



Short term Leydig cell stimulation by LH and hCG in a man with central hypogonadism

Background: The comparison between human chorionic gonadotropin (hCG) and luteinizing hormone (LH) has been performed in *in vitro* models. Despite their action being mediated by the same receptor and leading to a similar increase of testosterone (T) production, it is now clear that LH and hCG activate differently signal transduction. However, hCG administration remains the therapeutic option of choice to increase intratesticular T. A direct *in vivo* comparison between LH and hCG was not performed systematically so far in the male. Here, we report the first case in which the short-term action of LH and hCG was on compared in the same man. **Methods:** A 55-years-old patient presented with hypogonadotropic hypogonadism (HH) probably due to an atypical giant pituitary adenoma. HH was present both at the diagnosis and after trans-sphenoidal neurosurgery with complete removal of adenoma. Assuming that the long-standing HH could have reduced the Leydig cells responsiveness, three different schemes were consecutively administered: i) hCG (Gonasi HP, IBSA pharmaceuticals) 75 IU daily i.m. for 2 weeks; ii) recombinant LH (rh-LH) (Luveris, Merck) 75 IU daily i.m. for 2 weeks; iii) hCG again 75 IU daily i.m. for 2 weeks. Each stimulation scheme was followed by 2-weeks of wash-out. Serum total T levels were measured by liquid chromatography-tandem mass spectrometry. All three treatments led to a significant increase in serum total T levels compared to baseline ($p=0.004$, $p=0.010$ and $p=0.004$, respectively), which occurred immediately after the first injection. Although the maximal T increase reached after hCG administration seemed higher compared to rh-LH (3.46 vs 2.49 ng/mL), no significant differences were found ($p=0.245$). LH serum levels increased after LH administration from 2.7 to 5.7 mIU/ml, suggesting that a minimal, apulsatile LH increase was able to stimulate Leydig cells. **Conclusion:** This case report demonstrates, for the first time, that a daily injection of the same low dosage of either LH or hCG increases serum T levels *in vivo*, quickly reaching a steady state. Although hCG is expected to be more potent than LH by *in vitro* studies, both treatments equally increased serum T levels. Thus, a similar potency of LH and hCG on T production is supposed. Whether LH and hCG differently stimulate other Leydig cell functions (e.g. INSL3 production) remains to be determined. HH could represent the best *in vivo* model at comparing LH and hCG action and kinetics in the male.