Hormone abnormalities are not related to the erectile dysfunction and decreased libido found in many men with infertility

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Objective: To evaluate whether hormonal markers predict erectile dysfunction (ED) and symptoms of T deficiency syndrome (TDS), which are commonly found in the population of infertile men.
Design: Retrospective study utilizing a prospectively maintained infertility database.
Setting: A tertiary referral center.
Patient(s): A total of 1,750 of 2,783 men presenting for evaluation of infertility between 1995 and 2010 completed validated questionnaires.
Intervention(s): Androgen Deficiency in the Aging Male (ADAM) and Sexual Health Inventory for Men questionnaires were administered. Baseline risk factors for ED and TDS were also measured. Subjects underwent serum hormone evaluation for total T, calculated bioavailable T, sex hormone–binding globulin, E_2, LH, FSH, and PRL.
Main Outcome Measure(s): Multivariable logistic regression modeling was used to determine the significance of hormonal markers in predicting ED (Sexual Health Inventory for Men score <22) and/or a positive ADAM score.
Result(s): The prevalence of ED and a positive response to the ADAM questionnaire were 30.5% and 45.2%, respectively, in this population (mean age, 36 years). Low serum T (total T < 10 nmol/L) was found in 29.4%. Neither T nor bioavailable T was significantly associated with the symptoms of ED or TDS on multivariable regression analysis.
Conclusion(s): Erectile dysfunction and TDS in young, infertile men seem to be unrelated to hormone changes. (Fertil Steril® 2014;101:1594–8. ©2014 by American Society for Reproductive Medicine.)
Key Words: Infertility, erectile dysfunction, andropause

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The decline in T and the increase in sex hormone–binding globulin (SHBG) with age have been associated with loss of muscle strength and bone density, a decrease in libido, memory, alterations in mood, and erectile dysfunction (ED) (1). This constellation of symptoms, formerly termed *andropause*, has been more recently referred to as T deficiency syndrome (TDS), hypogonadism, or late-onset hypogonadism (2). We have previously reported that a significant proportion of male partners of infertile couples report symptoms like those of TDS (38%) and ED (28%) (3). It is unclear, however, whether these findings reflect the impact of the psychological stress of infertility, infertility evaluation, and therapy, or whether the underlying cause for the infertility (hypothalamic–pituitary–testis dysfunction) may also have an impact on the levels of circulating T, which in turn might have an impact on male sexual health and erectile function.

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Certainly the stress of infertility may result in sexual dysfunction. Male factor infertility poses significant psychological stress, and this alone is associated with sexual dysfunction (4, 5). Moreover, the diagnostic evaluation that infertile men undergo, including invasive procedures such as testicular sperm extraction, seems to further negatively impact erectile function (6). The cumulative impact of this on the couple's sexual function is likely magnified by the fact that female partners also report high rates of sexual and relationship problems (7). Shindel et al. (5) showed that male sexual function is directly predicted by partner sexual function. We sought to address the prevalence of male sexual dysfunction in couples with infertility and whether the sexual dysfunction reported in couples with infertility is primarily due to the stress of the infertility alone or whether there are organic factors that might cause both male infertility and sexual dysfunction. In particular, we were interested in evaluating whether serum hormonal levels, namely T and bioavailable T levels, were predictive of ED in this patient population.

MATERIALS AND METHODS

Study Design and Patient Population

We completed a retrospective cohort study utilizing a prospectively maintained infertility database at our institution, Mount Sinai Hospital. Men presenting for evaluation of infertility at Mount Sinai Hospital between July 1995 and April 2010 were enrolled in the prospective infertility database. Enrolled patients were administered demographic and medical history questionnaires along with select validated questionnaires. Institutional research ethics board approval was obtained before study commencement.

Questionnaires

The demographic and medical history questionnaire consisted of questions regarding demographic information, past medical history, current prescription medication history, and baseline risk factors, including smoking and illicit drug use (e.g., marijuana). The select validated questionnaires included the Androgen Deficiency in the Aging Male (ADAM) and Sexual Health Inventory for Males (SHIM) instruments, which assess TDS and erectile function, respectively (8, 9).

Inclusion/Exclusion Criteria

To be enrolled in the prospectively maintained infertility database, all men were required to understand English and be able to consent and complete the questionnaires. Physicians reviewed completed questionnaires with respondents at the time of patient interview to clarify any discrepancies, and appropriate corrections were made.

For our retrospective cohort study we excluded subjects with questionnaires in which SHIM and ADAM components were not completed in entirety. Additionally, men younger than 18 years and those with a history of pre-existing, surgical causes for sexual dysfunction were excluded (e.g., penile prosthesis or radical prostatectomy).

Serum Hormones

For our study, patient data from our prospective infertility database were merged with a separate database of serum hormones (total T, SHBG, E_2, LH, FSH, and PRL). These parameters are routinely evaluated initially in most men presenting for assessment. Using previously described methods, we calculated bioavailable T in all men who had SHBG levels available (10).

Outcomes

All men included in our study were classified into three categories (some overlap) as those with ED, low libido, or a positive ADAM score: [1] men with SHIM scores below 22 were classified as having ED; [2] those with a positive response to question 1 of the ADAM score were categorized as having low libido; and [3] respondents had a positive ADAM questionnaire if they responded "yes" to item 1 (relating to libido) or 7 (relating to ED) or if they answered "yes" to three or more of the other items (8).

Our principal outcomes were the determination of the prevalence of ED and the assessment of predictors of ED in this population of infertile men, specifically hormonal parameters.

Our secondary outcomes were the determination of the prevalence of low libido and positive ADAM score in male patients evaluated for infertility, along with the assessment of predictors of each of low libido and a positive ADAM score.

Statistical Analysis

For our univariate analysis, the χ^2 test (categoric variables) and single variable logistic regression (continuous variables) were used to assess for covariates significantly associated with ED, low libido, and a positive ADAM questionnaire, respectively. For each of the three respective outcomes, 12 covariates were assessed. These included demographic (age), comorbidity (diabetes mellitus [DM], hypertension, medications), and lifestyle variables (smoking, marijuana use), as well as serum hormonal markers (E_2, FSH, LH, T, bioavailable T, and PRL). The use of any medication known to affect ED was reviewed to construct a dichotomous variable to represent at-risk individuals. To account for the multiple testing of so many covariates, the Bonferroni test was used to adjust our *P* value accordingly.

In light of our specific interest in assessing the relationship between the hormonal markers and the likelihood of ED, we proceeded to perform multivariable logistic regression separately for each of FSH, LH, PRL, T, and bioavailable T. In doing so, this would allow us to get a more accurate estimate of the effect of each of these five hormones on the likelihood of ED, by controlling for any potential confounding by the other measured covariates. As such, using the Harrell method, five separate multivariable logistic regression models were constructed for each of the five hormonal markers, with the hormonal marker serving as the primary predictor in each model (11). Briefly, each hormonal marker was considered as the primary predictor, and each potential covariate was