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Medscape Medical News

DHEA May Be Effective for Depression Associated With HIV CME

News Author: Laurie Barclay, MD
CME Author: Charles Vega, MD, FAAFP

Complete author affiliations and disclosures, and other CME information, are available at the end of this activity.

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Jan. 24, 2006 — Dehydroepiandrosterone (DHEA) is an effective therapy for treatment of nonmajor depression in patients with HIV/AIDS, according to the results of a randomized trial reported in the January issue of the *American Journal of Psychiatry*.

"Subsyndromal major depressive disorder is common among HIV-positive adults," write Judith G. Rabkin, PhD, MPH, from the New York State Psychiatric Institute, Columbia University College of Physicians and Surgeons in New York, and colleagues. "DHEA is of particular interest for HIV-positive patients, because declining levels of DHEA have been associated with progression to AIDS in both cross-sectional comparisons of HIV-positive men and women at different stages of HIV illness and in longitudinal studies, including a previous study by our group."

In this 8-week trial, 145 patients with subsyndromal depression or dysthymia were randomized to receive either DHEA, using flexible dosing of 100 to 400 mg/day, or placebo. Study completion rates were 90% (69/77) of the DHEA-treated patients and 94% (64/68) of the placebo-treated patients. The primary efficacy endpoint, based on intent-to-treat analysis and completer analysis, was a Clinical Global Impression improvement rating of 1 or 2 (much or very much improved) plus a final Hamilton Depression Rating Scale (HAM-D) score of 8 or less. Safety outcomes included adverse effect reports and measures of CD4 cell count and HIV RNA viral load at baseline and at week 8.

In the intent-to-treat analysis, clinicians' ratings demonstrated that DHEA was superior, with response rates of 56% (43/77) for the DHEA group vs 31% (21/68) for the placebo group. In the completer analysis, response rates were 62% (43/69) for DHEA and 33% (21/ 64) for placebo. Based on intent-to-treat data, the number needed-to-treat was 4 vs 3.4 on the basis of completer data. There were few adverse events and no significant changes in CD4 cell count or HIV RNA viral load in either treatment group.

"Nonmajor but persistent depression is common in patients with HIV/AIDS, and DHEA appears to be a useful treatment that is superior to placebo in reducing depressive symptoms," the authors write. "The low attrition rate in this group of physically ill patients, together with requests for extended open-label treatment, reflect high acceptance of this readily available intervention."

Study limitations include lack of generalizability to patients with major depression or those with substance use disorders, small number of women, absence of long-term follow-up regarding maintenance of response or possible long-term endocrine or other effects of DHEA, and restriction of the study to HIV-positive individuals.

"Given the high acceptance rate and low side effect profile for DHEA in this group of patients with HIV/AIDS, nearly all of whom were taking multiple concurrent medications, it may be appropriate to evaluate the efficacy of DHEA in other groups of physically ill patients in which mild depression is common," the authors conclude. "We do not recommend widespread use of DHEA in the absence of confirmatory efficacy research and more data about longer-term use. For patients who are unwilling to take antidepressants, who express a strong preference for an 'alternative' treatment, and who have nonmajor depression, DHEA may be a reasonable choice."

The National Institutes of Mental Health supported this study.

Am J Psychiatry. 2006;163:59-66

Learning Objectives for This Educational Activity

Upon completion of this activity, participants will be able to:

- Describe the efficacy of DHEA treatment on mood.
- Compare DHEA vs placebo in the treatment of mild depression among patients with HIV infection.

Clinical Context

DHEA is a weakly active adrenal androgen that serves as a precursor to testosterone and estradiol, which are hormones that can have a positive effect on mood when administered exogenously. In addition, the authors of the current study describe that DHEA increases the amount of available insulin-like growth factor, which in turn can increase levels of growth hormone. Growth hormone deficiency has also been linked with depressed mood. Finally, DHEA may modulate inflammatory cytokines, such as tumor necrosis factor, which may be related to depressed mood.

Declines in DHEA levels may also be important in the progression to AIDS among patients infected with HIV. In their current study, researchers compare DHEA with placebo in the treatment of mild depression among a cohort of patients with HIV.

Study Highlights

- Study subjects were adults with HIV who met criteria for dysthymia or subsyndromal depression of at least 3 months' duration. Patients were excluded from study participation if they had current unstable medical conditions, substance abuse, or recent use of steroids.
- Participants were randomized to receive DHEA, which was titrated to a maintenance dose of 300 to 400 mg/day depending on patient response, or matching placebo.
- The duration of the trial was 8 weeks. Study outcomes included a score of very much or much improved on the Clinical Global Impression scale. The authors also measured scores from the HAM-D . A measure of participants' quality of life and the Beck Depression Inventory were also assessed. Serum DHEA levels were followed to judge their relationship to study treatment.
- 145 patients underwent randomization, and 92% of participants finished the 8-week trial. Baseline characteristics between the DHEA and placebo groups were similar. The mean age of the study cohort was 44 years old, and 84% of subjects were male. Ethnicity of the study was cohort was nearly evenly divided between black, white, and Hispanic subjects. The average duration since the diagnosis of HIV was 8.6 years, and two thirds of the group had a diagnosis of AIDS. 80% of the study cohort was receiving antiretroviral treatment, and 20% was receiving testosterone supplementation during the trial. 70% of the study group reported previously receiving treatment of depression, and 10% had DHEA levels below normal at baseline. The mean HAM-D score was 16.
- On intent-to-treat analysis, the clinical response rates of much improved or very much improved were 56% vs 31% in the DHEA and placebo groups, respectively, a significant difference. The mean endpoint HAM-D scores were 8.1 and 9.4,

respectively. This difference was not statistically significant. However, a reduction of at least 50% of the baseline HAM-D score was achieved in 57% of the DHEA group vs 35% of the placebo group (*P* = .009).
- Measures of quality of life and the Beck Depression Inventory did not significantly differ between treatment groups.
- Mean doses of DHEA did not differ between responders and nonresponders nor did final serum levels of DHEA. Similarly, the increase in serum DHEA during the study was not associated with improved study outcomes, and there were no sex differences for DHEA vs placebo therapy.
- Concomitant steroid therapy did not significantly affect the main study outcome.
- Serum testosterone levels increased with DHEA therapy in women, but not in men. DHEA did not significantly affect CD4 counts or the HIV viral load.
- Rates of adverse events were similar between the placebo and DHEA groups.
- An open-label continuation phase of DHEA therapy revealed that DHEA maintained its efficacy in treating depression for 8 months.

Pearls for Practice

- DHEA may improve mood by increasing levels of sex steroids, insulin-like growth factor, and growth hormone while reducing activity of inflammatory cytokines.
- In the current study, DHEA improved clinicians' assessment of mild depression vs placebo among a mostly male cohort of patients with HIV. However, DHEA was not more effective than placebo in the outcomes of HAM-D scores, the Beck Depression Inventory, or quality of life.

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Target Audience

This article is intended for primary care clinicians, psychiatrists, infectious disease specialists, and other specialists who care for patients with mild depression, dysthymia, or HIV infection.

Goal

The goal of this activity is to provide medical news to primary care clinicians and other healthcare professionals in order to enhance patient care.

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News Author

Laurie Barclay, MD
is a freelance writer for Medscape.

Disclosure: Laurie Barclay, MD, has disclosed no relevant financial relationships.

Clinical Reviewer

Gary Vogin, MD
Senior Medical Editor, Medscape

Disclosure: Gary Vogin, MD, has disclosed no relevant financial relationships.

CME Author

Charles P Vega, MD
Associate Professor, Residency Director, Department of Family Medicine, University of California, Irvine

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