

## Format for ANSWERING REVIEWERS

September 5, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (Treatment of Hypogonadotropic Male Hypogonadism: Case-Based Scenarios: 12060-review.doc).

**Title:** Treatment of Hypogonadism: Case-Based Scenarios

**Author:** Lindsey E Crosnoe-Shipley, Osama O. Elkelany, Cyrus D. Rahnema, Edward D. Kim

**Name of Journal:** *World Journal of Nephrology*

**ESPS Manuscript NO:** 12060

The manuscript has been improved according to the suggestions of reviewers:

**1 Format has been updated**

**2 Revision has been made according to the suggestions of the reviewer**

(1 - 2878065)

1. The title was altered to read: "Treatment of Hypogonadotropic Male Hypogonadism: Case-Based Scenarios"
2. The remaining revisions were corrected within the Manuscript and highlighted accordingly.

(2 - 615136)

1. Page 7: Clinical recommendation: The authors should make clear that this recommendation is applicable to mild hypogonadism, but not to severe hypoandrogenism which usually also present with oligo- or azoospermia even without testosterone replacement.
  - a. This comment has been added to the clinical recommendation.
2. The second case is ill-described. The authors should clarify the presumptive diagnosis that moved the physician to prescribe testosterone, and what other studies should be performed before starting clomiphene. Why not LH or hCG?
  - a. The use of hCG and LH is discussed in Case 3 as the patient in Case 2 had a normal baseline serum Testosterone level. Use of hCG or LH would be considered amperic therapy. We have improved the description of Case 2.
3. Page 18: Conclusion: the first affirmation (Exogenous testosterone use should be avoided in men desiring future fertility given the potential for long-term detrimental effects on spermatogenesis) is not sufficiently supported and cannot be used as a recommendation. The authors should smoothen their affirmation (e.g. saying that in a minority of cases, spermatogenesis is not recovered, although it is difficult to say whether this is due to testosterone treatment or to the natural evolution of the condition).
  - a. This comment has been added to the Conclusion.

(3 - 2977112)

1. Very short introduction. Would need to be more elaborated. This case series aimed fertility in hypogonadal men. The raising epidemic of hypogonadism is mostly related to longer life span and the men at the age of more than 60 are not very concerned about fertility. You can put this study in your introduction: Samplaski MK et al: testosterone use in the male infertility

population: prescribing patterns and effects on semen and hormonal parameters. *Fertil Steril*, 2014, 101 (1). This study shows 88.4% of men were azoospermic while on exogenous testosterone.

- a. The introduction was lengthened and improved. Samplaski article was added.
2. This article is a case series but authors did not provide the details of each case such as age, underlying disease, drug history, the duration of testosterone therapy, routes and type of testosterone therapy, details of semen analysis before and after testosterone therapy, primary and secondary hypogonadism. Putting comments rather than facts describing cases should be removed in the first section of each case.
  - a. These details were added to each case.
3. Needs to be more elaborated about each of treatment options and their side effects. Also, needs to be more elaborated what symptoms of hypogonadism would and would not improve with these different options. For example, hCG can exacerbate the depression and irritability in hypogonadal men.
  - a. Please find the hCG side effects included in Table 1. The following was added to the manuscript to address hCG side effects: "Occasionally, hCG can exacerbate depression and irritability in hypogonadal men. Cessation of the anabolic steroids with use of clomiphene may be the most beneficial."
  - b. The following section was added to page 14 of the manuscript: Clomiphene citrate results in similar satisfaction and efficacy to testosterone therapy.
4. The tried treatment approach for each case after stopping of testosterone treatment and the time frame and outcome in each case need to be more elaborated.
  - a. In case 2, we added the recommendation that cessation of T therapy should be the first treatment concern for each man. Recommendations for timeframe and outcome were added to each case.
5. Authors suggest alternative therapies to address the infertility in hypogonadal men. I think they also need to address how these treatments works on different symptoms of hypogonadism as well.
  - a. The following was added to our manuscript: "Katz *et al* [25] conducted a study demonstrating the efficacy of low-dose CC in 36 hypogonadal men. No major side effects were reported and 60% of these patients had an improvement in more than three items of the ADAM (Androgen Deficiency in Aging Males) questionnaire."

(4 - 2497108)

1. Case-Based Scenarios may provide some interesting information. However, a systematic review may provide clear conclusion. Other comments In the abstract, human chorionic gonadotropin should be spelled out at the first time.
  - a. This article was reflected by *World Journal of Nephrology* as a corollary article to our previous publication in *Fertility and Sterility* (F&S 14737R1). This previous article served as a systematic review with recommendations. Our present article makes clinical correlation using case studies.
  - b. The spelling of hCG was corrected in the abstract.

### **3 References and typesetting were corrected**

Thank you again for publishing our manuscript in the *World Journal of Nephrology*.

Sincerely yours,

Edward D. Kim, MD

Department of Surgery, Division of Urology

University of Tennessee Graduate School of Medicine

1928 Alcoa Highway, Suite 222

Knoxville, Tennessee 37920

[ekim@utmck.edu](mailto:ekim@utmck.edu)

tel: 865-305-9254

fax: 865-305-9716