Reviewer's report

Title: Management of cryptorchidism: a survey of clinical practice in Italy

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Reviewer: Faruk Hadziselimovic

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With help of the online questionnaire, Marchetti et al described current management of cryptorchidism in Italy concluding that high percentage of cryptorchid boys were inappropriately and unnecessarily treated with hormones to induce a testicular descent. This equivocal conclusion was based according to the guidelines released by Nordic consensus group.(1) The Nordic consensus on the treatment of undescended testis prohibited the use of hormones because of possible long-term adverse effects on spermatogenesis (1). Even if human chorionic gonadotropin (HCG) treatment induces increased apoptosis of the germ cells, it is still irrelevant for subsequent fertility outcome. The follow-up spermiogram performed in these patients showed no significant difference in fertility outcome between the treated and untreated groups. The second reason was the observation of decreased numbers of germ cells in cryptorchid boys aged 1–3 years who were previously unsuccessfully treated with HCG in comparison to the untreated group (1). These results, although statistically significant, are again irrelevant for the fertility outcome because the germ cell count in both groups was below 0.2 germ cells per tubular cross-section. If the germ cell count is <0.2, the majority of patients will develop infertility irrespective of whether they had only surgery or hormonal pre-treatment in addition to orchidopexy.

During the last 35 years, histological studies have contributed the most to our understanding of the aetiology of cryptorchidism. Only the comparison of histology and hormonal levels exemplify hypogonadotropic hypogonadism in the majority of cryptorchid boys and showed that unilateral cryptorchidism is a bilateral disease (2). It is important to realize that male fertility potential depends on the presence of Ad spermatogonia.(3) Therefore, early and successful orchidopexy does not improve fertility in a substantial number of cryptorchid males because it does not address the underlying pathophysiology of cryptorchidism namely endocrinopathy of mini-puberty (3,4) In contrast to the concerns raised by the Nordic consensus group, the results of our study showed that hormonal treatment for undescended testis improved the histopathology of the contralateral testis without harming the germ cells (5). Furthermore, neoadjuvant gonadotropin releasing hormone (GNRH) treatment was found to improve the fertility index (6,7). Maximum salvage of active germinal tissue is achieved by treating cryptorchidism before the end of the first year of life (7). Treatment with LH-RHa normalized sperm concentration in 86% of unilateral cryptorchid males, who were in the high-risk group for developing infertility. All males in the untreated group (surgery only) were severely oligospermic, with
20% being azoospermic (8). Recently, Biers and Malone performed a critical appraisal of the key papers in the world literature to evaluate the level of evidence for improved fertility indices, semen analysis and paternity rates following hormone therapy in undescended testes. They concluded that the evidence for hormonal treatment is sufficiently strong to recommend a change in clinical practice. (9)

Hormonal treatment as a first choice of treatment has a long tradition in Italy. (10) It abrogates the necessity of subsequent surgery and in case of non-responder it facilitates orchidopexy and contributes considerably to reduced incidence of unilateral and more seriously bilateral complete post surgical testicular atrophy. Therefore, hormonal treatment has to stay as the first choice of cryptorchidism treatment. Moreover, recognizing that the endocrinopathy of mini-puberty is responsible for ensuing infertility in cryptorchidism, post surgical hormonal treatment should be implemented in cryptorchid boys having had early successful orchidopexy but still having a risk of infertility.

5. Zivkovic D, Bica DTG, Hadziselimovic F. Relationship between adult dark spermatogonia and secretory capacity of Leydig cells in cryptorchidism. BJU, 2007; 100:1147-1149.
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests