

Pregnancies – *risk factor for Alzheimer's disease*

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Alzheimer's disease (AD) is the most common cause of cognitive impairment, affecting about 10% of the United States population over 65 years of age and 50% older than 85. Epidemiological studies revealed a higher risk of developing AD in post-menopausal women than in men of the same age. The more probably explanation of the gender-dependent incidence of late-onset AD is the reduction of estrogens levels that occurs in post-menopausal women. If this hypothesis is correct, hormone replacement therapy (HRT) would be a potential preventive therapy of AD in women.

However, observational studies did not confirm the protective effect of estrogens, and the only randomized clinical trial did not support a protective effect of HRT, at least in women aged 65 and older, indicating HRT as an important cardio- and cerebrovascular risk factor and suggesting HRT could double the risk of AD. Increased number of pregnancies is also a possible AD risk factor, showed that women with more pregnancies had an earlier onset of AD.

The aim of this study is to investigate whether a higher exposure to endogenous estrogens is associated with lower risk of dementia or not. It was also evaluated head trauma as a possible risk factor and the educational level as a protective factor for AD.

For this retrospective case-control study, were studied 204 women affected by AD and 201 age-matched women without neurological diseases, with a mean clinical 15 month follow up, randomly chosen amongst wives of AD patients (75.3 ± 6.8 years for AD group and 74.3 ± 6 years for control group).

Compared with the AD group, the control group had significantly higher educational levels, higher percentage of nulliparous women and higher number of women treated with HRT. In the AD group there was a significant higher incidence of head trauma, and a higher percentage of women with three or more pregnancies.

The risk of developing AD is 2.2-fold for women without HRT, and 2.1-fold for those with head trauma. The risk also increases with the number of pregnancies. Indeed, the risk of AD for women with one or two pregnancies, in comparison with the nulliparas, is 1.8-fold but it becomes 3.2-fold for those that had three or more pregnancies.

The AD patients with more than three pregnancies have an earlier onset of disease in comparison with the other AD patients (71.7 ± 7 years vs. 75.6 ± 6.7 ; $P = 0.01$).

No relationship was found between disease progression and number of pregnancies, reproductive period and iatrogenic menopause. All these negative data argue against the protective effect of estrogens for AD.

As during pregnancy estro-progestinic levels dramatically increase, the higher number of pregnancies in the AD group than in the control group suggest that a change in estro-progestinic ratio during pregnancy or an increased exposure to progesterone and/or estrogen could be potential factors able to raise the risk of developing AD.

In conclusion, the risk of developing AD increases with the number of pregnancies. Only a higher number of pregnancies were correlated with an earlier onset of disease.

Comment on the paper:

M. Colucci, S. Cammarata, A. Assini et al – The number of pregnancies is a risk factor for Alzheimer's disease. *European Journal of Neurology* December 2006; 13(12):1374-1377