

METABOLIC EFFECTS OF GONADOTROPIN RELEASING HORMONE AGONISTS IN TRANSGENDER YOUTH

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Purpose of study: Eligible transgender youth may receive gonadotropin-releasing hormone agonist (GnRHa) treatment to prevent the development of secondary sex characteristics that do not align with gender identity. Though GnRHa are linked to worse metabolic outcomes in adults (decrease in insulin sensitivity, increase in body fat, mixed effects on basal metabolic rate), there are few studies evaluating the effects in Tanner Stage 2-3 youth. We evaluated the changes in bone mineral density (BMD), body composition, resting energy expenditure (REE) and insulin sensitivity (IS) of transgender girls at baseline and 6 months after GnRHa initiation.

Methods used: Transgender youth with a male sex at birth (n=14, 9.9-13.6 yrs, Tanner 2-3) were enrolled in a longitudinal, observational study, with a baseline visit (prior to clinical GnRHa initiation) and 6 months later. Visits included fasted morning labs, a 3-hour 75g oral glucose tolerance test, REE via indirect calorimetry, and body composition and BMD by DXA. IS was estimated using the HOMA-IR and Matsuda index. Changes from 6-month time point vs. baseline were compared using one-sample Wilcoxon Rank Sum tests. Medians and interquartile ranges are presented.

Summary of Results: The median total bone mineral content (BMC, +49.5g [40.9,65.7], P=0.002), subtotal BMC (+47.9g [36.2, 66.5], P=0.002), total BMD (+0.023g/cm² [0.009,0.028], P=0.008) and subtotal BMD (+0.022g/cm² [0.013,0.033], P=0.002) increased after 6 months of GnRHa. Subtotal BMD Z-scores were not significantly different after 6 months of GnRHa (baseline: -1.7 [-1.7, -0.05], 6 months: -1.2 [-1.8, -0.80]). Total mass, (+2.2kg [1.9, 3.2], P=0.002) lean mass (+1.5kg [0.75,2.0], P=0.003), and fat mass (+1.1kg [0.22, 1.7], P=0.003) all increased after 6 months of GnRHa. The fat mass/height² (+0.3kg/m² [0, 0.4], P=0.021) increased. Neither the total %fat nor BMI percentile were significantly different after 6 months of GnRHa. There were no significant differences in REE or respiratory quotient. While not statistically significant, Matsuda Index decreased (-0.6 [-19.4, 4.6], P=0.415) and HOMA-IR increased (0.2 [-0.2, 0.3], P=0.625).

Conclusions: Though BMD z-scores were below average at baseline, they were not significantly different after 6 months of GnRHa, and BMC and BMD increased. Total mass, lean mass, fat mass, and fat/height² increased, however, total %fat and BMI percentile

were unchanged. There were no significant differences in REE or insulin sensitivity, though these should be investigated in a larger cohort.