New study suggests link between chronic estrogen exposure and high blood pressure

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For many years doctors believed the estrogen women consumed in the form of oral contraceptives and hormone replacement therapy (HRT) pills was good for their patients' hearts. Recent studies however have shown that long-term exposure to estrogen can be a danger to women as it has been associated with high blood pressure, a key link to heart- and brain-attacks (strokes). Although the process by which estrogen induces high blood pressure in females is unclear, Michigan State University (MSU) researchers have found that long-term estrogen exposure generates excessive levels of a compound, superoxide, which causes stress in the body. The build-up of this compound occurs in an area of the brain that is crucial to regulating blood pressure, suggesting that chronic estrogen induces a build up of superoxide that in turn causes blood pressure to increase. The study also found that the anti-oxidant resveratrol reverses the increase in both superoxide and blood pressure.

The study is entitled Chronic Estradiol-17β Exposure Increases Superoxide Production in the Rostral Ventrolateral Medulla (RVLM) and Causes Hypertension: Reversal by Resveratrol." It appears in the Articles in PresS section of the *American Journal of Physiology – Regulatory, Integrative, and Comparative Physiology*, published by the American Physiological Society.

Methodology

The researchers looked to the rostral ventrolateral medulla (RVLM), a

critical region in the brain stem known to be involved with the maintenance of blood pressure and thought to be associated with hypertension and heart failure. They theorized that chronic exposure to low levels of estrogen (in the form of estradiol-17β, also called E2) could influence this area of the brain. They hypothesized that E2 exposure could increase the anti-oxidant superoxide, which causes stress in the body and the RVLM to respond by increase the body's blood pressure. They also wanted to examine whether or not resveratrol, the anti-oxidant that has a strong beneficial impact on the brain, would have a positive effect on superoxide and blood pressure activity.

To test their hypotheses they conducted a two-phase experiment using rats. In phase 1, animals were divided into groups and used as either controls or implanted with E2. After 90 days of E2 exposure the animals were examined and key data collected. In phase 2, the animals were used as either controls or implanted with E2 and, in addition, fed resveratrol-laced chow for 90 days. As with phase 1, RVLM was subsequently isolated from each animal and examined for increases in superoxide, hypertension and other key health markers.

Results

The researchers found that chronic E2 exposure caused a significant increase in superoxide in the RVLM, and in blood pressure. In addition they determined that the increases in both indicators were reversed with resveratrol. Taken together, the findings demonstrate that chronic exposure to low levels of E2 is capable of causing hypertension, possibly by increasing superoxide generation in the RVLM.

Importance of the Findings

In an interview, lead study author Dr. P.S. MohanKumar said, "This is an

important study on at least two levels. First, it continues to confirm the negative effect that long-term estrogen exposure has for females. Second, it provides a new rationale for how and why this relationship occurs."

Dr. MohanKumar continued, "Because so many women use estrogen-only HRT to combat the effects of menopause, it is imperative that we better understand the risks that chronic exposure has for females and why these effects occur. In studies such as this we come one step closer to clarifying the relationship and have established a launch pad for identifying how the process might be interrupted in the future."

More information: ajpregu.physiology.org/content …0.2011.full.pdf+html

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