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# Testosterone prior to hypospadias repair: No clear-cut benefit or reassurance regarding long-term safety



Charles Van Praet, Anne-Françoise Spinoit

Department of Urology, Ghent University Hospital, Ghent, Belgium

Correspondence to:  
A.-F. Spinoit

[afspinoit@hotmail.com](mailto:afspinoit@hotmail.com) (A.-F. Spinoit)

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The benefit of androgenic stimulation prior to hypospadias surgery has long been debated. Its goal is to increase penile length and circumference, and widen the glans and urethral plate to make the surgery easier and decrease adverse events. Short-term side effects include transient growth of pubic hair, possible growth retardation, erections, and increased bleeding during surgery. Long-term side effects of pre-pubertal androgenic stimulation are ill studied.

Rynja et al. examined 58 adults (mean age 19.8 years) who underwent hypospadias repair as a child, including 24 patients who received testosterone pre-operatively [1]. They found no difference in postoperative complication rate, or in adult body or penile length or cosmesis with regard to testosterone use. Only 50% of the 121 eligible patients responded to the investigators' invitation. Selection bias may have influenced their results, and they have too few included patients to perform an accurate multivariate analysis. With the presented data from a retrospective analysis of 24 patients, it cannot be concluded, in our opinion, that pre-pubertal testosterone application has no long-term side effects. Statistics lose their power in such a small population, and no conclusion can safely be drawn from these series, especially when many surgical or anatomical parameters have not been taken into account.

In a rat model, pre-pubertal androgenic stimulation decreased genital size and germ cell count in adulthood [2], something which has not been reproduced in men but warrants further study. Also, the effect of testosterone on the androgen receptor, which seems to be less expressed in hypospadias, requires further investigation [3]. As 78% of pediatric urologists in the US apply androgenic stimulation pre-operatively, it is important to understand its possible long-term side effects [4].

The European Association of Urology guidelines give a level 1B recommendation for

androgenic stimulation, despite ambiguous evidence [5]. Recently, two randomized controlled trials (RCT) demonstrated that pre-operative testosterone application decreased complication rate [6,7]. However, testosterone use is associated with tissue healing problems and another RCT demonstrated more wound dehiscence following testosterone administration [8]. This could have resulted from increased tissue vascularization and edema. A French RCT is investigating the effect of topical estrogen on complication rates. The study is completed, and results are awaited (NCT01370798).

In our institution, androgen stimulation is exceptionally administered prior to hypospadias repair, as advantages have not been shown. We agree, however, that it can be considered in selected children with a very small glans, in the hopes of increasing size to facilitate surgery.

Further research is needed to determine whether pre-operative testosterone improves surgical outcome. Furthermore, possible long-term side effects should be assessed in large prospective cohorts. Parents should be informed about the benefits and risks of pre-operative androgenic stimulation.

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