Markers of Metabolic Health and Body Composition in Transgender Youth Before and After Gonadotropin Releasing Hormone Agonists

Beatrice M Bridge;[1] Samantha Bothwell, MS;[1] J Pinkans;[1] Kerrie L Moreau, PhD;[2] Kristen J Nadeau, MD, MS;[1] Natalie J Nokoff, MD, PhD[1]

[1]Department of Pediatrics, University of Colorado Anschutz Medical Campus; [2]Department of Medicine, University of Colorado Anschutz Medical Campus

Children's Hospital Colorado

Affiliated with University of Colorado Anschutz Medical Campus

Background

- 1.8% of adolescents in the U.S. identify as transgender or gender diverse (TGD)
- Eligible TGD youth may receive gonadotropin-releasing hormone agonist (GnRHa) treatment to prevent the development of incongruent secondary sex characteristics
- GnRHa treatment in adults is associated with increased adiposity, cardiovascular disease and diabetes risk
- GnRHa treatment in children with central precocious puberty is associated with increased adiposity and insulin resistance
- During puberty, youth have an increase in insulin resistance
- Little is known about the effects of GnRHa therapy in TGD adolescents on metabolic health and body composition, particularly in Tanner Stage 2-3 youth

Methods

- Longitudinal, observational study
- 14 transgender females with a male sex at birth (9.9-13.6 yrs, Tanner stage 2-3)
- Visits at baseline and 6 months after starting GnRHa therapy
- Fasting morning research visit with 3-hour oral glucose tolerance test (OGTT), resting energy expenditure (REE) via indirect calorimetry
- Body composition and bone density measured by dual-energy X-ray absorptiometry (DXA)
- Insulin sensitivity estimated with 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

Aims

To evaluate differences in metabolic health (bone mineral density, body composition, insulin sensitivity, resting energy expenditure) in transgender females at baseline and 6 months after starting GnRHa clinically

Figures: Changes after GnRHa therapy

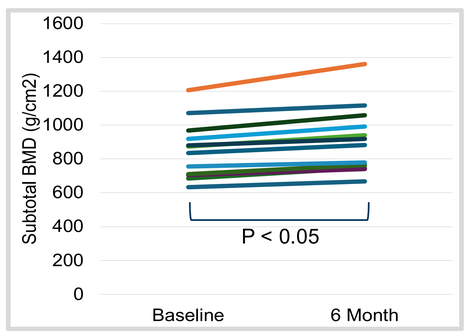

Figure 1: Subtotal BMD increases after 6 months of GnRHa therapy

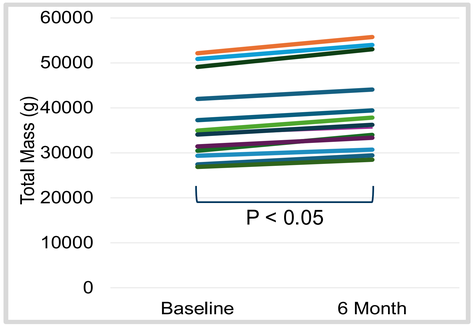

Figure 2: Total mass increases after 6 months of GnRHa therapy

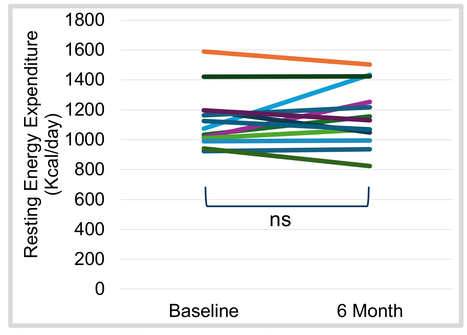

Figure 3: REE is not significantly changed after 6 months of GnRHa therapy

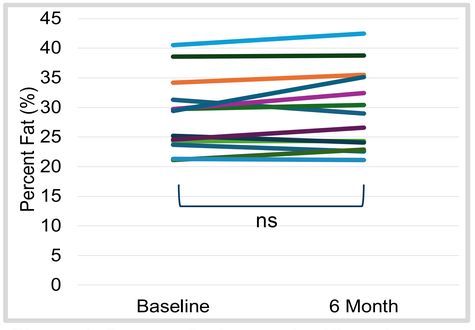

Figure 4: Percent fat is not significantly changed after 6 months of GnRHa therapy

