Nature Reviews Endocrinology | Published online 18 Apr 2017; doi:10.1038/nrendo.2017.45

PITUITARY FUNCTION

Pulsatile GnRH therapy in CCPHD

In patients with congenital combined pituitary hormone deficiency (CCPHD), the function of the hypothalamus–pituitary–testis axis can be restored with pulsatile gonadotropin-releasing hormone (GnRH) therapy, according to the results of a self-controlled clinical trial.

CCPHD is a rare disorder characterized by morphological anomalies in the pituitary stalk and multiple pituitary hormone deficiencies, resulting in short stature and absence of puberty. Pulsatile GnRH therapy is known to activate the pituitary–gonadal axis in patients with congenital hypogonadotropic hypogonadism. However, pulsatile GnRH therapy is only effective in patients with a gonadotrophic cell reservoir in the anterior pituitary, so was thought to be ineffective in patients with CCPHD owing to the morphological anomalies in the pituitary stalks of these patients. A team of researchers from China and the USA conducted a prospective, self-controlled clinical trial to assess this assumption.

The trial included 40 male patients with CCPHD (age 25.5 ± 4.5 years) who were treated with pulsatile GnRH that was administered subcutaneously via a portable infusion pump for 3 months. The initial dosage was 10 μg every 90 min, which was increased to try and maintain serum levels of testosterone of 6.94–17.35 nmol/l. After 3 months, 60% of patients had a good response to the therapy, with levels of luteinizing hormone and follicle-stimulating hormone in the normal range and an increase in serum levels of testosterone. Eight patients also achieved spermatogenesis. The researchers found no correlation between the response to therapy and the severity of the morphological anomalies.

The researchers suggest that their findings indicate that some patients with CCPHD have a functional gonadotropic cell reservoir. Pulsatile GnRH therapy could therefore be a viable option in these patients. More research is needed to determine the optimal dose and the length of therapy required to see a response.

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ORIGINAL ARTICLE Zheng, J. *et al.* Pulsatile GnRH therapy may restore hypothalamus–pituitary–testis axis function in patients with congenital combined pituitary hormone deficiency: a prospective, self-controlled trial. *J. Clin. Endocrinol. Metab.* http://dx.doi.org/10.1210/jc.2016-3990 (2017)