

PENIS GROWTH RESPONSE TO HORMONAL THERAPY IN CHILDREN WITH MICROPENIS AT HASAN SADIKIN HOSPITAL

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ABSTRACT

Objective: This study aims to determine the response of penis growth to testosterone injection. **Material & Methods:** The study was conducted on all cases of micropenis from January 2016 to December 2020. Each subject who met the criteria for micropenis received 25 mg of intramuscular testosterone ester injection, in 4 doses with an interval of 1 week. Evaluation is done at the beginning, before administration of testosterone, then an evaluation is carried out for each patient before testosterone injection until 1 week after the 4th injection. Penis measurement is done by fully stretched length measurement. **Results:** There were 62 patients who met the criteria for micropenis. The average age of patients with micropenis when they first came was 5.9 years. The patient's mean initial penile length was 2.13 cm. There was an increase in penis length of 32% in the first injection, 28% after the second injection, 18% after the third injection and 14% after the fourth injection. The average length of the penis at the first, second, third and fourth injections was 2.53 cm, 3.24 cm, 3.65 cm and 4.01 cm, respectively. At the end of treatment, there was an average increase in penile length of 75.8% compared to the beginning of treatment. **Conclusion:** In conclusion, it can be said that testosterone therapy in micropenis patients gave a good response in terms of increasing penile length by 75.8% and increasing the average from 2.13 cm to 4.01 cm.

Keywords: Micropenis, testosterone, growth.

ABSTRAK

Tujuan: Penelitian ini bertujuan untuk mengetahui respon pertumbuhan penis terhadap suntikan testosteron. **Bahan & Cara:** Penelitian dilakukan pada semua kasus mikropenis dari Januari 2016 hingga Desember 2020. Setiap subjek yang memenuhi kriteria mikropenis mendapat suntikan testosteron ester intramuskular 25 mg, dalam 4 dosis dengan selang waktu 1 minggu. Evaluasi dilakukan di awal, sebelum pemberian testosteron, kemudian dilakukan evaluasi pada setiap pasien sebelum penyuntikan testosteron hingga 1 minggu setelah penyuntikan ke-4. Pengukuran penis dilakukan dengan pengukuran panjang terentang penuh. **Hasil:** Terdapat 62 pasien yang memenuhi kriteria mikropenis. Usia rerata penderita mikropenis saat pertama kali datang adalah 5.9 tahun. Rerata panjang penis awal pasien adalah 2.13 cm. Terjadi peningkatan panjang penis sebesar 32% pada penyuntikan pertama, 28% setelah penyuntikan kedua, 18% setelah penyuntikan ketiga dan 14% setelah penyuntikan keempat. Rerata panjang penis pada penyuntikan pertama, kedua, ketiga, dan keempat berturut-turut adalah 2.53 cm, 3.24 cm, 3.65 cm, dan 4.01 cm. Pada akhir pengobatan, terjadi peningkatan rerata panjang penis sebesar 75.8% dibandingkan awal pengobatan. **Simpulan:** Terapi testosteron pada pasien mikropenis memberikan respon yang baik dalam hal peningkatan panjang penis sebesar 75.8% dan peningkatan rata-rata dari 2.13 cm menjadi 4.01 cm.

Kata Kunci: Mikropenis, testosterone, pertumbuhan.

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INTRODUCTION

Micropenis is a condition in which the length of the penis is below the average for the patient based on his age. Examination of the length of the penis is done in a stretched state (stretched). Micropenis in adult males of Caucasian race is less than 7.5 cm in size and less than 1.9 cm in neonates.¹

Micropenis occurs in 0.6% of men worldwide. In addition, according to a study conducted by Alsaleem and Saadeh in 2017, the incidence of micropenis in North America is 1.5 per 10,000 male infants.² In a study conducted in China in 2015 it was found that the prevalence of micropenis was 13%.³ Indonesia's own micropenis in a study conducted by Hakimi on 107 boys from

four kindergartens in Medan City, Indonesia, in 2010 found the prevalence of micropenis was 18.2% (20 children), and small penis was 72% (77 children).⁴

