Is megestrol acetate an effective appetite stimulator in HIV wasting syndrome?

Evidence-Based Answer
Among patients with anorexia-cachexia syndrome, which includes patients with HIV/AIDS, megestrol acetate (Megace®) increases weight gain by 1.9 kg, but does not significantly improve appetite or quality of life (SOR: B, systematic review of RCTs).

Megestrol acetate was approved by the US Food and Drug Administration in 1993 for treatment of anorexia-cachexia syndrome, otherwise known as HIV wasting syndrome, in AIDS patients.¹,²

A 2004 systematic review of 26 RCTs examined the effects of megestrol acetate on appetite, weight gain, and quality of life among 3,887 patients with cancer, AIDS, or other pathologies and anorexia-cachexia syndrome.¹ Megestrol acetate was compared with placebo, different doses of megestrol acetate, and other medications including prednisolone, dexamethasone, cisapride, dronabinol, and nandrolone decanoate.

For patients with HIV/AIDS, there was an improvement in weight gain (defined as any observed weight gain) compared with placebo (2 trials, n=287; RR 2.2; 95% CI, 1.5–3.2). However, data were insufficient to evaluate appetite and no significant improvements were seen in quality of life (described as improved or not improved) (7 trials, n=1,019; RR 1.6; 95% CI, 0.7–3.9). There were also no significant dose-based improvements in the comparison of ≥800 mg/d to <800 mg/d. Data were insufficient to compare megestrol acetate to other treatments in the subgroup of patients with HIV/AIDS. Edema was the only statistically significant adverse event found with megestrol acetate use among all of the trials (26 trials, n=3,887; RR 1.7; 95% CI, 1.2–2.3).³

Another systematic review, in 2013, examined 35 RCTs for the effect of megestrol acetate on the primary outcomes of weight gain, quality of life, and adverse events.² Through evaluation of 3,963 patients for efficacy and 3,180 patients for safety with a diagnosis of anorexia-cachexia syndrome in the settings of cancer, AIDS, and other pathologies, megestrol acetate was compared with placebo, different doses, and other medications. A subgroup analysis of the 5 trials that specifically evaluated HIV/AIDS patients did not provide sufficient data for individual results.

Weight gain improved with megestrol acetate in all comparisons among noncancer patients (10 trials, n=1,109; mean difference [MD] 1.9 kg; 95% CI, 0.06–2.9). In patients with HIV/AIDS, megestrol acetate provided no improvement in quality of life compared with placebo (3 trials, n=423; RR 1.5; 95% CI, 0.47–4.7). Both edema (12 trials, n=2,182; RR 1.4; 95% CI, 1.1–1.7) and thromboembolic phenomena (11 trials, n=1,544; RR 1.4; 95% CI, 1.1–3.2) were statistically significant adverse events.²

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Is phenobarbital effective in treating alcohol withdrawal?

Evidence-Based Answer
It may have a role. Adding IV phenobarbital to lorazepam in the emergency department (ED) decreases ICU admissions compared with lorazepam alone, decreases total ED lorazepam dosing, and reduces the need for continuous IV lorazepam. As individual agents, phenobarbital and lorazepam appear to have comparable effectiveness in lowering Clinical Institute Withdrawal Assessment (CIWA) scores in the ED (SOR: B, small RCTs).

One RCT from 2013 evaluated single-dose phenobarbital with benzodiazepines in adults presenting to an ED with alcohol withdrawal severe enough to require admission and treatment with benzodiazepines (N=102).¹ Patients were diagnosed with alcohol withdrawal based on physician judgment of the following symptoms: heart rate >100 bpm, tremor, paroxysmal sweats, agitation, anxiety, and hallucinations or clouded sensorium. Investigators excluded patients with severe hepatic impairment, pregnancy, or allergy to study medications.

Patients received 10 mg/kg phenobarbital IV in 100 mL saline or 100 mL IV saline placebo in a double-blind fashion. Both groups subsequently received oral or IV lorazepam for scores of ≥3 on a local modification of CIWA scoring, assessing 6 domains (tremor, sweats, agitation, hallucinations,