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The Addition Of Anastrozole To Standard Testosterone Enanthate Treatment Significantly Improves Penile Size In Adolescent Boys With *Micropenis*

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Background: Micropenis is treated preferably in infancy $(\leq 2 \text{ yrs})$ or at the onset of puberty, usually with 3 (2-4) monthly testosterone enanthate I. M. injections at the dose of 100 mg/m2. This short-term therapy may temporarily advance bone maturation but with a concomitant increase in height velocity and no apparent change in predicted adult height. Bone maturation depends on locally

produced estrogens by aromatization. Third generation aromatase inhibitors (AIs) are used as an off-label treatment to improve predicted adult height (PAH) in boys as well as in girls, either as monotherapy or in combination with growth hormone and/or puberty inhibition. They induce reverse binding inhibiting the activity of aromatase (a cytochrome P450 enzyme), which catalyzes the conversion of androstenedione and testosterone to estrone and estradiol, respectively, resulting in a substantial increase of the circulating testosterone concentrations. Aims: To compare the traditional treatment of isolated - idiopathic - relative micropenis in boys with testosterone enanthate monotherapy to its combination with anastrozole 1 mg×1 p. o. **Methods:** 164 boys with micropenis (stretched penile length \leq -2 SD) received testosterone enanthate 100 mg/m2 I. M./month either as monotherapy (n=63, mean age 10.8 yrs, group A) or in combination with anastrozole 1 mg/day (n=101, mean age 11 yrs, group B) for 3 months. Stretched penile length, bone maturation and auxological data were analyzed. All measurements were performed by the same examiner. The choice of the rapeutic intervention was made randomly. Groups A and B did not differ in terms of age at intervention onset, bone age, target height or predicted adult height. They underwent a 6-month follow-up that included clinical examination, bone age X-ray evaluated by BoneXpert ver. 3.2. 0 (Visiana, Denmark), and laboratory tests at 8: 00hrs (LH, FSH, testosterone, estradiol, estrone), prior and under treatment. Results: In both groups penile length normalized: for group A gain was +1.9 cm (+2.08 SD) and for group B +2.24 cm (+2.3 SD), with group B attaining a greater length by +18% (p=0.004) due to the higher testosterone concentrations attained by at least 50%. Group A presented a slight acceleration of height velocity with parallel advancement of their bone age maturation while group B with unchanged or lower estradiol and estrone concentrations maintained their height velocity with parallel movement of their bone age maturation. Conclusions: Addition of anastrozole 1 mg/day p. o. in testosterone enanthate treatment for idiopathic-isolated-relative micropenis at the beginning of puberty significantly improves penile length by almost 20% while the tempo of height velocity and bone maturation continue their previous track.

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