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Letter to the Editor

Revision of Sex Hormone Replacement Therapy for CKD Pediatric Cases

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According to the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS), children with Chronic Kidney Diseases (CKD) have considerable height deficits in comparison to the normal children. Additionally, short stature and poor growth of CKD children are associated with an increased risk of death [1]. Although complex medical regimens including bicarbonate therapy, iron, erythropoietin, salt-water supplementation, and Growth Hormone (GH) can improve final height, however, these children experience progressive height deficit after the age of 6 y compared to their normal counterparts [2]. We believe that CKD pediatric cases with short stature and delayed puberty should receive Sex Hormone Replacement Therapy (SHRT) at the same time when majority of the normal boys and girls have started maturation. We thus propose that SHRT should be started in CKD cases with the same rationale as in hypo/hyper-gonadothropic hypogonadism patients to improve their final height as adults.

Puberty

Ninety five percent of contemporary normal girls start their Thelarche by the age of 11 y [3] and the mean age of puberty stage 2a and 2b in contemporary normal boys are 12.1 and 12.7 y, respectively [4]. Sex hormones (estrogen and testosterone) have an essential role in pubertal growth spurt by enhancing synthesis and secretion of IGF1 that has anabolic effects on bone growth plates [5]. Despite good acid-base management and nutritional support, CKD can interfere with the hypothalamic-pituitary-gonadal axis at different levels which leads to delay in onset of puberty [6]. Pulsatile secretion of Luteinizing Hormone (LH) is impaired along with serum LH level elevation in CKD children due to uremia. Lack of nocturnal LH secretion causes delay in puberty in these patients [7]. Pediatricians should evaluate pubertal delay in CKD children, if no Thelarche starts by the age of 11 y in girls and no sign of puberty at 13 y in boys.

In normal children, standardized height averagely increases 1.3 SDS from pre-puberty to post-puberty, while patients with delayed puberty have significantly less increase in standardized height (+0.9 SDS) [7]. CKD Children have approximately 2.5 years lag in the onset and progression of gonadarche in comparison with their peers. In addition, their pubertal growth spurt is shortened by 1.5 y, and at start of the pubertal spurt, they have less mean height velocity in comparison with the healthy adolescents [7-9]. Thus, an irreversible height deficit occurs during puberty in CKD children [9] because of disturbed puberty and impaired pubertal growth spurt.

Growth Hormone

Practitioners have tried to enhance CKD children growth deficit with GH, however, optimal final height was not achieved with this treatment. In CKD children who received GH from late pre-pubertal stage, GH therapy had no overall effect on the improvement of pubertal height gain and they still had a prominent height deficit [8,10]. Also, the mean peak height velocity during the pubertal growth spurt was not significantly higher in GH treated CKD children compared to the control CKD children [8].

Conclusion

According to the best of our knowledge, CKD girls and boys with short stature who do not start puberty till 11 and 13 y respectively are at high risk of height deficit in spite of GH therapy. As 20 to 25 cm of FH was obtained by pubertal growth spurt [11], experts have referred this height deficit to the delayed puberty and shorten pubertal growth spurt duration in CKD children [7]. SHRT in boys with CKD and delay puberty is challenging and needs more personalized decision making because Testosterone could aggravate uremic side effects [12,13]. However, we recommended SHRT in short CKD girls with delay puberty at 11 y to enhance their final height besides improving bone density.

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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