Potential Beneficial Effects of DHEA in Humans

Wendy M Kohrt, PhD
Professor of Medicine
Division of Geriatric Medicine
University of Colorado Health Sciences Center
Denver, Colorado
Potential Beneficial Effects of DHEA in Humans

- overview of DHEA metabolism
- effects of DHEA administration
  - animal models
  - young men
  - older women and men
- summary
Potential Beneficial Effects of DHEA in Humans

- overview of DHEA metabolism
- effects of DHEA administration
  - animal models
  - young men
  - older women and men
- summary
DHEA/DHEAS

Androstenedione

Testosterone

DHT

Estradiol
DHEAS
“The Mother Steroid”

DHEAS is an abundant hormone that serves as a precursor to:

✧ ~50% of androgens in adult men
✧ ~75% of active estrogens in premenopausal women
✧ nearly 100% of active estrogens in postmenopausal women

DHEA/DHEAS

- Most abundant steroid in human plasma
- Concentrations in humans are much higher than in animals
- Lack of an appropriate animal model has limited the understanding of the metabolism of DHEA(S) and its biological effects in humans
- DHEA is widely distributed in the body:
  - brain > plasma > spleen > kidneys > liver
### Abundance of DHEAS

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>DHEAS</td>
<td>8,000 nM</td>
<td>10,000 nM</td>
</tr>
<tr>
<td>DHEA</td>
<td>32 nM</td>
<td>20 nM</td>
</tr>
<tr>
<td>T</td>
<td>3 nM</td>
<td>30 nM</td>
</tr>
<tr>
<td>$E_2$</td>
<td>0.22 nM</td>
<td>0.15 nM</td>
</tr>
</tbody>
</table>
Serum DHEAS vs Age

Serum DHEAS (µM)

Age (yr)

Men
Women
Serum DHEAS and Cortisol Levels in Premenopausal Women

Age (yr) 21-25 26-30 31-35 36-40
Serum DHEAS, ng/mL 3.2 ± 0.5 2.9 ± 0.4 2.5 ± 0.3 1.9 ± 0.2
-40%

Age (yr) 21-25 26-30 31-35 36-40
Serum Cortisol, µg/dL 8.5 ± 1.2 9.0 ± 1.3 9.5 ± 1.4 10.0 ± 1.5
Potential Beneficial Effects of DHEA in Humans

- overview of DHEA metabolism
- effects of DHEA administration
  - animal models
  - young men
  - older women and men
- summary
Effects of DHEA Supplementation in Rodents

- **Anti-obesity**
  - prevents fat gain in obesity-prone strains and reverses obesity

- **Anti-diabetogenic**
  - enhances insulin action

- **Anti-atherogenic**
  - diminishes atherosclerotic plaque
20 Months of DHEA Supplementation in Rats

Effects of a 12-wk Atherogenic Diet Plus DHEA on Aortic Plaque

Potential Beneficial Effects of DHEA in Humans

- overview of DHEA metabolism
- effects of DHEA administration
  - animal models
  - young men
  - older women and men
- summary
DHEA Reduces LDL Levels and Body Fat but does not Alter Insulin Sensitivity in Normal Men


- 10 men, aged 22-25 yr
- placebo or DHEA, 1600 mg/d, 28 d
- body composition - hydrodensitometry
- insulin action - euglycemic, hyperinsulinemic clamp
- no side effects noted in either group
<table>
<thead>
<tr>
<th></th>
<th>Placebo Baseline</th>
<th>∆</th>
<th>DHEA Baseline</th>
<th>∆</th>
</tr>
</thead>
<tbody>
<tr>
<td>DHEAS, µM</td>
<td>9.9</td>
<td>-1.2</td>
<td>10.9</td>
<td>27.9*</td>
</tr>
<tr>
<td>Total T, nM</td>
<td>29.0</td>
<td>1.4</td>
<td>26.6</td>
<td>3.3</td>
</tr>
<tr>
<td>Free T, nM</td>
<td>12.9</td>
<td>-1.3</td>
<td>11.0</td>
<td>5.9</td>
</tr>
<tr>
<td>Andro, nM</td>
<td>5.5</td>
<td>0.3</td>
<td>4.3</td>
<td>4.3*</td>
</tr>
<tr>
<td>E₂, pM</td>
<td>117</td>
<td>-26</td>
<td>117</td>
<td>-14</td>
</tr>
<tr>
<td>E₁, pM</td>
<td>193</td>
<td>35</td>
<td>194</td>
<td>38</td>
</tr>
<tr>
<td>SHBG, nM</td>
<td>17.9</td>
<td>2.9</td>
<td>17.5</td>
<td>-3.6</td>
</tr>
</tbody>
</table>

