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Secondhand tobacco smoke exposure is associated with prolactin but not thyroid stimulating hormone among nonsmoking women seeking in vitro fertilization

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ABSTRACT

Prolactin (PRL) and thyroid stimulating hormone (TSH) serve important roles in the reproductive and other systems. Active smoking is associated with changes in PRL and TSH secretion, but the relationship between secondhand tobacco smoke (STS) exposure and these hormones is unclear. We measured PRL and TSH in serum as well as cotinine in follicular fluid (to estimate STS exposure) among 314 nonsmoking women undergoing in vitro fertilization treatment. We observed a significant increase in PRL concentrations ($p = 0.03$) among STS-exposed nonsmokers compared to unexposed nonsmokers. There was no significant difference in TSH concentration ($p > 0.4$) among those exposed to STS compared to those who were unexposed. STS exposure is associated with an increase in circulating PRL but not TSH levels. Future studies are needed to confirm our results, identify biological mechanisms involved, and better understand the potential clinical and public health implications.

1. Introduction

Prolactin (PRL) and thyroid stimulating hormone (TSH; also known as thyrotropin) are important reproductive hormones. PRL is secreted by the anterior pituitary and was originally identified by its ability to stimulate mammary gland development and lactation. We now know that it is involved in over 300 separate actions in various vertebrates, including effects on reproduction, growth and development, metabolism, water and electrolyte balance, brain and behavior, and immunoregulation (Bole-Feysot et al., 1998). The largest group of actions for PRL pertains to reproductive processes.

Abbreviations: PRL, prolactin; TSH, thyroid stimulating hormone; T3, triiodothyronine; T4, thyroxine; STS, secondhand tobacco smoke; IVF, in vitro fertilization; ICSI, intracytoplasmic sperm injection; GIFT, gamete intra-fallopian transfer; FF, follicular fluid; MEIA, microparticle enzyme immunoassay; LOD, limit of detection; CV, coefficients of variation; ELISA, enzyme-linked immunosorbent assay; ANOVA, analysis of variance; BMI, body mass index; NHS, Nurses' Health Studies.

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TSH is also secreted by the anterior pituitary, and it stimulates the thyroid gland to produce and secrete thyroid hormones. TSH is regulated via negative feedback from thyroid hormones. Normal thyroid function is an important component of reproductive health. In females, thyroid dysfunction has been linked to menstrual disturbances, reduced fertility, spontaneous abortion and various late-pregnancy outcomes, including preterm birth and low birth weight (Krassas et al., 2010). Proper thyroid function is important to many other processes, as well, including energy balance, metabolism, and other functions in the nervous, cardiovascular, and pulmonary systems.

Studies have examined the effects of active smoking on TSH and thyroid function. McDonald et al. (2008) found that women who smoke during pregnancy had significantly lower TSH levels than nonsmokers. Triiodothyronine (T3) was not measured in that study, but free thyroxine (T4) concentrations did not differ between exposure groups, neither did cord blood TSH concentration from infants born of smokers compared to infants of nonsmokers (McDonald et al., 2008).

Shields et al. (2009) later confirmed some of these findings. For example, they also observed lower TSH concentrations in serum among pregnant smokers compared to nonsmokers and no significant difference in free T4 concentrations between exposure groups; though they did find significantly higher median free T3 concentrations among smoking mothers as well as significantly lower cord serum TSH concentrations in babies born to smoking mothers compared to those whose mothers were nonsmokers.

Active smoking is also associated with changes in PRL concentrations, but studies have had differing results. One study found a significant increase in PRL concentrations among men who were active smokers compared to nonsmokers (Xue et al., 2010). Two other studies reported increases and decreases, respectively, in PRL concentrations among animals exposed to tobacco smoke (Ng et al., 2006; Muraki et al., 1979).

Data is limited on the effects of secondhand tobacco smoke (STS) exposure on circulating TSH and PRL. Several studies have shown that exposure can disrupt the thyroid (Carrillo et al., 2009; Soldin et al., 2009; Flouris et al., 2008), but to the best of our knowledge no studies to date have examined the relationship between STS exposure and PRL concentrations. Thus, the present study is intended to increase our understanding of the relationship between STS exposure and circulating TSH and PRL. We hypothesized that STS exposure is associated with increased serum levels of PRL and decreased serum TSH.

2. Methods

2.1. Study population

Subjects for the present study are a subset of a larger study examining predictors of in vitro fertilization (IVF) success, including STS exposure, and have been previously described (Meeker et al., 2007; Cramer et al., 2003). Briefly, in the larger study, couples undergoing IVF or intracytoplasmic sperm injection (ICSI) between 1994–1998 (study 1) and 1999–2003 (study 2) were recruited through three Boston-area clinics. Protocols were approved by the Human Research Committees at Brigham and Women's Hospital, the Harvard School of Public Health, and the University of Michigan. Approximately 65% of couples approached agreed to participate in the study. Couples excluded from the study were those who were gestational carriers or who underwent gamete intra-fallopian transfer (GIFT), as well as those who required donor oocytes or donor semen. After exclusions, 2350 couples who underwent from one to six IVF/ICSI treatment cycles were enrolled in the parent study. A self-administered questionnaire was used to obtain information from each subject on medical history and lifestyle factors such as: demographics, ages of both male and female partner, medical and reproductive history, smoking history, and duration of infertility. Information on IVF treatment and outcome was abstracted from clinical records. 314 nonsmoking patients for whom a blood sample was analyzed for PRL and TSH and for whom first-treatment-cycle follicular fluid (FF) was analyzed for cotinine were included in the present analysis.

2.2. Hormone measurement

When possible, a basal blood sample was collected from study participants. This sample was taken sometime during days one through five of the menstrual cycle and designated as the "true baseline." When a blood sample timed with the menses could not be collected, a sample was collected before IVF treatment began and was designated the "initial" specimen. Samples were aliquoted and stored at −80 °C. PRL and TSH were measured in archived serum samples using the AxSYM Immunoassay system (Abbott Diagnostics, Chicago, IL), which was described previously (Cramer et al., 2003). Briefly, the tests for PRL and TSH are solid-phase double antibody enzyme immunoassays employing microparticle enzyme immunoassay (MEIA) technology. For PRL, the limit of detection (LOD) was 0.6 ng/ml and assay performance was monitored using three quality control sera (Abbott Diagnostics). The coefficients of variation (CV) for PRL in the three control sera were 8.3, 6.8, and 4.8%. TSH was analyzed using the MEIA technology (Ultrasensitive hTSH II). TSH levels were quantified as μIU/ml based on assay calibrators standardized using the World Health Organization TSH 80/558. The LOD was 0.03 μIU/ml. TSH assay performance was also monitored using three quality control sera and the CV were 7.1, 6.2, and 7.4%.

2.3. Cotinine measurement

Physicians and technicians were asked to retain FF during egg retrieval for each IVF cycle. FF was aspirated from follicles using a 16-gauge needle and constant suction from a Rocket pump apparatus. Fluid was collected from the largest visible follicle before using any flushing medium and then transferred to a sterile Petri dish. Oocytes were then scanned for and removed from the FF. The fluid, normally discarded at this point, was placed into a 15 ml conical tube and centrifuged for 15 min. The supernatant was placed into a clean storage tube, labeled, refrigerated, and transferred to the Brigham and Women's Hospital laboratory within 12 h. At the laboratory, the specimens were aliquoted into one to six 1.5 ml tubes, depending upon the volume collected, and frozen at