vitamin D status, but it explains only a minor part of its variation. Majority of Stockholm CF patients have insufficient s25OHD levels both in winter and in summer.

354 Are serum vitamin D levels >75nmol/L achievable in children with cystic fibrosis?

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Recent UK Cystic Fibrosis (CF) guidelines have recommended that serum 25-OH Vitamin D (25-OHD) levels should be maintained at 75–150 nmol/L to improve bone accretion and so prevent bone disease and low bone mineral density.
A previous review of 25-OHD levels in 2003–4 showed that only 11 patients (6%) had levels >75 nmol/L, mean(SD) 48(18) nmol/L. Our current practice is to prescribe a daily Vitamin D supplement to all pancreatic insufficient children of 10 ug per day, and following our previous review we implemented a more aggressive regime where the Vitamin D supplement is incrementally increased up to 50 ug daily if there is a persistently low serum 25-OHD.
Aim: To determine the prevalence of Vitamin D deficiency in our CF population, in response to the more aggressive management adopted and our perception that 25-OHD levels >75 nmol/L may still not be achieved with this regimen.
Methods: Retrospective interrogation of our CF database for 25-OHD levels of children attending for annual review in 2007, 2008 and 2009.
Results: See the table. The 2009 results were significantly better ($p < 0.001$) than either 2007 or 2008 (ANOVA).

	Serum 25-OHD levels			
	Result available, N	Mean (SD)	>75nmol/L, N (%)	<25nmol/L, N (%)
2007	107	50 (17.1)	9 (8)	4 (4)
2008	131	51.7 (25.3)	17 (13)	14 (11)
2009	122	65.7 (30.2)	45 (37)	10 (8)

Conclusion: Although, the proportion of children in our clinic with 25-OHD levels in the recommended range is increasing, a significant number remain below the recommended range. Our current supplementation regimen will need to be reviewed again to improve this further.
The question still remains: are serum 25-OHD levels >75 nmol/L achievable in all our population?

355 High dose colecalciferol increases vitamin D levels in adult cystic fibrosis patients

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Background: CF Trust guidelines state that vitamin D supplementation should be individualised with the aim of achieving serum 25-OH vitamin D (25OHD) between 30 and 60 mcg/L (CF Trust, 2007). We aimed to achieve recommended 25OHD levels by prescribing high dose vitamin D for patients who had levels <30 mcg/L.
Method: CF patients have their 25OHD levels checked annually and those with levels <30 mcg/L were given colecalciferol (vitamin D3) 100,000 units weekly for 6 weeks and levels rechecked after completion of the course (average 12.4 weeks).
Results: A total of 60 patients were given a course of high dose vitamin D between Aug 2008 and Dec 2009 (mean pre-course 25OHD level = 12.3 mcg/L).
Of these, 43 patients had a 25OHD level checked at the end of the course (mean post-course 25OHD level = 32.8 mcg/L). 42/43 patients had an increase in 25OHD levels and one patient's level remained the same (<5 mcg/L).
20/43 patients achieved levels of >30 mcg/L and of these 17 achieved the target levels of 30–60 mcg/L as recommended by the CF Trust. 3 patients had levels >60 mcg/L.
A total of 14 patients had levels rechecked at a later date (average 27 weeks after starting vitamin D course). Most patients' levels had decreased, but 6/14 remained at 30–60 mcg/L and all remained higher than their pre-course levels.
Conclusions: High dose vitamin D (as colecalciferol) is effective at increasing 25OHD levels in CF patients (mean pre level 12.3 mcg/L; mean post level 32.8d mcg/L). However, only 40% of patients achieved the CF Trust recommended level. Although levels decreased with time, they were still higher than baseline after an average of 27 weeks.