Results

Values as n (%) mean ± standard deviation if normally distributed or median (interquartile range) if not normally distributed

BMI: body mass index, BMC: bone mineral content, BMD: bone mineral density, REE: resting energy expenditure, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance

	Transgender females (n=14)
Age (years)	11.6 ± 1.15
Race	
White	13 (93)
Hispanic/Latino Ethnicity	1 (7)
Depression	0 (0)
Anxiety	3 (21)

Table 1: Baseline demographics

	Baseline (n=13)	6 month (n=13)	6 months - Baseline	p-value
BMI Percentile	34 [7.6, 68]	34 [6.1, 56.5]	0.3 [-1.4, 2.0]	0.961
BMC (g)	1231.8 [1072.7, 1291.3]	1297.1 [1102.5, 1363.5]	49.5 [40.9, 65.7]	0.002
Subtotal BMC (g)	873.5 [709.8, 919.4]	917.6 [765.1, 992.6]	47.9 [36.2, 66.5]	0.002
BMD (g/cm^2)	0.856 [0.79, 0.875]	0.857 [0.809, 0.891]	0.023 [0.009, 0.028]	0.008
Fat mass/height^2 (kg/m^2)	4.5 [3.8, 4.7]	4.3 [3.7, 6]	0.3 [0, 0.4]	0.021
Fat mass (g)	9,063.2 [8515.6, 10948.8]	9,961.7 [8732.5, 13857]	1,142.4 [218.8, 1651]	0.003
Lean mass (g)	24,203.7 [22005.1, 28904]	24,371.4 [22721.7, 29714.2]	14,68.4 [750.6, 1965.1]	0.003
BMD Z-score female norms	-0.8 [-1.3, -0.1]	-1.1 [-1.3, -0.6]	-0.2 [-0.3, 0.1]	0.130
BMD Z-score male norms	-0.9 [-1, -0.1]	-0.8 [-1, -0.7]	0 [-0.2, 0.2]	1.000
% Predicted REE	83 [81, 92]	82 [79, 89]	-2 [-7, 3]	0.529
HOMA-IR	0.6 [0.5, 0.7]	0.8 [0.7, 0.9]	0.2 [-0.2, 0.3]	0.625
Matsuda index	27 [16.3, 37.9]	16.4 [13.9, 24.4]	-0.6 [-19.4, 4.6]	0.415

Table 2: Body Composition and Indirect Calorimetry Values

Conclusions

- After 6 months of GnRHa therapy, growing youth had:
  - Increased bone mineral content
  - Increased bone mineral density
  - No change in bone mineral density Z-scores when compared to male or female norms
  - Increased total mass, lean mass, and fat mass
  - Increased fat mass/height^2
  - No change in % fat or BMI percentile
- OGTT results after 6 months of GnRHa therapy show:
  - No change in HOMA-IR (a measure calculated using fasting insulin and glucose values)
  - No change in Matsuda index (a measure calculated using insulin and glucose values across the OGTT)
- Resting energy expenditure via indirect calorimetry after 6 months of GnRHa therapy show:
  - No change in REE or respiratory quotient

Though BMD z-scores were below average at baseline, they were not significantly different after 6 months of GnRHa and there was an increase in BMC and BMD after 6 months.

Implications and Limitations

After six months of GnRHa therapy, transgender youth had unchanged bone density Z-scores and BMI percentiles, with increases in BMC, BMD, and total mass. This suggests that while on therapy these youths continued to grow and gain bone mass. There were no significant changes in estimates of insulin resistance or measured resting energy expenditure, though this study was limited by a small sample size and lack of controls. More research is needed to understand the long-term impact of GnRHa on metabolic health in youth, and how the metabolic effects of GnRHa use in early pubertal youth may be distinct from those in adults.

Acknowledgements

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