MINIPUBERTY PITUITARY-GONADAL HORMONE PROFILE IN INFANTS WITH 47,XXY

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Abstract

Purpose of the Study: Minipuberty in infant males is important for growth of the phallus, proliferation of Sertoli and germ cells, and has been shown to influence early body composition, with total testosterone (TT) correlating with adiposity, lean mass, and linear growth velocity. Previous studies examining the minipuberty hormone profile of infants with 47,XXY Klinefelter Syndrome (KS) are limited by contradictory results, disparate hormonal measurement techniques, and small sample sizes. Our aim was to describe the minipuberty pituitary-gonadal hormone profile in infants with KS.

Method used: Serum hormone concentrations from 85 infant males with KS participating in the eXtraordinarY Babies and/or TESTO studies at Children's Hospital Colorado were measured during the minipuberty period (median age = 2.3 months (range 1-3.6)). Blood was drawn by venipuncture, centrifuged, and stored at -80°C until batch analysis. TT was analyzed using ultra-high performance liquid chromatography tandem mass spectrometry; luteinizing hormone (LH), follicle stimulating hormone (FSH), anti-Müllerian hormone (AMH), and inhibin B (INHB) were analyzed via immunoassays. Body length and stretched penile length (SPL) were measured to the nearest 0.1cm. One-sample Wilcoxon tests were used to compare our sample's median with the male reference population 1-4 months of age; scatter and violin plots were constructed for data visualization. Spearman regression analyses were performed to evaluate the relationship between continuous variables with alpha set at 0.05. All analyses were conducted in R statistical package version 4.4.1 with R Studio build 764.

Summary of Results: The majority (~95%) of all hormone concentrations fell within the normal reference range for age, however medians were lower in XXY than the reference population for TT ($p<0.001$) and AMH ($p=0.001$), while median INHB ($p<0.001$), LH ($p<0.001$), and FSH ($p=0.027$) levels were higher. Positive correlations were observed between TT and LH ($r=0.28$,

p=0.010) and AMH and INHB (r=0.5, p<0.001), while negative correlations were observed between AMH and FSH (r=-0.3, p=0.007) and INHB and FSH (r=-0.3, p=0.008). No correlation was observed between TT and SPL, while weak negative correlations were observed between TT and length z-score (r=-0.22, p=0.043).

Conclusion: Although pituitary-gonadal serum hormone concentrations in infants with KS during minipuberty fall within the normal range, median values are lower in infants with KS compared to normative values. The lack of positive correlations between TT and body length or SPL challenges strong physiologic implications of TT in the mini-puberty period. Strengths of this study include a large sample size compared to prior studies, narrow age window, and uniform hormone measurement techniques. Future directions include exploring whether early hormone measures predict longitudinal outcomes in KS.