

Chapter 10

Summary

Dehydroepiandrosterone (DHEA) and its sulfated conjugate DHEA-S are two steroids synthesized in highest concentrations by humans from adrenal cortex (DHEA, 6-8 mg / day; DHEA-S, 15-18 mg / day). The pattern of secretion is characteristically age-related. The concentration of DHEA in the serum is low in early age, starts increasing at around 2 years before the onset of puberty, peaks at adult stage and declines after the age of 35 to 40 years. Based on this characteristic age-related pattern DHEA is alleged to be the YOUTH HORMONE. Many people are using DHEA and its conjugate DHEA-S as nutritive supplement or as anti-aging drug. Many reports suggest that DHEA/DHEA-S helps to cope up with age related consequence. It may be used as drug or supplement for disease like cancer, diabetes, atherosclerosis, heart disease, kidney disease, parasite infection, malaria etc. It is also known as neurosteroid and has a role in memory and cognition. But there are also some reports which showed no effect of DHEA treatment and on the contrary on over dose of DHEA as harmful or even lethal. Hence, there is a controversy about the role of exogenous DHEA and this leads to an unclear picture on DHEA being the youth hormone. This was the idea behind the present study.

In the present study effects of exogenous DHEA in development and aging were examined on brain and liver mitochondria using rat model. Mitochondrial respiration rates, other mitochondrial enzymes related to electron transport chain i.e. activity of ATPase, glutamate dehydrogenase (GDH), succinate DCIP reductase (SDR), Mitochondrial and cytosolic malate dehydrogenase (MDH) and content of cytochromes aa₃, b and c+c₁ were checked. Also lipid/phospholipid profile of mitochondrial membrane was scrutinized. DHEA was administered subcutaneously for 7 consecutive days to different age groups, age on the eighth day were 3 weeks, 5 weeks, young adult (8-10 weeks) and old animals (1.5-2 years)].

The first part of the study was dose standardization. For this young adult rats were injected subcutaneously (doses used 0.1 mg, 0.2 mg, 1 mg and 2 mg/kg body weight) for seven consecutive days. On the eighth day rats were sacrificed and the mitochondria were isolated from the brain and liver. We found that the DHEA treatment influenced the respiratory parameters in tissue specific and dose

dependent manner. Marginal effects were seen at lower dose (0.1 mg) and at higher dose (2 mg) in some cases adverse effects were observed. Lipid/phospholipid profile also altered in dose dependent and tissue specific manner. Hence, for further studies we have decided to use two doses (0.2 mg and 1 mg) where maximum effects were seen.

In the next part of the study, the effects of DHEA were investigated in development and aging. For this study the different age groups mentioned above were injected with two different doses (0.2 mg and 1 mg) in similar way. We have found that DHEA treatment positively influenced development and maturation of mitochondria of brain and liver from developing rats. The treatment also improved the respiratory parameters in old rats and the values were comparable to untreated young adults in most cases. Lipid/phospholipid profile was age specific. It was altered after DHEA treatment in all groups. For some parameters the values after DHEA treatment were more or less comparable to untreated young adult rats. In short DHEA treatment has helped development and aging.

Since, effects of DHEA were dose dependent, age dependent and tissue specific it is important to know how exactly DHEA exerts its effects. Because some parameter increases or decreases with increasing dose while in some cases increase or decrease were more with lower dose but effect declined at higher dose. Effects were more pronounced in developing and old rats than young adult rats which may be because at young adult age DHEA present in vivo is at the highest levels.

To further confirm this one could find out the serum and tissue levels of DHEA after different doses and then look for different gene expression in different age groups.