

Efficacy of hormone therapy on stretched penile length in micropenis: A systematic review

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Abstract

Background: While there have been clinical studies to prove the efficacy of testosterone in increasing the stretched penile size in cases of micropenis, giving various results, attempts to summarize them have been scant.

Objectives: This systematic review summarizes the efficacy of testosterone in the treatment of micropenis.

Materials and methods: This systematic review sought original English research articles in which patients with isolated micropenis were administered testosterone to increase their stretched penile length in PubMed, Scopus, and ProQuest. Search keywords were “micropenis” and “hormone”. We then assessed the selected articles using the Joanna Briggs Institute (JBI) Checklist for Case Series.

Results: Of the 1,181 articles, 8 articles (n = 171) met the inclusion criteria for this systematic review. Assessment of the articles showed that various hormones are used in the treatment of micropenis.

Discussion: Various hormones, mainly testosterone, are effective in treating micropenis. It is found that testosterone, especially topical testosterone, can increase stretched penile length 2 until 3 times the pre-treatment length in 3 months of treatment. However, other hormone treatments can also increase stretched penile length, but its effect is not as significant as testosterone. Dual hormone therapy is also used for micropenis and other hormone deficiencies to increase the efficacy of the results.

Conclusions: Hormone therapy is effective in increasing the stretched penile size in cases of micropenis. The use of hormones needs to be tailored to each patient to ensure optimal result.

Keywords: Hormone therapy; Testosterone; Micropenis; Stretched penile length

1. Introduction

Micropenis is occasionally reported but is seldom recognized by parents and children since the diagnosis is frequently wrong¹. Micropenis is a condition in which the stretched penile length is 2.5 standard deviations below the mean stretched penile length for age². Stretched penile length measurement might be subjective. As a result, in order to acquire an accurate volume of the cylindrical construction, penile circumference may also be an important measure in determining penile size³. Micropenis can present as its own abnormality or as a symptom of many syndromes. Micropenis may develop on the fetus due to abnormalities to the hypothalamic-pituitary-gonadal axis

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that occur after the 12th week of pregnancy, but cases of isolated micropenis also exist^{4,5}. Many countries do not publish their micropenis incidence rate, but the United States of America has around 15 cases of micropenis for every 100,000 male newborns⁶. The variability of causes in cases of micropenis guarantees thorough examination to ensure correct treatment. Meanwhile, various hormonal treatment has been proven to increase stretched penile length and resolve the issue of micropenis^{5,7-9}. However, attempts at summarizing these treatments are scant. This review aims to summarize these treatments so that future research on this topic would have some scientific basis.

2. Material and methods

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guideline¹⁰.

2.1. Article searching

We searched for articles in PubMed, Scopus, and ProQuest on 21 September 2022.

2.2. Selection criteria

Our inclusion criteria were as follows: (1) original research articles written in English in which (2) cases of micropenis (3) were treated only with hormone therapy. Our exclusion criteria were (1) non-standard penis measurement and (2) other major physical abnormalities. The measurement of micropenis follows Schonfeld's method, in which the penis is measured from the pubic ramus to the tip of the glans while the penis is stretched until resistance is found, while micropenis is defined as a stretched penile length at least 2.5 standard deviations below the mean.¹¹

2.3. Search keywords

Our primary search keywords were "micropenis" AND "hormone". These search keywords were adapted to each database's search engine because of the differences between the databases' search systems. The expanded search keywords are listed in Table 1.

2.4. Article compilation, screening, and quality assessment

We compiled the found articles using Microsoft Excel, deduplicated the articles using Rayyan¹². We screened the resulting list of articles by title, abstract, and full text. The screening process was presented with a ShinyApp flowchart for PRISMA 2020¹³. The screened articles were then appraised using Joanna Briggs Institute (JBI) Checklist for Case Series due to case series being the most common research method in the screened articles¹⁴. The articles are appraised as high-quality, medium-quality, or low-quality.

3. Results

3.1. Literature search and selection

Our search yielded 1,181 articles: 355 from PubMed, 483 from Scopus, and 343 from ProQuest. Two hundred forty articles were removed because they were duplicates, leaving 941 articles. Initial screening for irrelevant titles and abstracts of the articles eliminated 917 articles.

Three articles were irretrievable during the full-text retrieval. Of the remaining articles, seven were removed because they were published in languages other than English. Full-text assessment removed one article due to being an editorial, four articles due to nonstandard measurement (micropenis in these articles is defined as stretched penile length at least 2 standard deviations below the mean instead of 2.5), and one article due to the patients suffering from hypospadias, leaving at last 8 articles^{8,9,15-20}. The screening process is represented by a flowchart in Figure 1.

