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Could a longer reproductive period put women at greater risk for Alzheimer disease?

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Estrogen has been thought to play a role in a woman's risk of developing Alzheimer disease (AD). A new study has taken a different approach to identifying risk factors for AD by examining the association between a woman's reproductive life span as an indicator of endogenous estrogen exposure and levels of cerebrospinal fluid biomarkers. Study results are

published online in *Menopause*.

Alzheimer disease represents 60% to 70% of all dementia diagnoses, making it the most common form of dementia. Approximately two-thirds of those with AD are women. This is not surprising, because age is the greatest known risk factor for AD, and women tend to live longer than men.

The incidence of AD is rising quickly because of the aging population, so multiple studies have been undertaken to identify other risk factors, especially those that may explain any sex differences. Prior studies have shown a link between both higher and lower estradiol blood levels and risk of dementia, whereas others have identified no associations. Some studies have shown that hormone therapy after menopause can increase the risk of dementia, but others have documented a decreased risk. Similarly, cognitive decline has been linked with both longer and shorter reproductive periods.

Despite all the conflicting evidence, few, if any, studies have examined the association between estrogen and biomarkers for AD in cerebrospinal fluid, the clear body fluid found within the tissues surrounding the brain and spinal cord. In this new study, a small sampling of women who were free of dementia and underwent natural menopause were followed for 25 years. Based on the results from the cerebrospinal fluid samples, researchers concluded that a longer reproductive life was associated with increased levels of AD biomarkers in the preclinical phase of the disease; however, they suggested that larger studies should be conducted to confirm these findings.

Study results appear in the article "Reproductive period and preclinical cerebrospinal fluid markers for Alzheimer disease: a 25-year study."

"This small population-based study showed an association between

duration of the reproductive life span (a surrogate marker for exposure to endogenous estrogen) and biomarkers of Alzheimer disease in the cerebrospinal fluid of women without dementia. This finding needs to be confirmed in larger studies but may be another factor contributing to the increased burden of Alzheimer disease in women that, at least in part, likely relates to aging and the longer life expectancy in women compared with men," says Dr. Stephanie Faubion, NAMS medical director.

Provided by The North American Menopause Society