[1]*St Vincent's Hopspital, Sydney, Gastroenterology, Sydney, Australia,* [2]*The Australian National University, National Centre for Epidemiology and Population Health, Canberra, Australia,* [3]*The University of Western Australia, Centre for Microscopy, Characterisation and Analysis, Perth, Australia,* [4]*University of Western Australia, School of Medicine and Pharmacology, Faculty of Health and Medical Sciences, Perth, Australia,* [5]*St John of God Hospital, Centre for Inflammatory Bowel Diseases, Subiaco, Australia,* [6]*Telethon Kids Institute, Inflammation, Subiaco, Australia,* [7]*The Garvan Institute of Medical Research, Osteoporosis and Bone Biology, Sydney, Australia,* [8]*St Vincent's Hospital Sydney, Endocrinology, Sydney, Australia*

Background: Vitamin D deficiency is common among patients with Crohn's disease (CD) and has been a proposed risk factor for the development and flare of CD. It remains unclear, however, if this association is a result of the inflammatory process, or a cause. Furthermore, most studies have relied on radioimmunoassays to measure 25-hydroxyvitamin D (25(OH)D), which may be less accurate than the accepted gold standard of liquid chromatography tandem mass spectrometry (LC/MS/MS). Circulating 25(OH)D is metabolised to the metabolically active $1,25(OH)_2D$. The alternative pathway involves the production of the inactive $24,25(OH)_2D$ via 24-hydroxylase prior to elimination. The ratio of 25(OH)D:24,25(OH)D may be a more accurate measure of vitamin D status than 25(OH)D alone. We aimed to characterise vitamin D metabolism in patients with active and inactive CD using LC/MS/MS.
Methods: We report the baseline cross-sectional results of a prospective cohort study. Patients were included if they had active CD defined as ulceration at endoscopy; or a Crohn's disease Activity Index (CDAI) >220 and a CRP >10 mg/l or faecal calprotectin >250 mg/kg. Remission was defined as a CDAI <150 and normal inflammatory biomarkers. Patients were excluded if they received corticosteroids or vitamin D supplementation in the preceding 4 weeks. Serum was tested for 25(OH)D, epi-25(OH)D, 1,25(OH)D and $24,25(OH)_2D$ using an LC/MS/MS assay. Validated questionnaires were used to estimate vitamin D exposure from diet and sunlight. Spearman's correlation coefficient was used to test correlations and unpaired t-tests to test differences between active and remission CD groups.
Results: Forty-seven consecutive patients with CD (20 active and 27 remission) were recruited; 55% were male. Median age was 37years (range 23 to 76yr). Fewer patients in the active group were on immunomodulators (30% vs. 61% $p = 0.03$) or TNF inhibitors (25% vs. 89% $p < 0.001$). There was no difference in serum 25(OH)D, epi-25(OH)D or 1,25(OH)D between the groups. Serum $24,25(OH)_2D$ levels were significantly lower in the active group (mean 1.3 vs. 2.5ng/ml $p < 0.001$) and thus the 25(OH)D:$24,25(OH)_2D$ ratio was higher (49.4 vs. 26.1 $p < 0.001$). There was an inverse correlation between CDAI and $24,25(OH)_2D$ levels ($r^2 = 0.33$; $p = 0.01$). Dietary vitamin D intake and sunlight exposure were not different between the groups.
Conclusions: In the setting of active inflammation, levels of $1,25(OH)_2D$ are maintained by shifting the metabolism of 25(OH)D to $1,25(OH)_2D$ rather than $24,25(OH)_2D$, suggesting a reduction in 24-hydroxylase activity to maintain the active metabolite. The ratio of 25(OH)D:$24,25(OH)_2D$ is increased in active disease and may be a more sensitive marker of vitamin D status in patients with CD.

