

# Dynamics in blood pressure after pubertal suppression with GnRH analogs followed by testosterone treatment in transgender male adolescents

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Disclosure Statement: All authors have nothing to declare

## BACKGROUND

In 2017, the Endocrine Society published guidelines for the hormonal treatment of gender dysphoria. Adolescents who meet diagnostic criteria for gender dysphoria undergo pubertal suppression using gonadotropin-releasing hormone analogs (GnRHa) and induction of puberty with gender-affirming hormonal therapy (estrogen or testosterone). The Endocrine Society Clinical Practice Guidelines recommend blood pressure (BP) monitoring before and during treatment with GnRHa and/ or treatment with testosterone. Recommendations regarding GnRHa and blood pressure monitoring are based on a few case reports of hypertension during GnRHa treatment in precocious puberty in cis-gendered individuals. In the transgender youth population, there is a single case series describing three cases of GnRHa-induced arterial hypertension in adolescent natal girls with gender dysphoria, one patient also developed increased intracranial pressure and papilledema.

## AIMS

- To examine BP changes in transgender male adolescents treated with GnRHa and after the addition of testosterone.

## STUDY DESIGN, PATIENTS & METHODS

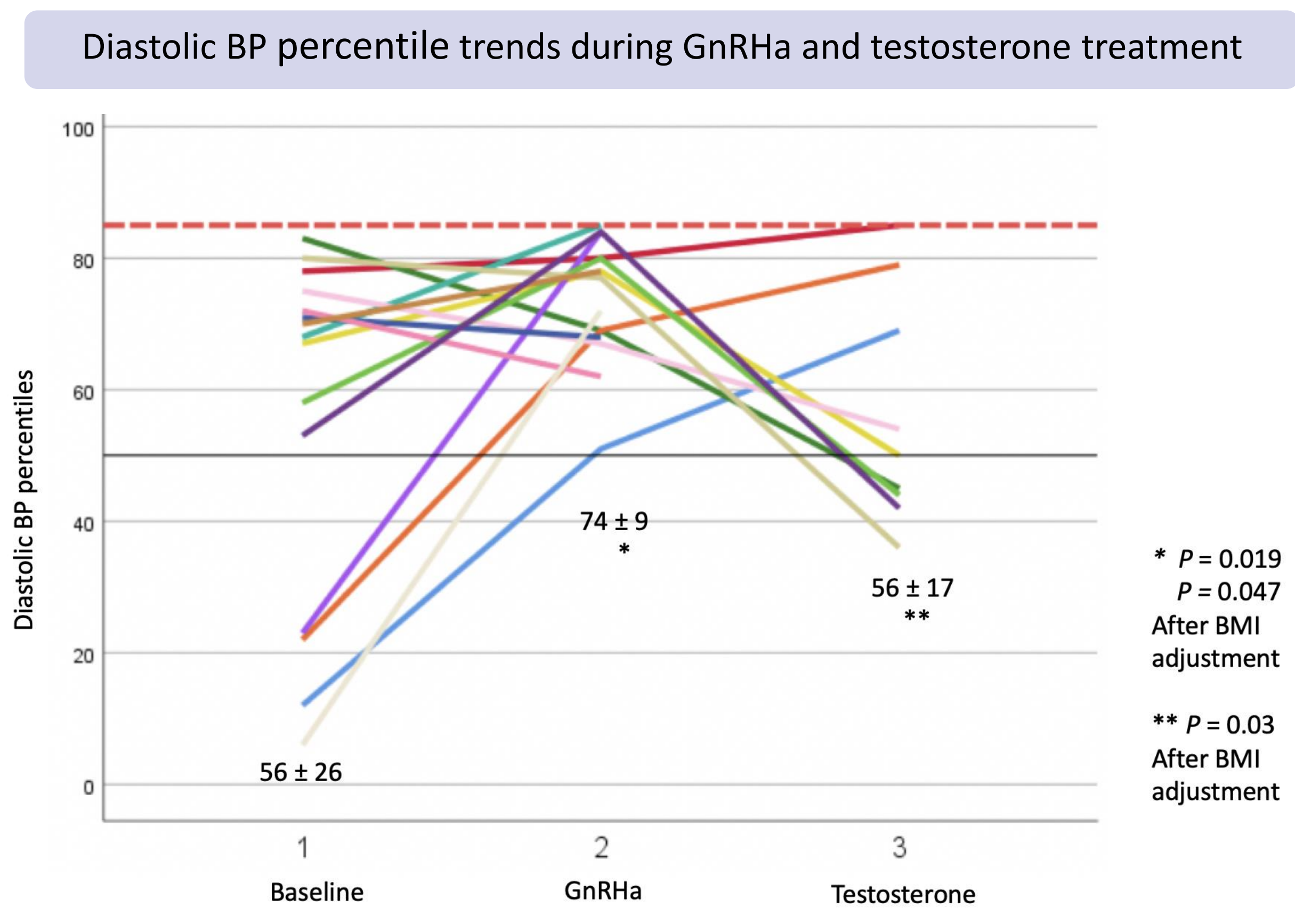
**Design:** Retrospective, single-center, observational study from the Israeli Pediatric Gender Dysphoria Clinic  
**Patients:** All consecutive transgender male adolescents who were treated solely with GnRHa for at least 2 months  
**Data:** Data extracted from medical records included vital signs, anthropometric measurements, and hormonal levels (LH, FSH, estradiol and testosterone)  
**Outcome measures:** Systolic and diastolic BP percentiles at baseline, after GnRHa and after testosterone treatment

