

CLINICAL INQUIRIES

Evidence-based answers from the
Family Physicians Inquiries Network

Frances K. Wen, PhD;
James Millar, MD
University of Oklahoma
School of Community
Medicine, Tulsa

Linda Oberst-Walsh, MD
University of Colorado
School of Medicine, Denver

Joan Nashelsky, MLS
Family Physicians Inquiries
Network, Iowa City

DEPUTY EDITOR

Rick Guthmann, MD,
MPH

Advocate Illinois Masonic
Family Medicine Residency,
Chicago

Q/ Is megestrol acetate safe and effective for malnourished nursing home residents?

EVIDENCE-BASED ANSWER

A/ NO. Megestrol acetate (MA) is neither safe nor effective for stimulating appetite in malnourished nursing home residents. It increases the risk of deep vein thrombosis (DVT) (strength of recommendation [SOR]: **C**, 2 retrospective chart reviews), but isn't associated with other new or worsening events or disorders (SOR: **B**, single randomized controlled trial [RCT]).

Over a 25-week period, MA wasn't as-

sociated with increased mortality (SOR: **B**, single RCT). After 44 months, however, MA-treated patients showed decreased median survival (SOR: **B**, single case-control study).

Consistent, meaningful weight gain was not observed with MA treatment (SOR: **B**, single case-control study, single RCT, 2 retrospective chart reviews, single prospective case-series).

Evidence summary

A 25-week double-blind, placebo-controlled RCT of 51 nursing home patients (mean age 76 years, range 50 to 95 years; 96% men) in 2000 found no difference in all-cause mortality between the MA treatment group and the placebo group (absolute risk reduction [ARR]=13.4%; 95% confidence interval [CI], -12.9% to 37.3%; number needed to harm [NNH]=7; 95% CI, -8 to 3).¹

A 2007 case-control study of 17,328 nursing home residents (mean age 84 years [standard deviation, 9]; 71% women) found increased mortality for residents treated with at least 6 days of MA (median survival=23.9 months; 95% CI, 20.2-27.5) compared with untreated residents (median survival=31.2 months; 95% CI, 27.8-35.9).² The decrease in median survival remained after adjusting for demographic variables, medical diagnoses, and cognitive and physical functioning (hazard ratio=1.37; 95% CI, 1.17-1.59). Follow-up ranged from 30 days to 44 months.

Risks related to megestrol acetate include deep vein thrombosis

The 2000 double-blind, placebo-controlled RCT of 51 nursing home patients found no difference in adverse events between the MA group and the placebo group (absolute risk increase=6.3%; 95% CI, -14.7% to 27.3%).¹ No DVTs were reported as adverse events.

A 2003 retrospective chart review of 246 nursing home residents (mean age 87 years, 77% women) who were given MA 400 mg/d found an overall incidence of DVT of 4.1% (10 residents); 3.2% (8) residents were on MA at the time of DVT occurrence.³

A 2000 retrospective chart review of 19 nursing home residents who were prescribed MA (mean age 83 years, range 66 to 92 years; 84% women) found 32% (6) who developed Doppler-confirmed DVT after 50 days of therapy.⁴ DVT was not associated with known risk factors, age, body mass index, numbers of medications, or other medical diagnoses. The authors didn't report MA dosage.

Patients on megestrol acetate don't gain weight...

The 2000 double-blind, placebo-controlled RCT of 51 nursing home patients found no difference between the MA (800 mg/d for 12 weeks) and placebo groups in percentage of patients who gained ≥ 1.82 kg (ARR=-6.6%; 95% CI, -30.2% to 18.2%).¹ At the 25-week follow-up (after the MA patients had been off the therapy for 13 weeks), a statistically, but not clinically, significant difference was observed in the number of MA patients who gained ≥ 1.82 kg (absolute benefit increase=40.2%; 95% CI, 13.4%-66.9%; number needed to treat [NNT]=2; 95% CI, 1-8). Of note, the authors based their statistics on a weight gain of ≥ 1.82 kg whereas 5 kg or 5% weight gain is the more commonly used definition for clinical significance.⁵