The presence of a congenital micropenis is largely due to a disturbance in the hypothalamic-pituitary-gonadal axis during fetal development, resulting in abnormal development of the penis. Micropenis can be caused by various factors such as deficiency of testosterone production (in Kallman's syndrome, Prader Willi syndrome, anorchia, gonadal dysgenesis, etc.), disturbances in the action of the hormone testosterone (androgen receptor defects), and developmental anomalies (aphallia). Meanwhile, acquired micropenis is caused by various factors such as Peyronie's disease, prostate cancer, post-priapismus, lichen sclerosis, and hypergonadotropic hypogonadism (due to failure of the testes to produce testosterone).⁵

The normal value of penis length is known to be different in each country. These differences occur due to racial, ethnic, genetic and nutritional factors. The Tanner classification from British Pediatrician is widely used by researchers as a reference for the normal length of the penis, including in Indonesia. Over time, many studies have been conducted to determine the average penis length by age in each country. By using normative data that is appropriate to the population, research is carried out to prevent under- or over-diagnosis which in turn causes the research to be biased. Research conducted by Wallad in 2017 at Hasan Sadikin Hospital Bandung can be used as a reference value for penis size in the population to be studied.⁶

Micropenis management is divided into hormonal therapy and surgical therapy. For hormonal therapy, testosterone enanthate 25-50 can be given intramuscularly every week for 1 month. Surgical treatment such as reconstructive surgery performed on patients with hormonal therapy failure.⁷

Testosterone is known to give promising results in increasing penis length.⁸⁻⁹ Testosterone is a sex steroid hormone which is a product of androgen hormones. The term androgen means a sex steroid hormone that has a masculinizing effect, which consists of the hormones testosterone, dihydrotestosterone (DHT), and androstenedione. Testosterone regulates the development and maintenance of the male sex organs and secondary male sex characteristics. Testosterone therapy is given over a short period of time to evaluate the response to penile development. Testosterone

therapy is known to be effective in treating micropenis due to testosterone deficiency and has minimal side effects.

In a study conducted by Abbas et al. 1 or 2 of a total of 3 injections of testosterone at a dose of 25-50 mg given at 4-week intervals in infancy or childhood increased penis size to reach the size according to age.¹⁰ Alsaem et al found that there was an increase in penile length in 50 children aged 5 months to 8 years who were given testosterone cream for 30 days.²

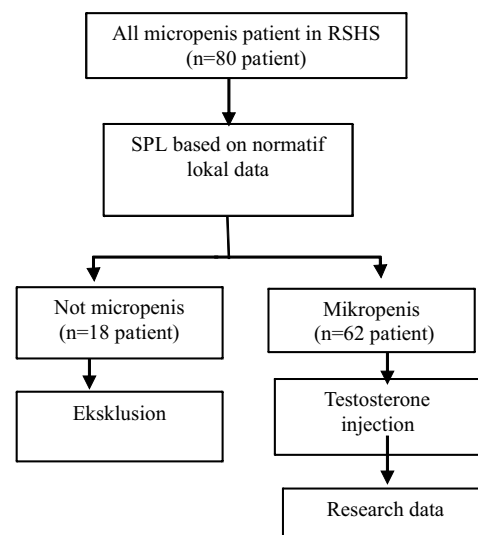
In a study conducted by Nerli, et al. Children under 11 years old are given hormonal therapy in the form of testosterone, while children over 11 years are given hCG. This difference in therapy depends on age, because in older children (over 11 years) hormonal therapy aims to trigger the production of the hormone testosterone from the testes themselves.¹¹

OBJECTIVE

This study aims to determine the response of penis growth to testosterone injection.

MATERIAL & METHODS

The study was conducted by taking secondary data from micropenis patients retrospectively from the medical records of the pediatric endocrine polyclinic at Hasan Sadikin Hospital in Bandung for the period 2016 to 2020, and the number of research samples was obtained as follows:



Picture 1. Research flow.

Data that met the inclusion criteria of penis length below the average determined using local normative data on penis length received injection of testosterone ester 25 mg intra-muscularly, given in 4 doses with an interval of 1 week. Evaluation is carried out at the beginning, before giving testosterone, and each time the patient comes to get a testosterone injection until 1 week after the 4th injection.

Penis length growth data was then analyzed using dependent T-test analysis using SPSS ver 25.0 data analysis tool.

