

# A Randomized Controlled Trial of Dehydroepiandrosterone in Postmenopausal Women with Fibromyalgia

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**ABSTRACT.** *Objective.* Patients with fibromyalgia (FM) consistently have adrenal hyporesponsiveness and low dehydroepiandrosterone (DHEA) levels. DHEA is promoted for and used by patients with FM. We tested the efficacy and safety of DHEA supplementation in ameliorating the symptoms of FM.

*Methods.* In a double-blind crossover study, postmenopausal women with FM were randomized to DHEA supplementation (50 mg/day) or placebo for 3 months, with a one-month washout period in between. Patients were assessed monthly for well-being and pain and by medical evaluations at the beginning and the end of each treatment period. The primary outcome was well being; secondary outcomes were pain, fatigue, cognition, sexuality, functional impairment, depression, and anxiety.

*Results.* A total of 52 patients were randomized, 47 patients completed the DHEA treatment period, and 45 the placebo treatment period. After 3 months of treatment with 50 mg of DHEA, median DHEA sulfate blood levels had tripled, but there was no improvement in well-being, pain, fatigue, cognitive dysfunction, functional impairment, depression, or anxiety, nor in objective measurements made by physicians. Androgenic side effects (greasy skin, acne, and increased growth of body hair) were more common during the DHEA treatment period ( $p = 0.02$ ).

*Conclusion.* DHEA does not improve quality of life, pain, fatigue, cognitive function, mood, or functional impairment in FM. (J Rheumatol 2005;32:1336–40)

*Key Indexing Terms:*

FIBROMYALGIA THERAPY  
RANDOMIZED CONTROLLED TRIAL

DEHYDROEPIANDROSTERONE  
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Fibromyalgia (FM) is a common clinical syndrome characterized by widespread pain and fatigue. Other common symptoms of FM include memory impairment<sup>1</sup>, psychological distress, morning stiffness, sleep disturbance, headache, and paresthesias. Pathogenesis is unknown, but altered pain modulation<sup>2</sup> and abnormalities in the neuroendocrine system<sup>3,4</sup> have been implicated. The current therapeutic approach to FM is multimodal, involving psychoeducational methods, exercise, and medications to relieve pain, improve sleep, and treat mood disorders. However these

therapeutic approaches are frequently unsatisfactory, and patients often seek alternative therapies<sup>5,6</sup>; among these dehydroepiandrosterone (DHEA) is commonly used.

DHEA and its sulfate ester (DHEA/S) are secreted by the adrenal glands under control of the adrenocorticotropic hormone. DHEA/S reaches its maximum concentrations in individuals at 20–30 years of age, and declines steadily during the following decades to less than 20% of the maximum after 70 years<sup>7</sup>. It is the most abundant steroid in plasma but its physiological function is not fully understood. Some of its activity is through transformation into other steroid compounds such as androgens (testosterone, 5 $\alpha$ -dihydrotestosterone) or estrogens (estradiol, estrone). Clinically DHEA is indicated in adrenal insufficiency, where DHEA supplementation improves well-being, sexual satisfaction, and depression<sup>8</sup>. DHEA also appears to reduce the number of flares in systemic lupus erythematosus (SLE)<sup>9,10</sup>, but has not been approved by the US Food and Drug Administration. DHEA is reported to improve quality of life, better depression, increase bone density, develop muscle strength, increase libido, and enhance cognitive function<sup>11</sup>, but clinical studies are conflicting<sup>7,12</sup>.

The potential usefulness of DHEA in FM is suggested by several clinical observations. Abnormal responses of the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis are seen in FM<sup>13–15</sup>. Particularly,

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adrenal hyporesponsiveness and low DHEA/S levels are observed<sup>13,16-18</sup>. Low levels of DHEA/S correlate with pain and poor physical functioning in FM<sup>16</sup>. Furthermore adrenal insufficiency and FM share similar clinical features and each can be misdiagnosed for the other<sup>19</sup>. Whether adrenal hyporesponsiveness and low DHEA/S levels are related to the pathogenesis of FM or are a consequence of the disease is unclear. Whatever its biological role, DHEA is widely used by FM patients<sup>20</sup>.

