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Brief report

A prospective study of hormonal treatment and anxiety disorders in community-dwelling elderly women (The Esprit Study)

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Abstract

Background: The impact of hormone therapy use on late-life anxiety disorder in elderly women has not been evaluated.
Methods: Anxiety disorders were evaluated in 838 community-dwelling postmenopausal women aged 65 years and over, randomly recruited from electoral rolls. Anxiety disorders were assessed using a standardized psychiatric examination based on DSM-IV criteria, at baseline and as part of the 2- and 4-year follow-up.
Results: Multivariate logistic regression analyses adjusted for socio-demographic variables, measures of physical health and cognitive impairment, as well as current depressive symptomatology indicated no significant association between hormone therapy and anxiety disorders at baseline or after the 4-year follow-up period, regardless of type of treatment. Compared to women who have never taken hormonal therapy, no significant difference was observed for women taking continuously hormone therapy over the follow-up or those who stopped their treatment.
Conclusions: The use of hormone therapy was not associated with improved anxiety symptomatology in elderly postmenopausal women.

Keywords: Anxiety; Estradiol; Postmenopausal; Progestogen; Transdermal

1. Introduction

Given the extensive protective effects of estrogens on neurotransmitter systems (see for reviews Behl, 2002; Garcia-Segura et al., 2001), the question currently being raised is whether hormonal therapy (HT) may play a role in the management of neuropsychiatric disorders in elderly women whose steroid levels, particularly estrogen, are dramatically lowered after the menopause. The majority of previous studies in this area have focused on the effects of HT on dementia and in the treatment of depression (see for reviews Ancelin and Ritchie, 2005; Ancelin et al., 2007). Despite methodological limitations and contradictory reports, most recent trials in women with clinically diagnosed depression, report a positive effect of short-term transdermal estrogen therapy (ET) in perimenopausal women (Schmidt et al., 2000; Soares et al., 2001), with the antidepressant

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response in depressed postmenopausal women being much weaker (Cohen et al., 2003; Morrison et al., 2004).

The specific effect of HT on anxiety disorders remains largely unknown. Studies conducted to date have seldom used validated psychiatric instruments or clinical diagnosis, relying principally on questionnaires evaluating psychosomatic menopausal symptoms, well-being, or quality of life. Frequent anxiety and depression co-morbidity further complicates the issue. A beneficial effect of estrogen on anxiety disorders might however, be expected, considering its role on various brain targets as well as it anxiolytic properties observed in animal models (see for recent review Walf and Frye, 2006). On the other hand, progestogen or its active metabolites, found in the majority of combined HT preparations, appear to have opposing anxiolytic and anxiogenic behaviors (Rupprecht, 2003; Strous et al., 2006).

Given the relatively high prevalence of anxiety disorders in older women (Ritchie et al., 2004), and differences in vulnerability across individuals, the potential effects of HT in treating these disorders remain an important question to be addressed. However, while it is unlikely to be answered in the near future by large-scale RCTs of long-term HT users, it is currently feasible to use existing data from longitudinal population-based studies with adequate information on hormone exposure and psychiatric evaluation.

The present study aimed to determine whether HT could alleviate anxiety symptomatology in a population-based cohort using validated instruments. In this study we controlled for socio-demographic variables, measures of physical health including insomnia, as well as cognitive impairment, which may independently contribute to anxiety disorder and HT prescription. We also took into account depression co-morbidity, as well as the type of HT used.

2. Subjects and methods

2.1. Study population

The data used for this analysis were derived from a longitudinal study of neuropsychiatric disorder in community-dwelling French elderly (the Esprit study) (Ritchie et al., 2004). Eligible participants, who were at least 65 years of age and non-institutionalized, were recruited from the electoral rolls of Montpellier (southern France), between 1999 and 2001. Ethics approval for the study was given by the national ethics committee. After obtaining written informed consent from all participants, interviews were administered by trained staff at baseline and every two years thereafter. Of the women recruited as part of the Esprit Study, only non-demented women with complete follow-up, who were assessed for current anxiety disorders, had detailed information relating to the use of HT and had no missing data for the main covariates considered in the multivariate logistic models ($n=838$) were included in this analysis.

2.2. Anxiety disorder

The diagnosis of lifetime anxiety disorders (general anxiety disorder (GAD), phobia, obsessional compulsive disorder, panic and post-traumatic stress disorder) was made using the Mini-International Neuropsychiatry Interview (MINI), a standardized psychiatric examination which has been validated in the general population (Sheehan et al., 1998) according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria (Ritchie et al., 2004). Cases detected by the MINI were reviewed by a panel of psychiatrists to validate the initial diagnosis. In longitudinal analyses, incident cases of anxiety symptomatology were identified from women free of anxiety disorder at baseline but who subsequently had incident anxiety disorder during at least one of the two follow-up examinations.

2.3. Hormone therapy and menopausal characteristics

All types of medications used during the preceding month (including HT and antidepressants) were validated by presentation of the prescription or the medication itself. Information was also recorded on past HT type and duration of use, as well as age at menopause (defined as one year without menses) and type of menopause (*i.e.* natural *vs.* surgical or following a treatment such as chemotherapy or radiotherapy).

2.4. Other measures

Participants were classified as disabled if they were unable to complete at least one task from either the Instrumental Activities of Daily Living (IADL) (Lawton, 1988) or the Activities of Daily Living (ADL) (Katz et al., 1963) scales. Cognitive function was assessed using the Mini-Mental State Examination (MMSE) (Folstein et al., 1975) and those scoring less than 26 (corresponding to the 15th percentile) were classified as having lower cognitive function. Insomnia was defined as scoring positive on at least two questions from the 5-item sleep subscale of the Nottingham Health Profile questionnaire (Ribet and Derriennic, 1999). Chronic disorders were defined as having a history of