RESULTS

In this study, there were 80 patients who met the criteria for micropenis based on Tanner stage, when calculating SPL based on local normative data it was found that 18 of them did not have a micropenis, bringing the total number of patients obtained to 62 patients. The average age of patients with micropenis when they first came was 5.9 years. All patients were in prepubertal status. 35 patients were in the age group 3-5 years (under fives group) and 27 patients were in the age group 6-11 years (children group).

The mean initial length of the patient's penis at first arrival was 2.13 cm. In table 1 it can be seen that there is an absolute response to testosterone administration. There was an increase in penis length of 32% in the first injection, 28% after the second injection, 18% after the third injection and 14% after the fourth injection. The average length of the penis at the first, second, third and fourth injections was 2.53 cm, 3.24 cm, 3.65 cm and 4.01 cm, respectively. At the end of treatment, there was an average increase in penile length of 75.8% compared to the beginning of treatment.

Table 1. Average penile length gain in micropenis patients on testosterone therapy.

Testosteron	Average Gain (cm)	P Value
Injection 1	0.73 ± 0.11	0.01
Injection 2	0.51 ± 0.13	0.02
Injection 3	0.40 ± 0.12	0.03
Injection 4	0.33 ± 0.10	0.15

In table 3, it is found that the average penis length increase in micropenis patients with testosterone therapy after the first to third injection has significant results.

DISCUSSION

Micropenis is a condition of the penis with a normal shape but with a size of less than 2.5 SD below the average for age and developmental status of puberty. There are several causes of a micropenis, such as a defect along the hypothalamic-pituitary-gonadal axis, damage to peripheral androgens, growth hormone deficiency, primary structural anomaly, or it may be part of a genetic syndrome.

Aaronson recommends parenteral administration of testosterone ester at a dose of 25 mg every 1 week 4 times. Control was carried out 1 week after the last injection. In neonates with micropenis, if the results are not satisfactory, it can be repeated at the age of 4-5 years. In this study, the protocol in accordance with Aaronson's recommendation turned out to produce a good response, not a single patient failed therapy. In patients who stopped treatment, everything had returned to normal at the time of discontinuation.^{3,11}

This study was conducted on 62 children with micropenis from the age of 3-10 years. Administered testosterone 25 mg at 1-week intervals. The result is an increase in penis length of 32% in the first injection, 28% after the second injection, 18% after the third injection and 14% after the fourth injection. The average length of the penis at the first, second, third and fourth injections was 2.13 cm, 3.24 cm, 3.85 cm and 4.01 cm, respectively. After receiving 4 injections of testosterone, the average penis length was 5 cm. or 75.8% increase in penis length.

In a study conducted by Abbas et al in America in 2000 showed the results that 1 or 2 doses of a total of 3 injections of testosterone (25-50 mg) given 4 doses at 1-week intervals in infancy or childhood is sufficient to increase the size of the penis to reach the appropriate size. with age.¹⁰ Research by Arisaka et al in 2010 in Japan showed that the use of 5% topical testosterone for 30 days was quite effective in childhood because there was an increase in penile length in 50 children with an age range of 5 months to 8 years.²

In a study conducted by Nihai in 2015 in India, it was found that the absence of androgens during childhood is crucial in the pathophysiology of micropenis. In this study, 4 doses of testosterone 25 mg were injected every 3 weeks for 3 months and there was an increase in SPL of 130%. Apart from injection, this study also shows that topical administration for 30 days also has promising

results. The results obtained were an increase in SPL of 100% and an increase in penis length of 3.5 cm. All cases in this study met normal SPL at their age after testosterone therapy.¹³ In this study, bone age and side effects of treatment were not investigated. Coal in 2016 in Indonesia found that giving testosterone 25 mg every 3 weeks 4 times did not accelerate the bone age of children with micropenis.¹³

According to Guthrie in 2015 in America, side effects that may arise from the use of testosterone can be said to be minimal and also rare, but testosterone as a micropenis therapy such as a temporary increase in growth rate, and an increase in the rate of bone age.

In a study conducted by Xu in China in 2016 that assessed the efficacy and safety of testosterone use in micropenis patients for 3 months, no side effects were found, only an increase in DHT after therapy without any symptoms.

CONCLUSION

In conclusion, it can be said that testosterone therapy in micropenis patients gave a good response in the form of an increase in penile length of 75.8% and an increase in the average from 2.13 cm to 4.01 cm. This study emphasizes that micropenis is a repairable condition with good outcomes.

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