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UROLOGICAL ONCOLOGY

Neo–adjuvant hormonal treatment for the undescendent testis – a benefit for the patient?

Raimund Stein

Division of Paediatric Urology, Department of Urology, University Medical Center, Johannes Gutenberg University, Mainz, Germany

With an incidence of around 3% isolated cryptorchidism represents one of the most common congenital anomalies in full–term newborns [1–9]. Until to the age of three month, up to 70% of these testes will descendent [4, 10]. Therefor at the age of one year, the incidence is around 1%. Complete spontaneous descensus after 6 months of life in a truly undescendent testis is rare [11]. In 20% the testis is non–palpable, a term missing in the publication of Kucharski and Niedzielski [12, 13]. The position of the testis is usually described at the time of exploration as in-traabdominal, intracaniclar (most probably in the article of Kucharski and Niedzielski called upper inguinal canal) extacanicular (supra– or infrapubic – in this article most probably lower inguinal canal) or ectopic, a group of boys also missing in the article. It is not clear, why the authors have chosen their own "new" classification. From the above mentioned entity, the retractile testis must clearly distinguished, which can be quite difficult in daily clinical praxis. A retractile testis is a testis, which can be "easily" brought down into the scrotum and remains in the scrotum after the traction is released. This testis needs no further therapy. However, some studies demonstrated that these retractile testes have a higher risk to become a ascendant testis later on [7, 14, 15, 16]. In 1966 Villumsen and Zacchau–Christiansen, demonstrated, that in 69 out of 4300 children (1.6%) with an orthotopic testis at birth had a secondary ascensus of the testis [17]. 40 years later a study from Finland had the identical result (8 out of 500 boys (1.6%) had a secondary ascensus) [18]. This could explain the quite high incidence of older boys in most studies. In the EAU / ESPU guidelines, treatment should be finished latest at the age of 18 months [19].

In the current study of Kucharski and Niedzielski, patients received a therapy with human chorionic gonadotrophin (hCG) for 5 weeks twice per week, if the parents agreed (101 boys). In 103 boys the parents disagreed (how many and why?) or the patients were older than 6 years of life. Unfortunately the age range is not given in the article as well as the reason for this age cut.

Especially retractile testes (most of them need only observation and no intervention in the long run) have a very good response to hormonal therapy [20]. So far there are no studies to demon-strate a clear benefit for the patient in respect to fertility and outcome.

Since 1930 hCG is used in patients with undescendent testis [21], and gonadotrophin–releasing hormone (GnRH /LH–RH) 45 years later [22, 23]. The hormonal therapy has following goals: a) to bring the testis down in the scrotum and b) to stimulate the germ cell maturation and improve the fertility index. Descent of the testis could be achieved in up to 20% in some randomized trails (LH–RH 21%; hCG 19% and placebo 4% [24]), however with the risk of re–ascending in up to 25% [24, 25]. Excluding retractile testis the success rate using LH–RH was 12% (8–15%), with hCG 19% (13–25%) and in the placebo group 5% (2–7%) [24]. In a double – blinded randomized study (n=252) the success rate of LH–RH was 9% (placebo 8%) [26]. The success rate was higher, if the testicle is located near the scrotum [27]. Some studies showed a benefit for the combination of hCG and GnRH [28], others not [29]. There are no difference between higher doses (e.G. 1500 IE/week) and lower doses (e.G. 1500 IE/week) [30].

In several randomized studies, the maximum success rate is around 20–25% with the risk of re–ascending in around 20%. In the report of Kucharski and Niedzielski 49 out of 110 testes descended to the scrotum and a re–ascensus was seen in 7 out of 62 patients.

However, there are also some side effects of the hormonal therapy including virilisation, increase of penile size, pain in the genitalia and injection site as well as a more aggressive behavior of the boys [31].

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After a 5–week course of hCG–Treatment Pirgon et al demonstrated that hCG treatment for cryptorchidism caused a significant increase in left ventricular mass due to high testosterone levels. They conclude that hCG therapy may not be safe for the cardiovascular sys-tem in boys with cryptorchidism [32]. Dundar et al described a case of a boy with right–sided hemiparesis 2 weeks after hCG–therapy for undescendent testis [33]. Dundar et al demonstrated in a group of 15 patients who had received an unsuccessful human chorionic gonadotropin (hCG) therapy before orchidopexy more apoptotic DNA fragmentation compared to non–hCG–treated patients. About 20 years later (16–30 years), volume of the testes treated with hCG the was lower (10,6 ml vs. 20,6 ml) and FSH was higher (6,2 IU/l vs. 3,1 IU/l) (34, 35).

Gonadotropin–releasing hormone (GnRH) treatment appears to improve fertility later in life by inducing germ cell maturation (e.G. transformation of the fetal stem cell pool (gonocytes) into the adult stem cell pool (adult dark spermatogonia) and transformation of adult dark spermatogonia into primary spermatocytes). Two small randomized studies demonstrated that neo–adjuvant GNRH treatment improves fertility index in prepubertal cryptorchidism (e.G. increase of the numbers of adult dark spermatogonia) [36, 37]. One study also demonstrated a positive effect of the number of adult dark spermatogonia using an adjuvant therapy with GnRH [38].

In boys with the risk of impairment of fertility (bilateral undescendent testis, small testicles or those with a reduced fertility–index in the biopsies taken during surgery, hormonal therapy should be discussed with the parents to improve the chance for fertility later on. These groups of patients may benefit from a neo–adjuvant or adjuvant hormonal treatment. Those patients with a testis located near the scrotum may also benefit from hormonal treatment in respect to bring the testis down in the scrotum. Due to the above mentioned side effects, GnRH Therapy should be preferred. In Germany, hormonal therapy will be recommended until the age of one year.

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Correspondence
Prof. Raimund Stein, M.D.
raimund.stein@unimedizin–mainz.de