

Impact of Vitamin D Supplementation on Vascular Function, Vascular Structure and Immune Regulation in Patients with Chronic Kidney Disease and Low Vitamin D Levels – A Pilot Randomised Trial

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BACKGROUND

Vitamin D deficiency contributes to the excess cardiovascular morbidity and mortality in patients with chronic kidney disease (CKD), yet there is limited evidence from randomised controlled trials (RCT) for a beneficial effect of vitamin D supplementation. Creative study methodology can avoid prohibitively large and lengthy trials of and contribute to understanding of mechanistic pathways.

METHODS

A pilot study was performed to assess the feasibility of a single-blinded RCT of cholecalciferol supplementation (5x 20,000 IU over 20 weeks) versus no supplementation in patients with CKD Stage 3-4 and serum total 25-hydroxyvitamin D <75 nmol/l on vascular function (assessed by flow mediated dilatation of the brachial artery), vascular structure (assessed by carotid intima media thickness), and absolute frequency and percentage of CD4+CD28null T lymphocytes and regulatory T cells (implicated in the immunoregulation of atherogenesis). The study tested methods of participant recruitment, participant retention, randomisation, acceptability and adherence to group-specific cholecalciferol supplementation instructions. Preliminary statistical analyses were performed to derive the necessary input for larger settings.

RESULTS

40.9% of eligible patients were recruited reaching 72% of target over 12 weeks. The retention rate was 91.6%. Cholecalciferol treatment and control groups were well-matched at baseline (see table). Quantitative and qualitative analysis of participant feedback demonstrated a largely positive attitude to participation with thematic analysis identifying a high prevalence of the theme of positivity of experience with subthemes of a beneficial feeling, confidence and altruism. The data showed strong evidence for a significant difference in the serum 25-hydroxyvitamin D levels at study completion between the cholecalciferol treatment and control groups, the higher levels in the cholecalciferol treatment group remaining significant after adjusting for the baseline 25-hydroxyvitamin D level with analysis of covariance (51.32 mmol/l difference between groups, 95% CI [36.28, 66.37], $p < 0.001$). This indicates adherence to the group-specific cholecalciferol supplementation instructions. At follow up there was no significant difference between the cholecalciferol treatment and control groups in flow mediated dilatation ($p = 0.49$), carotid intima media thickness ($p = 0.95$), percentage of CD4+CD28null T lymphocytes ($p = 0.43$), absolute frequency of CD4+CD28null T lymphocytes ($p = 0.21$), percentage of regulatory T cells ($p = 0.25$) or absolute frequency of regulatory T cells ($p = 0.45$).

CONCLUSION

A pilot trial performed using the methodology of this single-blinded pilot study of cholecalciferol supplementation generated results which can inform the planning of future a priori statistically powered similar experiments.