To our knowledge, DHEA has never been critically evaluated in FM. The purpose of our study was to evaluate the effects of DHEA supplementation on quality of life, pain, and cognitive function in patients with FM in a double blind, placebo controlled, randomized trial.

## MATERIALS AND METHODS

**Study design.** A double-blind, crossover design was used<sup>8</sup>. After a “run-in” phase of one month with placebo, patients were randomized to receive either DHEA or placebo during an initial treatment period of 3 months, followed by a washout period of one month, before the crossover treatment was given for 3 months (Figure 1). Three-month treatment periods were selected to capture potential neurobehavioral effects of DHEA<sup>12</sup>. Patients were examined at the beginning and at the end of each treatment period and were sent monthly questionnaires in between.

The patients were recruited through the Swiss Association of

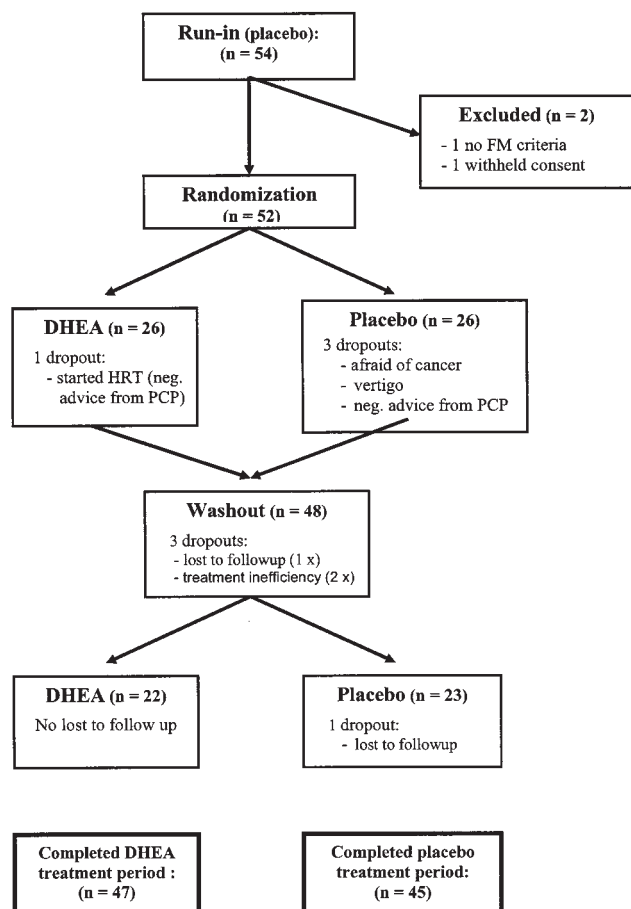


Figure 1. Flow diagram of the study.

Fibromyalgic Patients and the Rheumatology Clinic of University Hospital of Vaud (CHUV). The inclusion criteria were confirmed FM by 1990 American College of Rheumatology classification criteria<sup>21</sup>; female gender; postmenopausal status (or bilateral oophorectomy); and ability to complete questionnaires. The exclusion criteria were current treatment with narcoleptics or steroids; history of sex hormone-responsive cancer (breast, ovarian, or endometrial cancer); advanced liver, kidney, or heart disease; history of chronic inflammatory disease (i.e., rheumatoid arthritis, SLE). The local ethics committee approved the study protocol, and all patients signed informed consent.

**Intervention.** A daily dose of 50 mg DHEA restores low endogenous serum DHEA concentrations<sup>7,22</sup> in the aged, and is considered a replacement dose. The DHEA preparation was obtained through Hawkins Inc. Pharmaceutical Group, Minneapolis, MN, USA. Study capsules of DHEA 50 mg and identical opaque placebo capsules containing mannitol were produced and packed by the hospital’s pharmacy. Patients were asked to take 1 capsule a day and to report any side effects. New medications were given at each visit and exchanged for unused medications, to assess compliance by pill-count.

