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Tubal ligation does not affect hormonal changes during the early menopausal transition

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Abstract

Background: To determine if women with a bilateral tubal ligation (BTL) were more likely to experience hormonal changes indicative of the transition to menopause or an increase in menopausal symptoms compared to women without a BTL.

Methods: Menopausal symptoms and hormone profiles of 134 women reporting a BTL were compared throughout the course of a 4-year follow-up study to 172 women without a BTL. Generalized linear regression models for repeated measures were used to estimate the independent effect of BTL on menopausal symptoms and hormonal levels adjusted for covariates.

Results: Forty-four percent of women reported a BTL and over one-half of women with a BTL experienced hot flashes. Women with a BTL had similar hormonal levels over the study period compared to women without a BTL. In addition, no relationship was found between BTL and any of the menopausal symptoms, including hot flashes, decreased libido or increased anxiety adjusting for age, race, body mass index (BMI), education, menopausal status and parity.

Conclusion: These findings document that women with a BTL have similar changes in sex hormone levels over the perimenopausal period compared to women without a BTL independent of other covariates. In addition, the reporting of menopausal symptoms was similar between the groups.

Keywords: Tubal ligation; Menopausal symptoms; Sex hormones

1. Introduction

Bilateral tubal ligation (BTL) is a common form of birth control used in the United States with over 900,000 tubal sterilizations preformed annually [1,2]. This permanent method of birth control is considered one of the safest and most effective forms of pregnancy prevention. However, as the population ages, questions remain concerning the long-term consequences of BTL in terms of earlier onset of signs and symptoms indicative of menopause. At this time, given the high proportion of women undergoing BTL and the increasing number of women approaching the transition to menopause, assessing the role of tubal sterilization on subsequent hormonal changes and menopausal symptoms is extremely important.

There is evidence that BTL may compromise ovarian function and influence hormonal fluctuations and symptoms during the perimenopausal period. Two prior, small studies have reported a higher risk of menopausal symptoms among women with a history of tubal sterilization compared to women without a BTL, although a change in hormone measures was not measured. These studies were limited by small sample sizes and absence of multiple repeated

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hormone assessments during the perimenopausal period [3,4]. Bilateral tubal ligation itself may disrupt the vascular blood supply to the ovary, leading to increased ovarian vascular resistance and subsequent ovarian tissue necrosis [5,6]. Indeed, recent studies using Doppler ultrasound have reported increased localized resistance 3 months following tubal ligation but not immediately following tubal ligation among a small group of women [7,8]. There is also evidence that BTL is associated with a decline in ovarian function and increased gonadotropin output over a short period [9]. In addition, the reduction in ovarian cancer risk following BTL also adds to the evidence that tubal sterilization has an effect on ovarian physiology [10,11].

Given the potential of BTL to compromise long-term ovarian function, we conducted this evaluation to examine the influence of BTL on menopausal symptoms and fluctuations of sex hormone levels among a cohort of perimenopausal women followed for a 4-year period. Specifically, we examined the role of tubal ligation on menopausal symptoms, reproductive hormone changes and menopausal status among participants enrolled in the Penn Study of Ovarian Aging, an ongoing prospective study of ovarian aging in a population-based cohort of women. The objectives were (1) to compare the change in hormone levels and menstrual bleeding patterns indicative of the transition to menopause between women with and women without a tubal ligation, (2) to determine the association between tubal ligation and the occurrence of menopausal symptoms and (3) to examine the dose-dependent role of time since tubal ligation on the menopausal parameters collected in this cohort.

2. Material and methods

2.1. Data collection

The Penn Study of Ovarian Aging is an ongoing, longitudinal cohort study examining hormonal, clinical, behavioral and demographic factors potentially associated with ovarian aging. From 1996 to 1997, a population-based sample of women living in the city of Philadelphia was identified through random digit dialing. Over 70% of households identified were screened for eligibility. To ensure a racially diverse population, eligible women were stratified by race (African American or Caucasian), were between the ages of 35 and 47 years, reported menstrual cycles in the normal range (22–35 days) for the previous 3 months and had at least one intact ovary. Exclusion criteria included any serious illness that might compromise ovarian or hormonal function, such as diabetes, liver disease, breast or endometrial cancer; current use of exogenous hormones or psychotropic drugs; self-reported chronic alcohol or drug abuse within the past year; or current pregnancy, lactation or intention to become pregnant. The Institutional Review Board of the University of Pennsylvania approved the study and all women provided written informed consent.

At enrollment, eligible women were asked to participate in a long-term women's health study with no specific emphasis on the examination of menopause. Subjects participated in six follow-up assessment periods at approximately 8-month intervals over 4 years. At each assessment period, an extensive structured questionnaire was administered by trained research interviewers who collected information on demographic background information, menstrual cycle characteristics, menopausal symptoms, menstrual and reproductive history, general health status, medication use (including hormone replacement) and substance use. In addition, subjects completed a set of standard self-report questionnaires, including the Center for Epidemiological Studies Depression Scale (CES-D) [12] and the Zung Anxiety Scale [13]. Research interviewers were rotated among the study participants to reduce the influence of interviewer bias.

Within each assessment period, there were two study-related visits 1 month apart used to obtain blood samples for hormone measurements. Thus, each woman provided two blood samples per assessment period and a maximum of 14 blood samples per subject. The hormone levels from these two visits were used to calculate a mean hormone level for each assessment period. Each of these visits was scheduled within the first 6 days of the menstrual cycle and included anthropometric measures, completion of standardized questionnaires and blood sampling.

Blood samples were centrifuged and plasma frozen in aliquots at -80°C. Assays were conducted in the General Clinical Research Center at the Hospital of the University of Pennsylvania in batches that included four visits per subject in order to reduce the within-subject variability due to assay conditions. Estradiol (E_2), follicle stimulating hormone (FSH), luteinizing hormone (LH), dehydroepiandrosterone sulfate (DHEAS) and testosterone were measured by radioimmunoassay using Coat-A-Count (Diagnostic Products, Los Angeles, CA) commercial kits. Assays were performed in duplicate. The inter- and intraassay coefficients of variation were below 4%. Dimeric inhibin B was measured in serum by Dr. Patrick Sluss at the Massachusetts General Hospital using a sensitive, two-site nonisotopic immunoassay (Serotec) (Oxford BIO-Innovation LTD, Upper Heyford, Oxfordshire, England) (Distributor, Serotec, Raleigh, NC). The intra- and interassay coefficients were $<8\%$ and $<20\%$, respectively; values below the sensitivity threshold were given the threshold value.

2.2. Study measures

Tubal ligation status was determined with the question, "Have you ever had a tubal ligation or had your tubes tied?" To examine if duration since BTL influenced hormones or menopausal symptoms, a discrete time since BTL variable was created for each women reporting a BTL. This variable was categorized as BTL occurring