Effect of testosterone enanthate therapy on adult height, genital maturation, and bone mineral density in children and adolescents with male hypogonadotropic hypogonadism

Hironori Shibata, Tomohiro Ishii, Naoaki Hori, Goro Sasaki, Tsutomu Kamimaki, Makoto Anzo, Shinya Tamai, Seiji Sato, Nobutake Matsuo and Tomonobu Hasegawa

Department of Pediatrics, Keio University School of Medicine, Tokyo, Japan

Take Home Message

Testosterone enanthate therapy for male hypogonadotropic hypogonadism is effective in attainment of genetic height potential, maturation of genitalia, and improvement of BMD

Introduction

- Testosterone enanthate (TE) therapy was established for children and adolescents with male hypogonadotropic hypogonadism (c/a MHH).
- The effect of TE therapy on adult height (AH), genital maturation, and bone mineral density (BMD) in c/a MHH has not been described well.

Objective

To assess the effect of TE therapy in c/a MHH on the achievement of genetic height potential, pubertal development ,and bone acquisition, and the possible adverse effect on spermatogenesis by subsequent gonadotropin (Gn) therapy.

Methods

Design

Reviewed medical records retrospectively in a single center

Participants

<Inclusion criteria>

- c/a MHH patients followed at Department of Pediatrics, Keio University Hospital between April 1984 and March 2019
- Treated with TE intramuscular injection every 4 weeks
- Attained AH by TE therapy
- AH defined as height achieved at growth velocities < 1 cm per year or as height at bone ages ≥ 17 years

<Exclusion criteria>

- History of Gn therapy before TE therapy
- *DAX1* (*NR0B1*) mutation

Measurements

- Final growth status: AH, Target height (TH), Target range (TR)
- Pubertal development: Pubic hair (PH) Tanner stage, Stretched penile length (SPL)
- Bone mineral acquisition: Lumbar BMD by DXA
- Spermatogenesis: Sperm concentration by subsequent Gn therapy

Discussion

Effect of TE therapy on final growth status, pubertal development, and bone mineral acquisition

- All of AHs were greater than the lower limit of TR
- All of PH Tanner stages reached greater than stage 4
- SPL Z-scores were improved significantly
- Lumbar BMD Z-scores were increased significantly
  - TE therapy in c/a MHH is effective in achievement of appropriate AH for genetic potential, maturation of external genitalia, and improvement of BMD

Spermatogenesis by subsequent Gn therapy

- 6 of 7 (85.7%) achieved spermatogenesis
- One with azoospermia had untreated bilateral cryptorchidism at 22 years
  - Subsequent Gn therapy can induce spermatogenesis

Results

Table1. Causes of MHH (N=18)

Cause of MHH	No.
Isolated hypogonadotropic hypogonadism	6
Idiopathic hypopituitarism	5
Hypopituitarism due to brain tumors	4
Kallmann syndrome	3

Table2. Characteristics of participants (N=18)

Characteristics	Median (range)
Age at the first visit (yr)	12.1 (0.1 - 22.8)
Age at the start of TE therapy (yr)	15.1 (13.3 - 22.9)
Age at the attainment of AH (yr)	18.9 (17.1 – 24.8)
Duration of TE therapy until the attainment of AH (yr)	3.7 (1.8 - 6.3)

Table3. Final growth statuses (N=18)

Measurements	Median (range)
AH (cm)	175.5 (160.1 – 187.6)
TH (cm)	170.5 (160.9 – 179.2)
AH - TH (cm)	4.8 (-8.0 – 11.7)

Table4. PH Tanner stages before and after TE therapy (N=18)

PH Tanner Stage	Before TE therapy	At the attainment of AH
Stage Ⅰ (No.)	16	0
Stage Ⅱ (No.)	2	0
Stage Ⅲ (No.)	0	0
Stage Ⅳ (No.)	0	10
Stage Ⅴ (No.)	0	6

Fig1. SPL Z-scores before and after TE therapy (N=18)

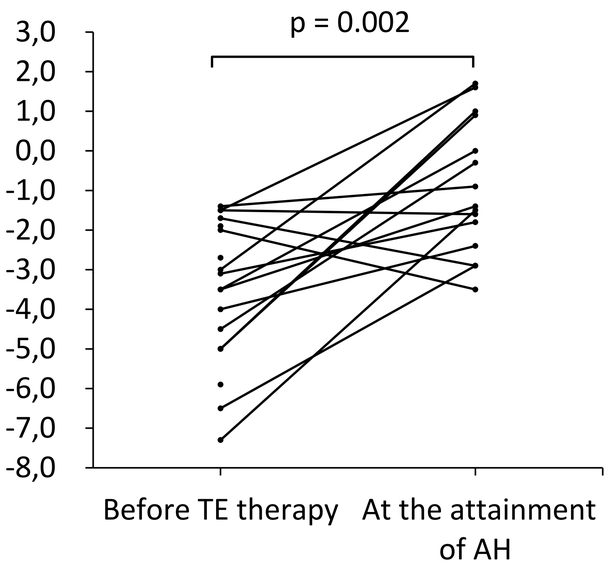

Fig2. Lumbar BMD Z-scores before and after TE therapy (N=16)

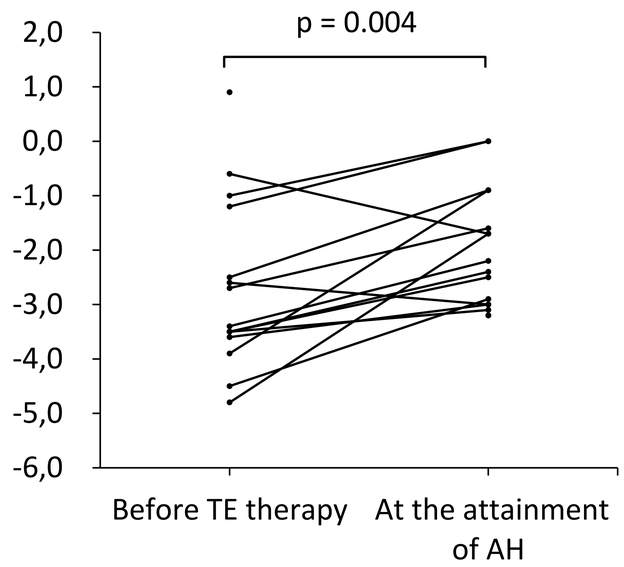

Table5. Sperm concentration by subsequent Gn therapy (N=7)

Sperm concentration (10^6/mL)	No. (%)
≥ 15	3 (42.9%)
> 0, < 15	3 (42.9%)
0	1 (14.2%)