**Randomization/blinding.** Patients were randomized to either DHEA or placebo in balanced blocks of 6 by means of a random number generator. The medication codes were kept in sealed envelopes until the end of the study. Both patients and investigators were blinded to the treatment group assignment.

**Outcome measures.** Patients were assessed at the beginning and at the end of each treatment period, at baseline, at 3 months, after the washout phase at 4 months, and at 8 months. In between these visits, patients received a monthly questionnaire assessing their quality of life and pain level. The primary outcome was quality of life measured by the Psychological General Well Being Index (PGWBI), which is sensitive to change in FM<sup>23</sup>. The PGWBI is a generic self-administered instrument composed of 6 subscales for a total of 22 items measuring vitality, self-control, positive well-being, general health, anxiety, and depression. The total score ranges from 0 to 110, with higher values indicating better quality of life. Secondary outcomes were pain measured by the Regional Pain Score (RPS)<sup>23</sup>, the number of analgesic pills taken during the last week, depression and anxiety measured by the Hospital Anxiety and Depression Scale (HAD)<sup>24</sup>, functional impairment measured by the Fibromyalgia Health Assessment Questionnaire (FHAQ)<sup>25</sup>, cognitive function as measured by the Cognitive Difficulties Scale (CDS)—short form<sup>26</sup>, and fatigue measured on a 10 cm visual analog scale<sup>27</sup>. Because DHEA is converted into androgens, assessment of sexual satisfaction and libido using the McCoy Female Sexuality Questionnaire (McCoy FSQ)<sup>28</sup> was felt to be of interest. All questionnaires exist in validated French versions. Patients were also asked about potential androgenic side effects such as greasy skin, acne, and increased body hair. During the medical evaluation, cognitive performance was tested with the verbal memory subscale of the revised Wechsler Memory Scale (WMS-R)<sup>29,30</sup> and bodily pain was rated by the physician using the Total Myalgic Score<sup>27</sup>.

**Statistical analyses.** We calculated the sample size based on previous data on the PGWB index in FM<sup>31,32</sup> with the goal of being able to detect a difference at least as large as the effect size found in previous studies (5.4 points). Using these, at least 44 patients would give our study a power of 0.80 with an alpha error of less than 0.05.

Continuous variables were tested for the normality of their distribution with the Shapiro-Wilk test. Comparison of the baseline disease characteristics were based on t tests for continuous normal variables, on Wilcoxon signed rank tests for continuous non-normal variables, and on the chi-square test for dichotomous variables. Efficacy analyses were performed on the intent-to-treat basis. Sporadic missing outcomes (essentially single unreturned questionnaires) were assumed to be missing completely at random.

Quality of life (PGWBI) and pain (RPS), measured at monthly intervals, were correlated and thus a repeated measure analysis was conducted. A profile analysis was used to compare the area under the curve of these

outcomes. Outcomes measured only at the beginning and the end of each treatment period were compared using their change scores during treatment periods with analysis of variance (ANOVA) for data from 2 period, repeated measures, crossover designs<sup>33</sup>. We used the Wilcoxon signed rank test to analyze non-normally distributed change scores and the McNemar's test to contrast differences in proportions. We tested the possibility of a carry-over effect for patients who received DHEA as their first treatment by adding the treatment sequence into the model. We also analyzed the possibility of effect modification by other therapies taken concomitantly by including an interaction term between DHEA and these medications. Only significant covariates or confounding variables were kept in the model. All analyses were conducted with SAS version 8 software.

