

# Comment on “Hypogonadotrophic hypogonadism due to a mutation in the luteinizing hormone $\beta$ -subunit gene”

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Song et al. [1], report a new case of a homozygous p.Leu72Arg mutation in exon 3 of the luteinizing hormone  $\beta$  (*LHB*) gene leading to hypogonadism in a 19-year-old male patient, which is one of only a handful of cases reported to date. As more physicians become aware of diagnosing luteinizing hormone (LH) deficiency, an important point that remains unresolved is the issue of the best therapeutic strategy to offer to these patients.

In patients with *LHB* mutations, the absence of LH during post-natal life leads to the characteristic pathological features seen on testicular biopsy, including immature Leydig cells, a reduction of Sertoli cells, hypomorphic seminiferous tubules, markedly decreased inhibin B, and low testicular volume. Although testosterone administration may induce virilization, it does not stimulate testicular development, as shown by Song et al. [1]. It has been suggested that gonadotropin treatment early after the diagnosis of hypogonadotrophic hypogonadism may significantly improve the fertility potential of these patients through mimicking of the “mini puberty” state [2].

Our three male patients with documented *LHB* mutations that were treated with human chorionic gonadotropin (hCG) (Pregnyl, MSD, Brussels, Belgium) 5,000 IU/week for nearly 2 years had virilization and testicular growth, and

spermatogenesis can occur, although it is usually suboptimal [3-5]. Our initial male patient successfully underwent assisted reproduction [4], and had recently a second child via the same method. Taking into account this experience and the available literature on this very rare disorder, we propose that young males with LH deficiency due to a documented *LHB* mutation should be initially treated with gonadotropins (hCG, recombinant LH) rather than testosterone, to promote Sertoli and Leydig maturation as well as to improve spermatogenesis and maximize the potential for fertility.

## Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Received: February 26, 2017

Accepted: April 24, 2017

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