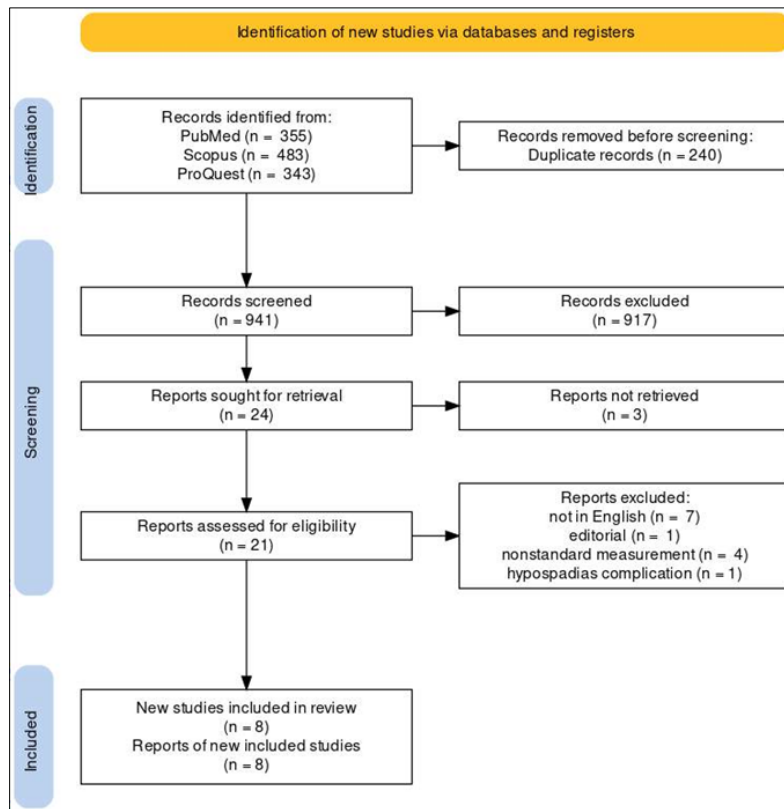


Figure 1 PRISMA 2020 flowchart of the systematic review

3.2. Study characteristics and quality

Table 1. Characteristics of screened articles.

	Ben-Galim <i>et al</i> ⁸	Burstein <i>et al</i> ⁹	Guthrie <i>et al</i> ¹⁵	Kim <i>et al</i> ¹⁶	Klugo <i>et al</i> ¹⁷	Levy <i>et al</i> ¹⁸	Liu <i>et al</i> ¹⁹	Sasaki <i>et al</i> ²⁰
Were patient’s demographic characteristics clearly described?	+	+	+	+	+	+	+	+
Was the patient’s history clearly described and presented as a timeline?	+	+	+	-	+	+	+	-
Was the current +clinical condition of the patient on presentation clearly described?	+	+	+	+	+	+	+	+
Were diagnostic tests or assessment methods and the results clearly described?	+	+	+	+	+	+	+	+
Was the intervention(s) or treatment procedure(s) clearly described?	+	+	+	+	+	+	+	+
Were adverse events (harms) or unanticipated events identified and described?	+	-	+	+	+	+	+	+
Does the case report provide takeaway lesson?	+	+	+	+	+	+	+	+

4. Discussion

4.1. Limitations

Our review and meta-analysis have several limitations. The reliability of our conclusions depended on the quality of other studies. However, few articles satisfied the criteria and thus could be used in this study. We also only included patients with isolated micropenis and excluded patients with other abnormalities thus limiting analyzable data.

4.2. Implications

Our study found that significant results related to hormone therapy are effective in increasing the stretched penile size in cases of micropenis in children and adults by performing reviews. Hormone therapy ought to be done in patients with micropenis before they undergo surgery⁹. As expected, all of the articles which included in the study showed significant results of hormonal therapy to patients with micropenis^{5,9}. A study conducted by Burstein et al. involved 14 patients with micropenis, but only 5 patients had micropenis without abnormalities such as hormone deficiencies. These patients were treated with systemic testosterone, using testosterone enanthate injected intramuscularly. The therapy was administered every month for 3 months and showed an increase in penis length of ± 0.62 standard deviations. In a study by Guthrie et al., patients with micropenis were administered 25mg testosterone cypionate intramuscularly every 3 weeks for 3 months. The general growth and osseous maturation of the patients were also assessed. The results showed that the treatment had a positive effect on enhanced penis length and was still in the normal range after 9-12 months post treatment. General growth and maturation also accelerated in three of the four patients as long as the treatment was administered. All of the subjects' bone age growth rapidly rose before falling down after 9 months of follow-up post-treatment. Another study showed testosterone treatment successfully gave increment in penis length on micropenis patient 1.37 ± 0.68 SD ($p = 0.0008$; SD, $p = 0.02$).

4.3. Analysis

According to the articles included in this study, hormone therapy, whether utilizing testosterone, GH, or gonadotropin, was beneficial in treating patients with micropenis. There are variances in how medications are administered to patients, which is most noticeable with testosterone. Ying Liu's research with the largest sample size of 90 patients succeeded in restoring normal penis size in all patients following the third course of orally given testosterone undecanoate. It is showed that low dose testosterone that administrated to the patients worked effectively. These patients were children approximately 1.7 years old with 5 α -reductase enzyme deficiency. Testosterone can improve the dihydrotestosterone conversion process, which has been disturbed caused by lack of 5 α -reductase enzyme or mutation of SRD5A2 which might results in a decrease of 5 α -reductase enzyme activity. Testosterone and dihydrotestosterone playing important role. With its relationship directly to androgen receptors, testosterone and dihydrotestosterone play a significant role in the development of male genital organs and the secondary features of puberty. However, the effects of hormone treatment might also be affected by the patient's other diseases or other variables such as age when the treatment was firstly administered. The efficacy of the treatment depends on the underlying source of the patient's hormonal pathway dysfunction.

5. Conclusion

Hormonal therapy Is very effective to treat patient with micropenis problem. It is show that testosterone gave the most significant effect on the penile length. Hormonal combination therapy also used in patient with other underlying diseases to increase the effectiveness of the therapy. This systematic review was made due to the lack of comparison data of hormonal therapy used and we hope that this paper can be one of the data to assist in micropenis therapy.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

Authors' contributions

Conceptualization: FA, OMS, JTS; methodology: FA; investigation: FA data curation: OMS; formal analysis: OMS; supervision: RI; writing — original draft: FA; and writing — review and editing: RI.

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