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A systematic review to evaluate the efficacy and safety of high-dose vitamin D supplementation in adults with cystic fibrosis

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Cystic fibrosis (CF) is an autosomal-recessive condition that is caused by a mutation in the CFTR gene[(1)]. As CF patients' prognoses are improving due to highly effective modulator therapy, (HEMT) managing comorbidities such as bone disease is pertinent. This could be exacerbated by vitamin D insufficiency which has been estimated to be as high as 98% in adults with CF[(1)]. This systematic review aimed to evaluate the efficacy and safety of high-dose cholecalciferol (vitamin D_3) supplementation in correcting inadequate serum 25-hydroxyvitamin D (serum 25(OH)D) concentration in adults with CF.

The systematic search included studies that examined the impact of high-dose cholecalciferol on serum 25(OH)D concentration. Eligible RCTs included study designs that involved adults with CF and a high-dose cholecalciferol supplementation protocol (defined as any dose above basal) compared with basal doses (800IU-1000IU/day)/no supplementation. A systematic search was conducted and a meta-analysis of RCTs was produced to calculate the change in serum 25(OH)D concentration in the intervention group in comparison to control as the primary outcome measure.

The systematic search yielded five RCTs that were collated and analysed. The results of the metaanalysis demonstrated that the high-dose cholecalciferol group and control group achieved a serum 25(OH)D concentration of 40.19ng/ml ± 10.21ng/ml and 28.50ng/ml ± 7.35ng/ml respectively ($p<0.01$), indicating that high-dose cholecalciferol is an effective intervention to achieve optimal serum 25(OH)D concentration (>30ng/ml). A high heterogeneity was observed across the studies ($I2 = 87\%$)[(2,3)]. Doses varied from daily supplementation of 1,700IU to a 250,000IU single dose. There were minimal adverse effects reported in the RCTs from high-dose cholecalciferol and there were no instances of hypervitaminosis D or hypercalcaemia reported[(3)].

The results infer the effectiveness of high-dose cholecalciferol in correcting low serum 25(OH)D concentration in adults with CF. The most effective regimen identified was a single weekly dose of 50,000IU for 12 weeks, which achieved serum 25(OH)D concentration of 45.91ng/ml ± 11.24ng/ml (control: 23.61ng/ml ± 4.37ng/ml) ($p<0.01$) after a 12-week intervention[(2)].

The key findings suggest that annual monitoring of serum 25(OH)D concentration would be beneficial with a tailored high-dose cholecalciferol protocol. A high level of heterogeneity was observed across the studies, with small sample sizes, meaning a larger multi-centre, multi-nation RCT study that considers the context of advances in HEMT should be conducted to corroborate the results before implementation into clinical guidelines.

High-dose cholecalciferol supplementation is an effective and safe method to increase serum 25(OH)D concentration in adults with CF that may lead to improved bone health outcomes. More studies are required before revising current vitamin D supplementation guidelines. Future research should focus on establishing dosing guidelines to optimise vitamin D status, exploring the longterm health outcomes of sustained adequate serum 25(OH)D concentration.

References

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