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Standard GnRH Analogue Doses Do Not Adequately Suppress Puberty In Adolescent Patients

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1. INTRODUCTION

Adolescent patients presenting with gender dysphoria can be administered standard doses of gonadotrophin releasing hormone analogues (GnRHa) to downregulate the hypothalamic-pituitary-gonadal axis and suspend undesired pubertal development[1]. It is unclear whether this treatment is sufficient to achieve full biochemical suppression of serum gonadotrophin (LH, FSH) and sex hormone (testosterone, oestradiol) production. We retrospectively reviewed the biochemistry of patients attending the Gender Identity Clinic at UCLH who were administered the GnRHa triptorelin (Gonapeptyl®).

2. MATERIALS & METHODS

Patients

Data was obtained from routine investigations of patients attending the UCLH Gender Identity Clinic (2012-2014) and who were treated with monthly injections of triptorelin (3.75mg, Gonapeptyl®). Biochemistry results (LH, FSH, testosterone, oestradiol) were extracted from the laboratory information management system whilst other information (age, height, weight, treatment) was available on electronic patient records.

	Natal Female	Natal Male
N	49	25
Age (y)	16.9 (16.1-17.2)	17.0 (16.2-17.4)
BSA (m^2)	1.67 (1.55-1.81)	1.79 (1.69-1.87)
Treatment Duration (m)	7 (6-7)	7 (6-8)

Result are median (interquartile range)

Patients administered other analogues or cross-sex hormones were excluded.

Measurement of LH, FSH, Testosterone, Oestradiol

All hormones were measured by immunoassays on the Roche Cobas platform. Assay limits of quantitation were 0.1mIU/mL (LH, FSH), 0.4nmol/L (testosterone), and 44pmol/L (oestradiol). Measurements were performed prior to and after commencement of treatment.

Data Analysis

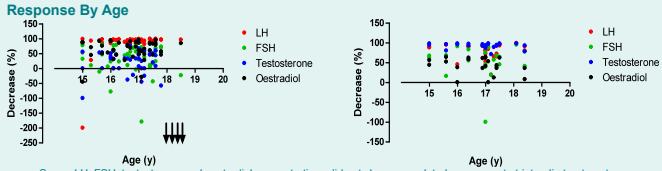
For the purposes of data analysis, results below the assay measuring limit were substituted for the limit of quantitation. Two-tailed paired t-tests were used to determine the significance between pre- and post-treatment results. P<0.05 was deemed to be statistically significant.

3. RESULTS

Natal Female

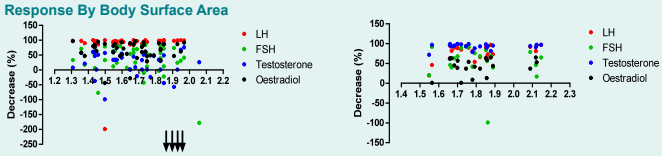
Natal Male

Response By Age



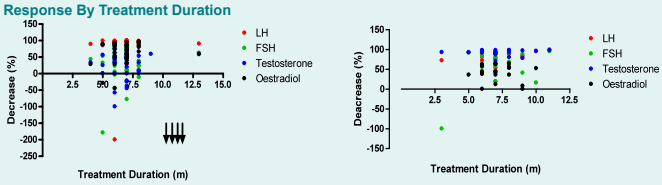
Serum LH, FSH, testosterone and oestradiol concentrations did not show age-related responses to triptorelin treatment. Arrows indicate the number of patients whose responses were not plotted.

Response By Body Surface Area



Serum LH, FSH, testosterone and oestradiol concentrations did not show responses to triptorelin treatment that correlated with body size (body surface area). Arrows indicate the number of patients whose responses were not plotted.

Response By Treatment Duration

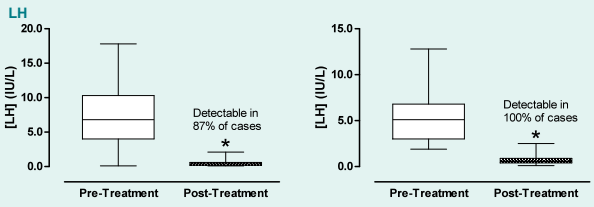


Serum LH, FSH, testosterone and oestradiol concentrations did not show responses to triptorelin that correlated treatment duration. Arrows indicate the number of patients whose responses were not plotted.

Natal Female

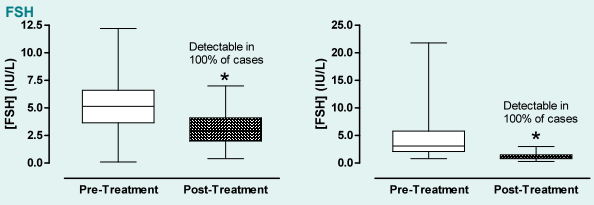
Natal Male

LH



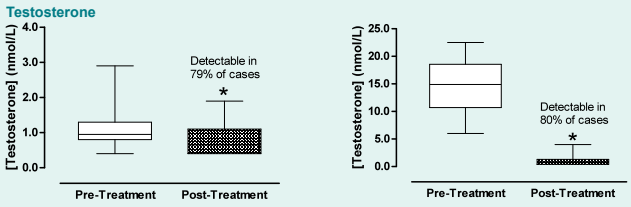
Serum LH concentrations were significantly suppressed in both natal males and females following treatment with triptorelin. LH remained detectable in all male and 87% of female patients. * = $P < 0.01$

FSH



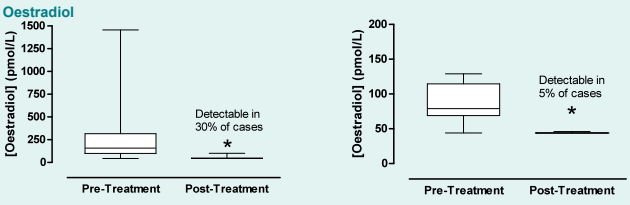
Serum FSH concentrations were significantly suppressed in both natal males and females following treatment with triptorelin but remained detectable in all cases. * = $P < 0.01$

Testosterone



Serum testosterone concentrations were significantly suppressed in both natal males and females following treatment with triptorelin. However, testosterone remained detectable in 80% of male and 79% of female patients. * = $P < 0.01$

Oestradiol



Serum oestradiol concentrations were significantly suppressed in both natal males and females following treatment with triptorelin, becoming undetectable in most cases. However, it remained measurable in 5% of male and 30% of female patients. * = $P < 0.01$

4. DISCUSSION

Using a standard dose of the GnRHa triptorelin, no patient achieved complete suppression of LH, FSH, testosterone and/or oestradiol. Using the biochemistry assays available LH, FSH and testosterone remained measurable in the majority of cases, whilst oestradiol was mostly undetectable after treatment. There was no association of the magnitude of response to age, treatment duration or body size. The results may have been affected by variations in sensitivity to GnRHa or to differences in the clearance rate of the drug. In addition, biochemistry measurements were not made at a defined time after the last GnRHa dose. The optimal treatment to arrest puberty in gender dysphoria patients needs a consensus view. The current protocol does not indicate complete suppression of hormone secretion. These biochemistry results need to be correlated with clinical outcomes to indicate sufficient suppression of the hypothalamic-pituitary-gonadal axis.

References

1. Hembree WC *et al.* Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2009; 94: 3132-3154