## RESULTS

A total number of 54 women started the "run-in" phase of the trial, and after a medical assessment, 52 were randomized to received DHEA or placebo (Figure 1). The baseline characteristics of these subjects at randomization showed no significant differences (Table 1). Subjects ranged from 36 to 83 years of age and were all Caucasian. Compliance to the treatment, as estimated by the number of used pills, was 87 (interquartile range, IQR: 7, about 95%) with DHEA and 89 (IQR: 7, about 98%) with placebo ( $p = 0.72$ , Wilcoxon). Eight patients did not complete the whole trial; the most common reason to drop out was treatment's inefficiency to improve symptoms. Forty-seven individuals (98%) finished the DHEA treatment period compared to 45 individuals (92%) in the placebo treatment period ( $p = 0.18$ , chi square). Before DHEA treatment, the enrolled patients with FM had low serum DHEA/S concentrations (1.4  $\mu\text{mol/l}$ , IQR: 4.2). During treatment with DHEA, serum DHEA/S concentrations increased (4.5  $\mu\text{mol/l}$ , IQR: 6.2) to normal ranges for younger women (1.1–7.3  $\mu\text{mol/l}$ )<sup>7</sup>.

Treatment with DHEA did not significantly improve quality of life ( $p = 0.45$ ) nor any of the secondary outcomes (Table 2). Surprisingly, no placebo effect was observed which could be explained by the presence of a run-in phase during which most of the placebo effect may have occurred. As expected, blood DHEA/S levels were significantly higher at the end of the DHEA treatment period ( $p = 0.0001$ ) and androgenic side effects were more common with DHEA: 11

patients (25%) complained of greasy skin, acne, or increased growth of body hair, compared to 2 patients (4%) with placebo ( $p = 0.023$ , McNemar). For sexual satisfaction, the percentage of sexually active women was too low (about 45%) to provide sufficient power to demonstrate an effect. We also examined the possibility of an effect modification by concomitant hormone replacement therapy (HRT), antidepressant medication, or low baseline DHEA/S levels. We found no evidence that DHEA supplementation was more effective in patients without HRT ( $p = 0.31$ ), without antidepressant medication ( $p = 0.34$  respectively), or with low baseline DHEA/S levels ( $p = 0.58$ ).

## DISCUSSION

DHEA is sold in large quantities as "dietary supplement" in the USA<sup>34,35</sup> and is promoted as "antidote for aging," to increase libido, strengthen the immune system, prevent memory loss, and treat FM<sup>20</sup>. We conducted a randomized, controlled, crossover study of the effects of DHEA supplementation on common complaints of patients with FM. After 3 months of treatment with 50 mg of DHEA, median DHEA/S blood levels had tripled, but there was no improvement in well-being, pain, fatigue, cognitive dysfunction, functional impairment, depression, or anxiety, nor in objective measurements made by the physicians. On the contrary, patients reported more androgenic side effects (greasy skin, acne, and increased growth of body hair) while on DHEA.

FM shares adrenal hyporesponsiveness and low DHEA/S levels with other diseases such as SLE or adrenal insufficiency, where DHEA treatment has shown some beneficial effects<sup>8-10</sup>. Baseline DHEA/S levels in this study were low (1.4, IQR: 4.2  $\mu\text{mol/l}$ ), consistent with DHEA/S levels found in FM by others<sup>3,17</sup>. This is the first controlled study, to our knowledge, that investigates the effects of a DHEA supplementation in patients with FM and is totally negative. Our results do not support the hypothesis of a primary role of the HPA axis in the pathogenesis of FM<sup>3</sup> and suggest that adrenal hyporesponsiveness may be a secondary phenomenon, possibly associated with chronic pain.

This study had a relatively small sample size, which allows the possibility of a false negative result. However, the sample size had a predicted power of 80% to detect changes in quality of life, the study's primary outcome. The fact that DHEA had no significant effect on the 10 secondary outcomes also strongly suggests that this is not a false negative result. The number of sexually active women was too small to allow a definitive conclusion regarding the effects of DHEA on sexual satisfaction in this population.

Studies using crossover designs assume that the effect induced by the medication is short lived, removed after discontinuation during the washout period and with no carry-over effect thereafter. The pharmacological half-life of DHEA is about 24 h in healthy elderly<sup>7</sup>; therefore a one-month washout period seems adequate. In the analysis, we

*Table 1.* Baseline characteristics. There were no significant differences for any of the patient characteristics. Values are given as mean (standard deviations), medians (interquartile ranges), or as absolute numbers (proportions).