## RESULTS

- 15 transgender males, mean age at baseline was  $14.4 \pm 1.0$  years and Tanner 5 stage of puberty (13 subjects)
- GnRHa was administered for a mean period of  $3 \pm 1$  months
- Testosterone treatment, in 9 transgender males was added at a mean age of  $15.1 \pm 0.9$  years
- Diastolic BP percentiles increased significantly after GnRHa treatment
- Diastolic BP percentiles decreased significantly after adding testosterone therapy, only after adjusting for the change in BMI SDS
- No significant correlations were found between BP percentiles and estrogen, LH or FSH levels

Parameter	Pubertal suppression (n=15)			Gender-affirming hormonal therapy (n=9)		
	Baseline	GnRHa treatment	P value	GnRHa treatment	Testosterone treatment	P value
Age (y)	14.4 ± 1.0	14.8 ± 1.0		15.1 ± 0.9	15.8 ± 0.9	
BMI (kg/m²)	21.3 ± 4.7	22.0 ± 4.8	0.240	23.3 ± 5.6	24.2 ± 4.6	0.199
BMI SDS	0.2 ± 0.9	0.4 ± 0.9	0.198	0.6 ± 1.0	0.8 ± 0.8	0.207
SBP (mm Hg)	115 ± 7	116 ± 5	0.532	117 ± 4	116 ± 6	0.776
SBP percentiles	71 ± 19	76 ± 14	0.443	76 ± 14	72 ± 21	0.57
DBP (mm Hg)	64 ± 10	71 ± 3.0	0.009	71 ± 3.0	68 ± 5	0.212
DBP percentiles	56 ± 26	74 ± 9.0	0.019	74 ± 9.0	56 ± 17	0.059
LH (mIU/mL)	6.6 ± 6.0	0.2 ± 0.4	0.02	0.2 ± 0.3	0.1 ± 0.2	0.429
FSH (mIU/mL)	6.2 ± 2.4	2.5 ± 1.2	<0.001	2.4 ± 1.0	2.0 ± 1.3	0.341
Estradiol (pmol/L)	264.6 ± 238.2	0 ± 0	0.003	0.0 ± 0.0	38.6 ± 42.0	0.035
Testosterone (nmol/L)	1.4 ± 1.2	0.4 ± 0.4	0.03	0.4 ± 0.5	7.1 ± 4.6	0.007

Data are presented as mean and SD, statistical analysis by ANOVA, ANCOVA and paired T test



## DISCUSSION

Our preliminary findings suggest that pubertal suppression with GnRHa increases diastolic BP in transgender male adolescents and that induction of puberty with gender-affirming testosterone treatment restores diastolic BP percentiles. One plausible explanation in which GnRHa might cause hypertension is the abrupt decline in estrogen and progesterone in pubertal trans male. Estrogen and progesterone influence the vascular system inducing vasodilatation, and so, their decline might reduce this effect. Induction of puberty with gender-affirming testosterone treatment might restore and lower diastolic BP percentiles through local aromatase activity in vascular tissue, thus increasing estrogen levels and vasodilatation. Further studies with larger cohorts are needed to elucidate the effect of BP dynamics in gender dysphoric adolescents on the metabolic and cardiovascular consequences in young adulthood.