WS15.4 Cystic fibrosis bronchial epithelial cells have impaired ability to activate vitamin D

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Objectives: Respiratory epithelial cells convert inactive 25-hydroxyvitamin D3 (25OHD3) to its active form. The active 1,25-dihydroxyvitamin D [1,25(OH)2D] induces the expression of the antimicrobial peptide cathelicidin (LL-37) and suppresses the production of pro inflammatory cytokines. Cystic fibrosis (CF) is characterized by a vicious circle of infection and inflammation in the lungs. We aimed to assess the ability of CF bronchial epithelial cells (CFBE) to convert inactive 25OHD3 to the active 1,25(OH)2D and its impact on LL-37 production.
Methods: Human bronchial epithelial cells (HBE) and CFBE cells were seeded in protein-coated plates and grown for 22 or 48 hours, when 25OHD3 was added to the media (100 nmol/L). After one day of incubation, media was harvested. 1,25(OH)2D and LL-37 concentrations were measured by EIA and ELISA, respectively.
Results: Adding 25OHD3 increased the concentration of 1,25(OH)2D in the media from both HBE and CFBE cells. However, the amplitude of the increase was significantly lower in CFBE cells (12.0±8.0 pmol/L) compared to HBE cells (33.2±12.4 pmol/L), $p < 0.01$. The LL-37 concentration in media from HBE or CFBE cells did not change upon 25OHD3 treatment.
Conclusion: CFBE cells activate vitamin D with a significantly lower efficacy than HBE cells. The data indicates that the ability to activate vitamin D may be impaired in CFBE cells. This may translate into lower local active vitamin D concentrations and contribute to the dysregulated immune response and the increased infection susceptibility in CF lungs. More experiments using other cell lines and primary epithelial cells are needed to confirm these findings.

WS15.5 A ten year review of serum vitamin D levels in children with cystic fibrosis

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Background: UK CF guidelines recommend serum 25-OH Vitamin D (25-OHD) levels are maintained at 75–150 nmol/l to help prevent CF bone disease. To achieve this, the CF unit at Great Ormond Street Hospital, London (GOS) has monitored and sequentially increased Vitamin D supplementation over the last 10 years. Since 2010 our protocol is to supplement 1500–3000IU cholecalciferol daily for 12 weeks for 25-OHD levels <50 nmol/l, then re-check serum levels. If levels remain <50 nmol/l, high dose supplementation is continued and levels reviewed 3 monthly.
Objectives: To determine the prevalence of sub-optimal serum 25-OHD levels in our CF paediatric population in response to increased supplementation protocols over a 10 year period.
Methods: Retrospective interrogation of all patients on the GOS CF database with a serum 25-OHD level measured at their annual review from 2003–2012.
Results: See the table.

Table: GOS Serum 25-OHD levels 2003–2012

Year of annual review	No. of patients	Mean (SD) 25-OHD (nmol/l)	Daily vitamin D supplementation (IU)	N (%) with 25-OHD >75 nmol/l
2003	148	50 (17)	400–600	12 (8)
2005	128	51 (17)	400–2000	11 (9)
2007	144	49 (17)	400–2000	11 (8)
2009	136	65 (29)	400–2000	43 (32)
2012	144	78 (27)	400–3000	83 (58)

The proportion of patients with a 25-OHD >75 nmol/l increased significantly. By 2012, 83 (58%) patients had a vitamin D level >75 nmol/l compared to only 12 (8%) in 2003 ($p < 0.0001$).
Conclusion: In the last decade we have observed a significant increase in mean vitamin D levels paralleling changes in supplementation protocols. Despite this, 42% of our population are yet to achieve serum 25-OHD levels >75 nmol/l. Our current regimen will need to be reviewed again to improve this further.