Patient Characteristics	Group 1	Group 2
N	26	26
Age, yrs, mean (SD)	59.2 (8.8)	58.7 (9.7)
Disease duration, yrs, median (IQR)	13 (10)	10 (12)
Working	7 (27%)	6 (22%)
Retired or social insurance	17 (65%)	15 (58%)
Hormone replacement therapy	10 (38.5%)	13 (50%)
Antidepressants	17 (65%)	14 (54%)
DHEA/S level, $\mu\text{mol/l}$ , median (IQR)*	2.2 (4.2)	1.4 (1.6)

\* Serum DHEA/S measurements after 4 months of placebo.

Table 2. Outcome measures before and after treatment with DHEA or placebo. Values are given as mean (standard deviation) unless otherwise indicated. When not normally distributed, variable medians (IQR) are reported.

Outcomes [range]*	DHEA		Placebo		p
	Baseline (n = 49)	3 Months (n = 47)	Baseline (n = 48)	3 Months (n = 45)	
DHEA level, $\mu\text{mol/l}$ , median		4.5 (6.2)		1.4 (4.2)	< 0.0001
Quality of life					
PGWBI [0–110]	59.2 (5.7)	59.6 (4.8)	58.5 (4.7)	58.9 (5)	0.45
Pain					
RPS [0–105]	55.8 (16)	55.2 (18)	55.4 (20)	58.9 (5)	0.79
Myalgic score [0–54]	29.6 (11)	28.4 (13)	27.9 (12)	28.5 (14)	0.28
Analgesic pills/wk, median*	14 (26)	11 (21)	10 (20)	14 (25)	0.26
Depression and anxiety					
HAD-D [0–21]	8.4 (4.3)	8.7 (4.4)	8.1 (4)	8.4 (4.3)	0.61
HAD-A [0–21]	11.6 (4.8)	10.9 (4.9)	11.1 (4.9)	10.9 (4.8)	0.10
Cognitive dysfunction					
CDS [0–80]	48.6 (15)	47.4 (15)	48.5 (15)	46.8 (16)	0.76
WMS-R [0–150]	67.3 (16)	69.8 (19)	68.8 (18)	71.5 (19)	0.52
Functional impairment					
FHAQ [0–24]	8.3 (4.1)	8.5 (3.6)	8.4 (4.2)	9.5 (4.3)	0.06
Fatigue (VAS) [0–100], median	78 (41)	74 (31)	80 (36)	78 (24)	0.43
Sexual function					
McCoy FSQ [9–63], median	35 (12)	36.5 (10)	35 (12.5)	32 (11)	0.50
	(n = 20)	(n = 20)	(n = 22)	(n = 22)	

PGWBI: Psychological General Well Being Index, higher score indicate better quality of life; RPS: Regional Pain Score, higher scores indicate more severe pain; Myalgic score: higher scores indicate more severe pain; HAD-D: Hospital Depression Scale, higher scores indicate more severe depression; HAD-A: Hospital Anxiety Scale, higher scores indicate more severe anxiety; CDS: Cognitive Difficulties Scale, higher scores indicate more subjective memory impairment; WMS-R: Wechsler Memory Scale-Revised, verbal memory subscale, higher scores indicate better memory function; FHAQ: Fibromyalgia Health Assessment Questionnaire, higher scores indicate more functional impairment; Fatigue (VAS): Visual analog scale for fatigue, higher scores indicate more fatigue; McCoy FSQ: McCoy female sexuality questionnaire, higher scores indicate more sexual satisfaction. The number of women who answered this questionnaire was lower. \* Comparison of outcome change scores during the 2 treatment periods. Analysis of variance (ANOVA) for normally distributed continuous variables and Wilcoxon test for non-normally distributed variables.

examined a possible effect of treatment sequence, but found no statistically significant carryover effect. We cannot exclude the possibility that a beneficial effect of DHEA might have appeared after 3 months. A DHEA dose of 50 mg/day was chosen because this dose is sufficient to restore physiological levels of DHEA in individuals with adrenal insufficiency<sup>22</sup>. Because FM is a chronic disease, it was felt unethical to expose patients to suprphysiologic hormonal doses for a longer period. Also 50 mg/day of DHEA is the most commonly studied dose in trials for cognition and well-being in healthy individuals<sup>12</sup>; it is however possible that a higher dose of DHEA could have been more effective. The compliance with DHEA treatment was confirmed with serum hormone measurements and returned pill counts. We could not exclude concomitant self-medication with other sources of DHEA, but DHEA is not sold over-the-counter in Switzerland, which makes it difficult to obtain. Furthermore, serum DHEA levels while taking placebo were low, suggesting no significant external source of DHEA.

