Empirical Medical Therapy for Idiopathic Male Infertility: A Survey of the American Urological Association

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Purpose: We determined empirical medical therapy practice patterns for idiopathic infertility.

Materials and Methods: We performed a survey of 7,745 practicing American Urological Association members from July to November 2010. Respondents were questioned on empirical medical therapy use, patient evaluation and selection, and preferred medications.

Results: A total of 387 urologists (5%) participated in the survey, of whom 16% had infertility fellowship training, two-thirds used empirical medical therapy and 78% treated with empirical medical therapy and surgery. Laboratory values important for identifying ideal candidates include sperm concentration, serum follicle-stimulating hormone and serum testosterone. The most common medications used were clomiphene citrate, human chorionic gonadotropin and anastrozole. Of respondents 25% would treat infertile males with testosterone while the patient actively pursued pregnancy. Overall 60.5% of respondents would treat with empirical therapy for 3 to 6 months. Of fellowship trained and general urologist respondents 70% and 47%, respectively, counseled patients that empirical medical therapy has unknown effects on pregnancy and sperm count.

Conclusions: Empirical medical therapy is used by two-thirds of survey respondents for idiopathic male infertility. There is no clear, universal pattern to the evaluation or identification of the ideal patient for such therapy among those surveyed. There is no consensus on the optimal medication and considerable ambiguity exists as to perceived effects on fertility. Of concern is that 25% of respondents use exogenous testosterone, a medication known for its contraceptive potential, for male infertility treatment. These findings confirm the need for additional studies to establish recommendations on the empirical use of medical therapy in the setting of male infertility.

Key Words: testis; infertility, male; oligospermia; physician's practice patterns; health care surveys

Abbreviations and Acronyms

AUA = American Urological Association

BMI = body mass index

CME = continuing medical education

EMT = empirical medical therapy

FSH = follicle-stimulating hormone

FTU = fellowship trained urologist

GU = general urologist

LH = luteinizing hormone

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Study received institutional review board approval.

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THERE is currently no consensus on the management of idiopathic oligospermia. While the role of hormonal therapy for men with specific abnormalities is well defined,[1] the literature remains inconclusive and controversial on hormonal manipulation with EMT for men with idiopathic infertility. Urologists use EMT despite the lack of large, randomized, controlled studies.

We assessed decision making and treatment practices, identified treatment patterns and evaluated the prevailing attitudes toward EMT in the urological community. Medications used

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for EMT are not Food and Drug Administration approved specifically for male infertility.

MATERIALS AND METHODS

Recruitment

An online survey using SurveyMonkey® was emailed to practicing AUA members in July 2010. Additional mailings in September and October 2010 were sent to nonrespondents. The study closed in November 2010. No incentives were provided to respondents.

Survey

The survey consisted of 3 sections, including demographics, clinical practice and clinical case scenarios. Demographics included practice duration, percent of practice involving male infertility, and training and education. Participants were queried on completion of a male infertility fellowship. Residents and fellows were excluded from study.

Respondents reported on EMT use for idiopathic infertility. They also provided information on medications used, clinical and laboratory criteria used to determine candidates for therapy and therapy duration. Participants were asked to provide expectations on EMT effectiveness for semen analysis and the pregnancy rate. Responses were compared between GUs and male infertility FTUs.

Cases

Three case scenarios were presented to evaluate participant practice patterns when treating infertile males with different clinical presentations. Each clinical scenario presented an infertile patient with a different semen analysis and laboratory parameters. The first 2 cases focused on the severity of oligospermia necessary to initiate EMT. The third case included changing hormone levels to the case scenario to evaluate the clinical variables at which treatment patterns would be influenced.

Statistical Methods

A medical biostatistician performed the statistical analysis using SAS® 9.2. The Fisher exact test was used for categorical variables and the Wilcoxon rank sum test for continuous variables with statistical significance considered at $p < 0.05$.

RESULTS

A total of 7,745 practicing AUA members in the United States were invited to participate in the survey by e-mail, of whom 387 (5%) urologists participated. Of respondents 74.8% had been in practice for at least 5 years and 63 (16%) had completed a male infertility fellowship. Of FTU respondents 66.7% treated at least 30% infertility cases while 95.3% of GU respondents treated less than 10% in their practice ($p < 0.0001$). Of respondents 9% treated no patients with infertility. This trend was also reflected in the amount of infertility CME obtained annually. FTU respondents were more likely than GUs to attend fertility related CME courses (58.7% vs 8.0%, $p < 0.0001$).

Significant practice pattern differences existed between FTU and GU respondents in medication use (fig. 1), therapy selection based on obesity and EMT outcome expectations. GUs were more likely than FTUs to use testosterone as therapy for idiopathic oligospermia (29.8% vs 6.8%, $p = 0.001$). FTUs administered anastrozole more commonly than GUs (61% vs 6.4%, $p < 0.001$). GUs were more likely than FTUs to use clomiphene citrate to treat obese males (BMI 30 kg/m^2 or greater) (79.5% vs 29.3%, $p < 0.001$).

Similar practice patterns were observed among respondents for medical or surgical therapy, EMT, medication type, laboratory evaluation, the sperm count cutoff threshold to initiate therapy, laboratory variables used to guide medication for EMT, treatment duration, medication choice for nonobese males (BMI less than 30 kg/m^2) and physical findings or laboratory values that would predict an inferior outcome of therapy (see Appendix).

Most respondents did not initiate EMT until the sperm concentration decreased below 20 million per ml. Of respondents 20% had no minimum threshold at which they would initiate EMT (fig. 2). Of respondents 61% would treat patients for between 3 and 6 months (fig. 3), including 24% for up to 12 months and only 0.9% beyond 1 year.

Of respondents 41% expected EMT to increase the sperm concentration while 47.4% and 13.5% expected EMT to have an unknown or no effect, respectively. There appeared to be even more uncertainty in regard to the pregnancy rate with 70.2% of respondents expecting an unknown effect, 21.5% ex-

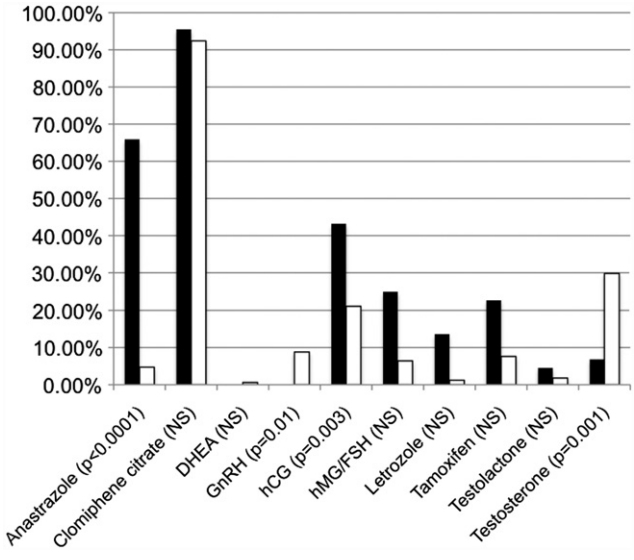

Figure 1. Medications used for EMT by fellowship trained (black bars) vs general urologist (open bars) respondents treating idiopathic male infertility. *NS*, not significant. *DHEA*, dehydroepiandrosterone. *GnRH*, gonadotropin-releasing hormone. *hCG*, human chorionic gonadotropin. *hMG*, human menopausal gonadotropin.