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Characterising and managing issues with food-related quality of life in inflammatory bowel disease: a qualitative study of patients and healthcare professionals

W. Czuber-Dochan[1]*, M. Morgan[2], M. Lomer[1], J.O. Lindsay[3], G. Robert[4], K. Whelan[1]

[1]*King's College London, Faculty of Life Sciences and Medicine, Department of Nutritional Sciences, London, UK,* [2]*King's College London, Institute of Pharmacological Sciences, London, UK,* [3]*Bart's and the London NHS Trust, Gastroenterology Department, London, UK,* [4]*King's College London, Faculty of Nursing, Midwifery and Palliative Care, London, UK*

Background: Inflammatory bowel disease (IBD) has a profound impact on diet and nutrition that creates limitations in psychosocial functioning and impacts quality of life (termed food-related quality of life, FR-QoL). The issues experienced and the management methods used by patients with IBD and healthcare professionals (HCPs) regarding FR-QoL are not well understood.
Methods: Individual semi-structured interviews with 15 IBD patients reporting issues with FR-QoL; and two focus group interviews with 11 HCPs were audio recorded and transcribed verbatim. Pragmatic thematic analysis was used to analyse data, with NVivo 11 used for data management.
Results: Fifteen patients with IBD (10 CD/5 UC) were purposively selected from UK hospital outpatient clinics (7 females, mean age 34.4 years; range 21–51 years). Individual interviews ranged from 39–70 min. Eleven HCPs (3 consultant gastroenterologists, three IBD registrars, two specialist dietitians, two IBD specialist nurses and one psychologist) participated in two focus groups over 2 h each. Patients perceived IBD as having a direct impact on their diet, particularly their food choices and enjoyment of food. This limited their daily life such as going out, socialising with friends and family, or personal relationships. Several factors, including limited understanding of IBD impact on body function and food digestion, fear of triggering a flare through eating, anxiety about making the right food choices, were perceived to contribute to impaired FR-QoL. Patients attempted various methods to improve FR-QoL including trial and error, food avoidance or exclusion, reducing portion size or frequency of eating; but few approaches were perceived to have the desired improvement in FR-QoL. Limited or no dietary advice from HCPs left patients feeling that food-related issues do not receive the same level of attention as medical management. During the focus groups, HCPs identified the factors affecting patients' diet and FR-QoL that needed greater attention and they were: IBD-related (e.g. newly diagnosed, acute inflammation, functional symptoms, strictures and stoma) and non-IBD related (e.g. pregnancy, allergies, likes/dislikes). HCPs acknowledged FR-QoL advice as a low priority in a consultation. HCPs recognised insufficient time in clinical consultations to address more complex issues. Some felt inadequately prepared to offer diet-specific advice, or assumed that other members of the multidisciplinary team provide diet-related care and advice.
Conclusions: Both, patients and HCPs emphasised the need for more individualised care in relation to food and IBD and required quality and timely sources of information. The development and testing of interventions designed to address FR-QoL is required.

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Vitamin D activates human intestinal fibroblasts

L. Gisbert-Ferrándiz[1]*, P. Salvador[1], D.C. Macias-Ceja[2], J. Cosín-Roger[2], D. Ortiz-Masiá[3,4], F. Navarro-Vicente[5], S. Calatayud[1,4], C. Hernández[2], M.D. Barrachina[1,4]

[1]*University of Valencia, Pharmacology, Valencia, Spain,* [2]*Fisabio Hospital Dr Peset, Valencia, Spain,* [3]*University of Valencia, Medicine, Valencia, Spain,* [4]*CIBERehd, Valencia, Spain,* [5]*Hospital of Manises, Servicio de Cirugía, Valencia, Spain*

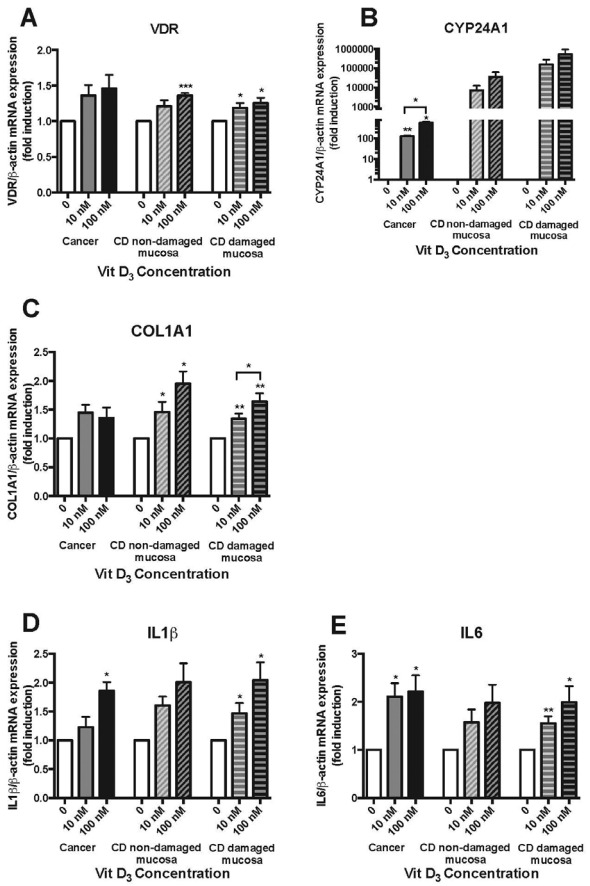
Background: Vitamin D signals through the vitamin D receptor (VDR) which is a member of the nuclear receptor family of transcription