To increase the potential generalizability of this study we did not exclude patients taking antidepressants or HRT, which

represents a substantial proportion of postmenopausal FM subjects. We examined the possibility of an effect modification of DHEA by these drugs and found no significant effect. However, larger studies in different subgroups of patients with FM would be necessary to confirm these results.

To our knowledge, this is the first placebo-controlled study of DHEA supplementation for FM. DHEA supplementation, although apparently frequently used by patients with FM, does not improve quality of life, mood, pain, fatigue, cognitive function, or functional impairment.

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#### REFERENCES

1. Sephton SE, Studts JL, Hoover K, et al. Biological and psychological factors associated with memory function in



- fibromyalgia syndrome. *Health Psychol* 2003;22:592-7.
2. Desmeules JA, Cedraschi C, Rapiti E, et al. Neurophysiologic evidence for a central sensitization in patients with fibromyalgia. *Arthritis Rheum* 2003;48:1420-9.
  3. Dessein PH, Shipton EA, Stanwix AE, Joffe BI. Neuroendocrine deficiency-mediated development and persistence of pain in fibromyalgia: a promising paradigm? *Pain* 2000;86:213-5.
  4. Adler GK, Manfredsdotir VF, Creskoff KW. Neuroendocrine abnormalities in fibromyalgia. *Curr Pain Headache Rep* 2002;6:289-98.
  5. Pioro-Boisset M, Esdaile JM, Fitzcharles MA. Alternative medicine use in fibromyalgia syndrome. *Arthritis Care Res* 1996;9:13-7.
  6. Poyhia R, Da Costa D, Fitzcharles MA. Pain and pain relief in fibromyalgia patients followed for three years. *Arthritis Rheum* 2001;45:355-61.
  7. Legrain S, Massin C, Lahlou N, et al. Dehydroepiandrosterone replacement administration: pharmacokinetic and pharmacodynamic studies in healthy elderly subjects. *J Clin Endocrinol Metab* 2000;85:3208-17.
  8. Arlt W, Callies F, van Vlijmen JC, et al. Dehydroepiandrosterone replacement in women with adrenal insufficiency. *N Engl J Med* 1999;341:1013-20.
  9. Chang DM, Lan JL, Lin HY, Luo SF. Dehydroepiandrosterone treatment of women with mild-to-moderate systemic lupus erythematosus: a multicenter randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2002;46:2924-7.
  10. Petri MA, Lahita RG, Van Vollenhoven RF, et al. Effects of prasterone on corticosteroid requirements of women with systemic lupus erythematosus: a double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 2002;46:1820-9.
  11. Larkin M. DHEA: will science confirm the headlines? *Lancet* 1998;352:208.
  12. Huppert FA, Van Niekerk JK. Dehydroepiandrosterone (DHEA) supplementation for cognitive function. *Cochrane Database Syst Rev* 2001:CD000304.
  13. Crofford LJ, Pillemer SR, Kalogeras KT, et al. Hypothalamic-pituitary-adrenal axis perturbations in patients with fibromyalgia. *Arthritis Rheum* 1994;37:1583-92.
  14. Ferraccioli G, Cavalieri F, Salaffi F, et al. Neuroendocrinologic findings in primary fibromyalgia and in other chronic rheumatic conditions. *J Rheumatol* 1990;17:869-73.
  15. Pillemer SR, Bradley LA, Crofford LJ, Moldofsky H, Chrousos GP. The neuroscience and endocrinology of fibromyalgia. *Arthritis Rheum* 1997;40:1928-39.
  16. Dessein PH, Shipton EA, Joffe BI, Hadebe DP, Stanwix AE, Van der Merwe BA. Hyposecretion of adrenal androgens and the relation of serum adrenal steroids, serotonin and insulin-like growth factor-1 to clinical features in women with fibromyalgia. *Pain* 1999;83:313-9.
  17. Margaux J, Gervy C, De Maertelaer V, Gangji V, Steinfeld S, Appelboom T. Low serum concentrations of DHEA sulphate in fibromyalgia [abstract]. *Arthritis Rheum* 2001;44 Suppl:S70.
  18. Adler GK, Kinsley BT, Hurwitz S, Mossey CJ, Goldenberg DL. Reduced hypothalamic-pituitary and sympathoadrenal responses to hypoglycemia in women with fibromyalgia syndrome. *Am J Med* 1999;106:534-43.
  19. Kaganov Y, Gattas N, Rimon D. Fibromyalgia-like syndrome secondary to Addison's disease. *J Clin Rheumatol* 2000;6:27-9.
  20. Lichten M. Fibromyalgia: New treatments with DHEA, and growth hormone may bring improvement! [Internet] [cited 2005 Mar 02]. Available from: <http://www.usdoctor.com/fibro.htm>
  21. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990;33:160-72.
  22. Arlt W, Justl HG, Callies F, et al. Oral dehydroepiandrosterone for adrenal androgen replacement: pharmacokinetics and peripheral conversion to androgens and estrogens in young healthy females after dexamethasone suppression. *J Clin Endocrinol Metab* 1998;83:1928-34.
  23. Finckh A, Morabia A, Deluze C, Vischer T. Validation of questionnaire-based response criteria of treatment efficacy in the fibromyalgia syndrome. *Arthritis Care Res* 1998;11:116-23.
  24. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361-70.
  25. Wolfe F, Hawley DJ, Goldenberg DL, Russell IJ, Buskila D, Neumann L. The assessment of functional impairment in fibromyalgia (FM): Rasch analyses of 5 functional scales and the development of the FM Health Assessment Questionnaire. *J Rheumatol* 2000;27:1989-99.
  26. Poitrenaud J, Israël L, Kozarevic D. Factorial structure and empirical validity of a shortened french version of the McNair and Khan' Scale on cognitive difficulties in activities of daily living. In: Beregi E, Gergely IA, Rajczi K, editors. Proceedings of the XVth Congress of the International Association of Gerontology 1993, July 4-9; Budapest. Bologna: Monduzzi; 1993.
  27. Littlejohn GO. A database for fibromyalgia. *Rheum Dis Clin North Am* 1995;21:527-57.
  28. McCoy N, Matyas R. McCoy female sexuality questionnaire. In: Davis CM, editor. Handbook of sexuality-related measures. Thousand Oaks: Sage; 1998:249-50.
  29. Wechsler D: Wechsler Memory Scale — revised. New York, Psychological Corporation/Harcourt Brace Jovanovich, 1987.
  30. Grace GM, Nielson WR, Hopkins M, Berg MA. Concentration and memory deficits in patients with fibromyalgia syndrome. *J Clin Exp Neuropsychol* 1999;21:477-87.
  31. Cedraschi C, Desmeules J, Rapiti E, et al. Fibromyalgia: a randomised, controlled trial of a treatment programme based on self-management. *Ann Rheum Dis* 2004;63:290-6.
  32. Deluze C, Bosia L, Zirbs A, Chantraine A, Vischer TL. Electroacupuncture in fibromyalgia: results of a controlled trial. *BMJ* 1992;305:1249-52.
  33. Kleinbaum DG, Kupper LL, Muller KE, Nizam A. Applied regression analysis and other multivariable methods. Pacific Grove: Duxbury Press; 1998.
  34. Parasrampur J, Schwartz K, Petesch R. Quality control of dehydroepiandrosterone dietary supplement products [letter]. *JAMA* 1998;280:1565.
  35. Skolnick AA. Scientific verdict still out on DHEA. *JAMA* 1996;276:1365-7.