

Evidence Update: Megestrol Acetate, Vitamin D

Q Some of my CKD patients are malnourished; in fact, some of those on dialysis do not eat well and have low albumin levels. Previously in this column, it was stated that higher albumin levels (> 4 g/dL) confer survival benefits to dialysis patients. Should I consider prescribing megestrol acetate to improve appetite? If I do prescribe it, what dose is safe for CKD and dialysis patients?

Malnutrition affects one-third of dialysis patients,¹ and malnutrition-inflammation complex syndrome (MICS) is common in those with stage 5 CKD. Albumin is used as an indicator of MICS in dialysis patients; however, since other factors (stress, infection, inflammation, comorbidities) affect nutritional status,² serum albumin alone may not be sufficient to assess it.

In fact, a recent consensus statement on malnutrition from the Academy of Nutrition and Dietetics and the American Society for Parenteral and Enteral Nutrition excluded serum albumin as a diagnostic characteristic; the criteria included percentage of energy requirement, percentage of

weight loss and time frame, loss of body fat and muscle mass, presence of edema, and reduced grip strength.³ These may be better measures of malnutrition in dialysis patients and could be used as criteria for determining when to prescribe an appetite stimulant, such as megestrol acetate.

In recent years, megestrol acetate (an antineoplastic drug) has been used to improve appetite, weight, albumin levels, and MICS in patients receiving maintenance dialysis.^{1,4-6} Rammohan et al found significant increases in weight, BMI, body fat, triceps skinfold thickness, protein/energy intake, and serum albumin in 10 dialysis patients who took megestrol acetate (400 mg/d) for 16 weeks.⁴

In a 20-week randomized, double-blind, placebo-controlled trial, Yeh et al found significant increases in weight, body fat, and fat-free mass in elderly hemodialysis patients receiving megestrol acetate (800 mg/d). The treatment group also demonstrated greater improvement in ability to exercise.⁵

Monfared and colleagues looked specifically at megestrol acetate's effect on serum albumin levels in dialysis patients.¹ Using

a much lower dose (40 mg bid for two months), they found a significant increase in serum albumin in the treatment group. Although an increase in appetite was noted, the researchers did not observe any significant change in total weight following treatment.¹

In a letter to the editor of the *Journal of Renal Nutrition*, Golebiewska et al reported their use of megestrol acetate in maintenance hemodialysis and peritoneal dialysis patients.⁶ Hypoalbuminemic patients were given megestrol acetate (160 mg/d). Significant increases in weight, BMI, subjective global assessment scores (a measure of nutritional status based on clinical indices such as weight, appetite, muscle, and fat mass), and serum albumin levels were seen. Only 12 of the 32 patients completed the study; the others dropped out due to adverse effects, including high intradialytic weight gain (the amount of fluid gained between dialysis sessions), dyspnea, diarrhea, and nausea.⁶

Currently, there is no consensus in the literature regarding the most effective dosage of megestrol acetate. Furthermore, evidence is lacking as to whether megestrol acetate-induced increases in appetite, oral intake, weight, and serum albumin level bestow any survival benefit or affect outcomes in dialysis patients.⁴ However, the increased sense of well-being a patient experiences when appetite returns and weight is restored may be worth the effort. —LD

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Q One of my patients came in and said he had read that vitamin D supplementation will help with hypertension. Now he wants to quit his blood pressure meds and use vitamin D instead. Do you have any background on this?

Vitamin D is critical for utilization of calcium, a vital nutrient for multiple metabolic and cellular processes; deficiency is associated with worsening of autoimmune disorders, osteoporosis, and certain cardiovascular conditions, among others.⁷ An association between vitamin D level and blood pressure has been recognized for some time, but the pathophysiology is not well understood.

A literature review of studies from 1988 to 2013 found contradictory results regarding vitamin D deficiency and concurrent elevated blood pressure (systolic and/or diastolic), as well as the impact on blood pressure with restoration of vitamin D levels. The findings were limited by several factors, including differences in study design, variables evaluated, and type of vitamin D compound used. The results suggested a link between the renin-angiotensin-aldosterone system, fibroblast growth factor 23/klotho axis, and vitamin D level.⁸

A study of 158 subjects (98 with newly diagnosed essential hypertension, 60 with normal blood pressure) found significantly lower 25(OH)D3 serum levels in hypertensive patients. Furthermore, the 25(OH)D3 level was significantly correlated with both systolic ($r = -0.33$) and diastolic

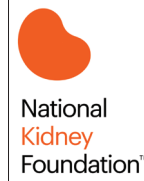
blood pressure ($r = -0.26$). Using multiple regression analysis, after adjustment for age, smoking status, and BMI, the impact of 25(OH)D3 level accounted for 10% of the variation in systolic blood pressure.⁹

In a mendelian randomization study of 108,173 subjects from 35 studies, an inverse association between vitamin D level and systolic blood pressure ($P = .0003$) was found. A reduced risk for essential hypertension with increased vitamin D level ($P = .0003$) was also noted. However, no association was found between increasing vitamin D level and a reduction in diastolic blood pressure ($P = .37$).¹⁰

With the ever-increasing access to health information from sources such as “Doctor Google,” it can be difficult for a non-health care professional to separate hype from evidence-based recommendations. While current evidence suggests optimal vitamin D levels may be beneficial for improving blood pressure control and may be a useful adjunctive therapy, there is no evidence to support discontinuing antihypertensive therapy and replacing it with vitamin D therapy. —CAS **CR**

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The National Kidney Foundation Council of Advanced Practitioners' (NKF-CAP) mission is to

serve as an advisory resource for the NKF, nurse practitioners, physician assistants, clinical nurse specialists, and the community in advancing the care, treatment, and education of patients with kidney disease and their families. CAP is an advocate for professional development, research, and health policies that impact the delivery of patient care and professional practice. For more information on NKF-CAP, visit www.kidney.org/CAP

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