factors that play an immunoregulatory role in the gut. Defective signalling due to vitamin D deficiency or decreased mucosal VDR levels has been related to Crohn's disease (CD). We aim to analyse the acute effects of Vitamin D in the activation of human intestinal fibroblasts.

Methods: Fibroblasts were isolated from non-damaged and damaged intestinal resection of CD patients and control patients (non-damaged intestine from colon cancer). Fibroblasts were treated with 1,25 Vitamin D_3 (10 nM and 100 nM) for 24 h. Gene expression of pro-inflammatory cytokines and COL1A1 was quantified by qPCR and protein levels were determined by western blot. Statistical significance was measured by ANOVA.

Results: Vitamin D increased the mRNA expression of VDR in fibroblasts obtained from the inflamed and non-inflamed mucosa of CD patients (Figure 1A) and it increased the mRNA of CYP24A1, a VDR target (Figure 1B). Treatment with vitamin D rised in a dose-dependent manner COL1A1 mRNA expression in fibroblasts from CD patients (Figure 1C) and in parallel it induced the expression of pro-inflammatory cytokines (IL1β , IL6) (Figure 1D, 1E). Protein levels of phospho-NFκB and phospho-STAT3 were also higher in fibroblasts treated with Vitamin D from CD patients.

Conclusions: Our study indicates that an acute treatment of Vitamin D activates an inflammatory pathway and a collagen I expression in human intestinal fibroblasts which may be involved in the initial response in the wound healing.



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The effect of necrosis inhibition on acute DSS colitis model of inflammatory bowel disease

D. Lee[1,2*], J.S. Koo[2], C.H. Kim[1], S.H. Hwang[1], J.W. Choe[2], S.Y. Kim[2], S.W. Jung[2], H.J. Yim[2], Y.T. Jeen[2], S.W. Lee[2]

[1]Korea University Ansan Hospital, Internal Medicine, Seoul, South Korea, [2]Korea University College of Medicine, Seoul, South Korea

Background: Inflammatory bowel diseases (IBD) were characterised by uncontrolled chronic inflammation, which lead to cell death and organ damage. In contrast to apoptotic cell death, necrosis is characterised by destruction of cell membrane, which released substances from the cells causing the inflammatory reaction and a cascade of vicious inflammatory cycle resulting in increased necrosis. Although necrosis is thought be a main cell death mechanism of IBD, few attempts have been made to reduce necrosis in IBD. A novel necrosis inhibitor (NI, NecroX-7) is recently developed, which blocks the opening of mitochondrial permeability transition pore and inhibits necrosis effectively. The aim of this study investigated the effect of necrosis inhibition in acute murine colitis model and in-vitro study.

Methods: Cleaved PARP-1 fragment band was analysed using western blot assay in intestinal epithelial cell line (IEC-18, rat) in order to confirm the necrosis inhibition effect of NI. And acute dextran-sodium sulfate (DSS) induced colitis was generated in C57BL/6 mice. NI (30 mg/kg) was administered once a day via oral gavage for 8 days from the day before DSS administration. The severity of colitis was assessed by weight, colon length and histologic score. And HMGB1 immunochemistry was performed on harvested intestine for evaluating necrotic cell death qualitatively. The inflammatory cytokines mRNA expressions were measured by quantitative RT-PCR.

Results: In the necrosis inhibition group, the expression of cleaved PARP-1 (55kDa, necrosis marker) was reduced compared with the control group, whereas the cleaved PARP-1 fragment (89 kDa, apoptosis marker) was not different between groups. In vivo study, NI treatment significantly reduced colitis represented by colon length and histologic score.