The 2007 case-control cohort study of 17,328 nursing home residents, who had lost 5% of total body weight in 3 months or 10% of total body weight in 6 months, also found no significant difference in weight gain between MA-treated patients (median dose=486 mg, range 20 to 2400 mg; median duration=90 days, range 7 to 934 days; median change=1 lb, interquartile range [IQR]=-8 to 10) and controls (median change=2 lb, IQR=-4 to 9) after 6 months of treatment.²

...And some lose weight

In a 2005 prospective case series of 17 nursing home residents (mean age 92 years [standard deviation, 6], 88% women), MA (400 mg/d for 63 days) was associated with weight loss (mean=-2.13 \pm 9.32 lb).⁶ Nine patients (53%) lost weight (mean=9.3 \pm 5.4 lb), and 8 patients (47%) gained weight (mean=5.9 \pm 4.9 lb).

A retrospective chart review in 2000 of 14 nursing home residents (mean age 84 years, range 74 to 97 years; 85% women) who received MA 40 to 800 mg/d for one to 15 weeks showed that 43% gained weight (mean=3.1 kg), 43% lost weight (mean=2.0 kg), and 14% had no weight change.⁷

A 2002 retrospective chart review of 50 nursing home residents (mean age 79 years, range 31 to 93 years; 74% women) who were treated with MA 200 to 2400 mg/d for at least 6 months found a mean weight loss of 1.1 to 2.2 kg.⁸ In the 6 months after MA discontinuation, weight gain for available subjects (5 to 16 patients) varied (mean monthly change=-0.17 kg to 3.07 kg). The study had a high attrition rate (26 patients were lost 6 months after MA initiation; 39 were lost 6 months after MA discontinuation).

Recommendations

The 2015 American Geriatrics Society Beers Criteria for potentially inappropriate medication use in older adults strongly advises against the use of MA because of limited increases in weight and increased risk of thrombotic events.⁹

JFP

References

1. Yeh SS, Wu SY, Lee TP, et al. Improvement in quality of life measures and stimulation of weight gain after treatment with megestrol acetate oral suspension in geriatric cachexia: results of a double-blind placebo controlled study. *J Am Geriatr Soc.* 2000;48:485-492.
2. Bodenner D, Spencer T, Riggs AT, et al. A retrospective study of the association between megestrol acetate administration and mortality among nursing home residents with clinically significant weight loss. *Am J Geriatr Pharmacother.* 2007;5:137-146.
3. Kropsky B, Shi Y, Cherniack EP. Incidence of deep-venous thrombosis in nursing home residents using megestrol acetate. *J Am Med Dir Assoc.* 2003;4:255-256.
4. Bolen JC, Andersen RE, Bennett RG. Deep vein thrombosis as a complication of megestrol acetate therapy among nursing home residents. *J Am Med Dir Assoc.* 2000;1:248-252.
5. Colman E. Food and Drug Administration's Obesity Drug Guidance Document: a short history. *Circulation.* 2012;125:2156-2164.
6. Simmons SF, Walker KA, Osterwell D. The effect of megestrol acetate on oral food and fluid intake in nursing home residents: a pilot study. *J Am Med Dir Assoc.* 2005;6(3 Suppl):S5-S11.
7. Cicero LA, Rosenberg JM, Miyashiro A, et al. Megestrol acetate suspension for the treatment of involuntary weight loss in elderly nursing home residents: a retrospective chart review. *Consult Pharm.* 2000;15:811-814.
8. Dickerson LM, Jones KW. Retrospective review and intervention in the use of megestrol acetate in residents of skilled nursing facilities in South Carolina. *Consult Pharm.* 2002;17:1040-1042.
9. The American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc.* 2015;63:2227-2246.



Megestrol acetate is neither safe nor effective for stimulating appetite in malnourished nursing home residents.



PHOTO ROUNDS FRIDAY

Each Friday, *The Journal of Family Practice* posts a new photo with a brief description and challenges you to make the diagnosis.

Test your skills today!

jfonline.com