Brief Communication

Congenital adrenal hyperplasia - experience from a tertiary centre in South India

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ABSTRACT

Congenital adrenal hyperplasia is a group of autosomal recessive disorders caused by enzyme deficiency which leads to defects in biosynthesis of steroid precursors. Most common is 21 hydroxylase deficiency. Clinical spectrum varies from non-classical CAH to classic CAH, and it may be simple virilising form or salt-wastinfg type. 29 patients were included in our study from January 2012 to October 2012. 76% were females. Male babies typically presented with adrenal crisis between 3rd to 6th week of life. Around 20% of females were identified and appropriately treated only after late adolescence. Short stature was seen in 1/3rd of patients. 1/3rd of patients had suppressed 17 OHP levels suggestive of over-replacement therapy which may contribute to final reduction in adult height.

Key words: CAH, 21 hydroxylase deficiency, adrenal crisis, genital ambiguity

Introduction

Congenital adrenal hyperplasia (CAH) refers to a group of autosomal recessive disorders caused by an enzyme deficiency which leads to defects in biosynthesis of steroid precursors. The most common deficiency encountered is 21 hydroxylase.[1] It accounts for more than 95 % of cases with CAH. Depending on the severity and degree of 21 hydroxylase deficiency, the clinical spectrum may vary from mild form of non classical CAH to classic CAH. It may be either simple virilizing form or salt wasting type of CAH. The incidence of classic CAH ranges from 1 in 10,000 to 1 in 20,000. However, the non classical CAH variant is more common with a prevalence rate of 1 in 1000. Management of CAH primarily consists of replacing the deficient corticosteroids.[2] It also helps in maintaining normal levels of precursors by suppressing adreno cortico trophic hormone (ACTH). During childhood, the management is largely focused on achieving normal growth and attaining appropriate final adult height.[3]

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Materials and Methods

This study was conducted in St. Johns Medical College Hospital, Bangalore by the Department of Endocrinology on patients diagnosed to have CAH and seen in the outpatient clinic between January 2012 and October 2012. During this period cross sectional data was collected and analyzed from this cohort of CAH patients. Data regarding demography, clinical presentation at time of diagnosis, treatment details, height SDs and BMI were collected. All patients underwent biochemical testing for 17 hydroxy progesterone (17 OHP) levels for assessment of adequacy of therapy. Bone age assessment with left hand and wrist X-ray using Greulich Pyle method was done in all children. Short stature was defined as height SDs lesser than -2.0. BMI was calculated for all patients and obesity was defined using WHO charts as values above 95th percentile. 17 OHP levels between 1 ng/ml and 12 ng/ml were considered appropriate; values below 1 ng/ml suggested suppression and over treatment and values above 12 ng/ml suggested under treatment.

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Results

29 patients were included in the study of which 22 were females (76%) and 7 were males (24%). Based on the cross sectional data collected, 11 patients were adults (age > 18) and 18 patients were children (62%). Among the males, one child was identified at birth via a neonatal screening program, one child presented with early pubarche, the other 5 infants presented between their 3rd and 6th week of life with features suggestive of adrenal crisis - poor feeding, vomiting and failure to gain weight. One of the male patients incidentally also had a penoscrotal hypospadias which was surgically corrected. Among the females, 9 infants were identified at birth due to presence of genital ambiguity (40%), 1 presented with symptoms of adrenal crisis at 4 weeks of life, 4 patients presented in the pre pubertal period due to early onset adrenarche (18%), 5 patients presented in the late adolescent period with marked virilization (23%) and 3 patients presented with features of poly cystic ovarian disease (PCOS).

All the five patients who presented in the late adolescent period had obvious genital ambiguity from birth, however, they sought medical attention only much later due to marked virilization and failure to attain menarche. One among them had actually been evaluated and even underwent a clitoroplasty at a young age, but unfortunately, the diagnosis of CAH was missed as she was mistakenly categorized as probable ovo testicular DSD due to presence of Mullerian structures with a phallic length of around 6cm. All these 5 women had a masculine built at presentation with poor breast development, severe hirsutism, muscular body habitus, temporal balding and varying degrees of deepening of voice. The non classical CAH (NCCAH) patients presented in adulthood with complaints of irregular cycles and hirsutism; they had no features of virilisation. Diagnosis was made on basis of stimulated 17 OHP levels. All women in this series had varying degrees of clitoromegaly +/- posterior labial fusion except for the three patients who had NCCAH. Hirsutism was a common complaint and was seen in more than 50% of patients.

Simple virilizing was the most common sub class seen among the women (81%) whereas the salt wasting type was predominant among boys (85%). Around 35% of patients had short stature as defined by height SDs < -2.0; 2 patients who presented with adrenarche had increase in height SDs, however, their bone age was also correspondingly advanced. Obesity was seen only in 16% of female patients with CAH. None of the male patients had obesity. High blood pressure was documented in two women among the cohort of 29 patients. All the children were treated with hydrocortisone; almost all adult patients were on dexamethasone. None of the NCCAH patients were treated with glucocorticoids; they were on anti-androgen therapy along with oral contraceptive pills. Most adult classic CAH patients with complaints of hirsutism were treated with either spironolactone or finasteride. Pubertal induction with ethinyl estradiol was initiated for three of the adult patients who sought medical care late. Analysis of 17 OHP levels revealed that 32% were suppressed with levels less than 1ng/ml; appropriate in 47% and inadequate in 21% of patients.

Discussion

We report the phenotypic features of a cohort of patients with CAH being evaluated and managed in a tertiary centre in southern India. In this series, the typical presentation of male babies were with adrenal crisis between the 3rd and 6th week of life. Around 20% of female patients with classic CAH were identified and appropriately treated only after late adolescence even when genital ambiguity was present since birth. Short stature was seen in one third of patients on therapy and the average final adult height among patients with classic CAH was 142.37, which was significantly lower than the mean adult height for females in our population. The mean final adult height of 157.5cm for those with NCCAH was better than their classic CAH counterpart. Obesity and hypertension were not found to be significantly higher in this cohort of CAH patients. One third of patients had suppressed 17 OHP levels suggestive of over replacement therapy which may also contribute to the reduction in the final adult stature.

References

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