Effect of DHEA Supplementation on Body Composition

Lack of an Effect of DHEA in Obese Men


- 6 men, aged 21-37 yr, BMI 28-38 kg/m²
- **DHEA, 1600 mg/d, 28 d**
- body composition - hydrodensitometry, BIA, anthropometry
- no side effects of DHEA
Effect of Oral DHEA on Serum Testosterone and Adaptations to Resistance Training in Young Men


- 19 men, aged 19-29 yr
- placebo or DHEA, 150 mg/d, wks 1,2,4,5,7,8
- body composition – hydrodensitometry
- strength – 1 repetition maximums
- no side effects reported
Androstenedione (nM)

10
5
0

T-TOTAL (nM)

20
15
10
5
0

T-FREE (pM)

105
95
85
75
0

Weeks

0 2 4 6 8

Estrone (pM)

- 75
- 85
- 95
- 105
- 115

Estradiol (pM)

- 230
- 240
- 250
- 260
- 270

Estriol (pM)

- 180
- 200
- 220
- 240
- 260

Weeks

0 2 4 6 8

Potential Beneficial Effects of DHEA in Humans

- overview of DHEA metabolism
- effects of DHEA administration
  - animal models
  - young men
  - older women and men
- summary
<table>
<thead>
<tr>
<th>M/W</th>
<th>Age</th>
<th>Treat</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morales et al. 13/17*</td>
<td>40-70</td>
<td>3 mo 50 mg</td>
<td>↑ IGF-1, ↓ HDL-C (W), ↑ well-being</td>
</tr>
<tr>
<td>(2 W, facial hair)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morales et al. 8/8*</td>
<td>50-65</td>
<td>6 mo 100 mg</td>
<td>↑ IGF-1, ↑ FFM, ↓ FM (M)</td>
</tr>
<tr>
<td>(no AE)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Casson et al. 0/13</td>
<td>&gt;50</td>
<td>6 mo 25 mg</td>
<td>↑ IGF-1, ↓ HDL-C</td>
</tr>
<tr>
<td>(no AE)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Villareal et al. 16/20</td>
<td>64-82</td>
<td>6 mo 50 mg</td>
<td>↑ IGF-1, ↑ FFM, BMD, ↓ FM</td>
</tr>
<tr>
<td>(1 W, acne)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baulieu et al. 140/140</td>
<td>60-79</td>
<td>12 mo 50 mg</td>
<td>??</td>
</tr>
<tr>
<td>(no AE)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Effects of DHEA Replacement on Bone Mineral Density and Body Composition in Elderly Women and Men


- open-label study of oral DHEA replacement, 50 mg/d
- 10 women, 8 men; aged 64 to 82 yr (18 sex- and age-matched convenience controls)
- serum DHEAS <20% of mean value in young subjects
Serum DHEAS (nmol/L)

Men

Women

Baseline 3 mo DHEA 6 mo DHEA

Young Controls

Older

Serum IGF-1, ng/mL

Comparing 0 months, 3 months, and 6 months for Men and Women.

Potential Beneficial Effects of DHEA in Humans

- overview of DHEA metabolism
- effects of DHEA administration
  - animal models
  - young men
  - older women and men
- summary
Summary

- There have been few controlled trials of DHEA supplementation. Available data do not provide evidence that DHEA enhances performance.
Summary

- There are intriguing data that suggest that DHEA supplementation (replacement) can increase lean mass and decrease fat mass, but these findings are not uniform. Potential mechanisms include increases in androgens and/or growth factors in response to DHEA.
Future Research Directions

- In general, additional controlled trials are needed to better understand the sex- and age-specific responses to DHEA supplementation and the mechanisms of action.

- Preliminary studies should evaluate potential effects of DHEA supplementation in eugonadal and hypogonadal athletes.