

Abstract

J Nutr Biochem. 2004 Apr;15(4):210-9.

Suppression of steroidogenesis and activator protein-1 transcription factor activity in rat adrenals by vitamin E deficiency-induced chronic oxidative stress.

Abidi P, Leers-Sucheta S, Azhar S.

Geriatric Research, Education and Clinical Center, Veterans Affairs Palo Alto Health Care System, Palo Alto, CA 94304, USA.

BACKGROUND: Excessive oxidative stress and associated macromolecular damage are considered to be key features of aging, and appear to contribute to the age-related decline in steroid hormone production in adrenal and testicular Leydig cells.

OBJECTIVE: The current studies were initiated to examine the potential mechanism by which excessive oxidative stress during aging attenuates the functional expression of the oxidant-responsive transcription factor Activator protein-1.

METHODS: Chronic oxidative stress was induced in vivo by maintaining groups of rats on a diet deficient in vitamin E for 6 months.

RESULTS: Plasma, liver, and adrenal tissues from vitamin E-deficient animals had negligible levels of this vitamin and showed high susceptibility to in vitro lipid peroxidation. Synthesis and secretion of corticosterone in response to corticotropin (ACTH), dibutyryl-cAMP, or 20alpha-hydroxycholesterol in vitro was significantly reduced in adrenocortical cells prepared from rats deficient in vitamin E. AP-1 DNA-binding activity was diminished approximately 55 % in adrenal extracts from vitamin E-deficient rats with no corresponding change in the binding activity of SP-1. The vitamin E deficiency-mediated loss of AP-1 activity was not due to an alteration in the dimeric composition of constituent proteins, but rather to a general down-regulation of steady-state levels of members of the Fos and Jun families of proteins. Interestingly, vitamin E deficiency also reduced the expression of the redox-regulated Ref-1 protein.

CONCLUSION: Collectively these data demonstrate that chronic oxidative stress specifically down-regulates essential components of the AP-1 transcription factor complex, and suggest that aberrancies in AP-1 expression may adversely affect processes crucial for intracellular cholesterol transport and steroid hormone production.

PMID: 15068814