Letters to the editor

SHOULD WE BE GIVING ENHANCED VITAMIN D INTAKES TO ALL?

Author’s response to letter from H Rhein (J R Coll Physicians Edin 2012; 42:93)

Dr Rhein makes a plea for replenishing deficient vitamin D stores, and suggests that failure to do so would be unethical. Low vitamin D level are indeed common, but in the absence of good trial evidence that population-level supplementation improves overall health, such supplementation itself could be argued to be unethical. We need to treat the patient, not the number.

Existing data from meta-analyses are derived mostly from trials in older people with osteoporosis; mortality was not a pre-specified outcome in these trials, and there is a world of difference between such targeted supplementation and indiscriminate population-level supplementation. While I agree that doses of vitamin D up to 4,000 units/day have not been associated with acute vitamin D toxicity or significant hypercalcemia in such selected populations, this does not mean that supplementation is ‘safe’ in the longer term – we don’t have the necessary long-term trial data to conclude this. The closest to population level trial data that we have showed a 16% increase in kidney stones when supplementing healthy middle-aged women with calcium plus vitamin D, the combination shown to have most effect on falls in selected patient groups.1

We need to conduct large, population-based trials of vitamin D supplementation before we bring this intervention into clinical practice. Until the evidence is in, the best course of action would be to stop measuring 25-hydroxyvitamin D levels on most patients until we have the necessary long-term trial data to conclude this. The closest to population level trial data that we have showed a 16% increase in kidney stones when supplementing healthy middle-aged women with calcium plus vitamin D, the combination shown to have most effect on falls in selected patient groups.1

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References

HYPONATRAEMIA AND ALCOHOL EXCESS ARE ASSOCIATED WITH PROTEAN CENTRAL NERVOUS SYSTEM DAMAGE

The recent descriptions in the Journal of both central pontine myelinolysis (CPM) associated with correction of electrolyte abnormalities other than a low sodium and of CPM developing in the more classical way, with subsequent good recovery,2 highlights the continuing problem of central nervous system damage that is associated with electrolyte disturbance and often alcohol abuse, but also appears to suggest that sometimes we still administer rapid corrective treatment that may compound the problem. It is therefore important that we ensure that physicians in training are aware of the potential risks of electrolyte abnormalities and their correction. Another aspect is the development of central nervous system lesions other than CPM during the management of hyponatraemia. Rapid correction of a low serum sodium has been associated with both infarct and haemorrhage in the pons and in other areas of the brain, but without any sign of the typical lesions of CPM.3 Clearly, the damage to nervous tissue caused by such electrolyte disturbances is variable and CPM is not the only pathology associated such clinical presentations.

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References

COELIAC DISEASE AND GRANULOMATOUS GUT COMPLICATIONS IN COMMON VARIABLE IMMUNODEFICIENCY DISORDERS

Dr A Dhar and colleagues recently reported a case of granulomatous ileocolitis in coeliac disease, but the possibility of granulomatous variant of common variable immunodeficiency disorder (CVID) was not explored. Chronic diarrhoea is seen in up to 90% of patients with CVID and if a strict gluten-free diet results in a failure of clinical response or complicated by persistent granulomas, it merits testing for serum immunoglobulin levels (IgG, IgA, IgM) in order to exclude hypogammaglobulinaemia. Villous blunting with an increase in intraepithelial lymphocytes (CD8+ T cells) in the lamina propria (i.e. a coeliac disease-like pattern but without plasma cells) and granulomas are found in 30–50% and 8–22%, respectively
in CVID. The diagnosis of CVID has significant implications as patients with the granulomatous variant on regular immunoglobulin replacement therapy were reported to have a median survival of 13.5 years in one study while median age at death was 37.5 years in another study.

Gut pathologies in CVID include coeliac disease, *Helicobacter pylori* infection, nodular lymphoid hyperplasia, inflammatory bowel disease (IBD), chronic atrophic gastritis with or without pernicious anaemia and hepatitis. IBD is reported in 2–13% of CVID patients, but differs from classic IBD with features of lymphocytic colitis, collagenous colitis and/or graft-versus host disease, lymphoma and gastric adenocarcinoma. The granulomatous variant has a higher incidence of auto-immune complications (up to 50% compared to 18% without granulomatous disease). A profound deficiency of isotype-switched memory B cells and abnormal genetic, cellular (CD8+ T cell expansion and low CD4+ T cells), cytokine environment or defective TLR9 signalling probably leads to the autoimmune/granulomatous complications. Mononuclear cells from the lamina propria produce significantly higher levels of interferon-gamma (IFN-γ) and interleukin-12 (IL-12), but not IL-23, IL-17, or tumour necrosis factor-alphas (TNF-α), as seen in Crohn's disease, suggesting a NOD2-independent pathway of inflammation.

The management of CVID enteropathy can be particularly challenging as regular replacement doses of human normal immunoglobulin does not reverse the colitis, perhaps due to continuous antigen trigger and inflammation driven by a dysregulated immune system. Immunoglobulin replacement and/or immunosuppressive therapy have led to a resolution of granulomas in exceptional cases only. Patients may not always have the typical symptoms of an immunodeficiency in the form of recurrent sinopulmonary infections, pneumonias and may only have gut symptoms such as chronic diarrhoea or unusual gut histopathology. If antibody deficiency is found, clinicians should consider antigen-based testing in these patients as infectious aetiologies must definitely be excluded.

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REFERENCES:


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