Central Precocious Puberty Complicating Congenital Adrenal Hyperplasia: North Indian Experience

Sir,

Increased androgen production often leads to peripheral precocious puberty (PPP) in congenital adrenal hyperplasia (CAH).[1] The chronic hyperandrogenemia may activate hypothalamic-pituitary axis and cause central precocious puberty (CPP) with advancement of bone age (BA) that compromises stature.[1] Short stature is indeed common in adults with CAH in less developed countries.[2] Gonadotropin-releasing hormone analogs (GnRHa) reduce the rate of linear growth and BA advancement and are considered an effective adjunct to steroids in the treatment of CPP complicating CAH.[3] However, data on GnRHa use are scarce from resource poor settings.[2,3]

Of the 55 patients diagnosed as precocious puberty (PP), five (four girls and one boy) treated as CPP complicating CAH between 2007 and 2016 were retrospectively reviewed. Four had simple virilizing CAH whereas one had classic salt-wasting form. The diagnosis of CPP was based on either basal serum LH of ≥ 0.3 IU/L or peak stimulated LH ≥5.0 IU/L. The presenting features were premature breast or pubic hair development in girls and testicular enlargement in boy. The mean chronological age (CA) at onset of PP and at start of treatment was 3.6 ± 0.74 years (range 2.7–4.3 years) and 4.7 ± 1.2 years (range 3.5–6.5 years), respectively. All had an advanced BA (mean 8.0 ± 2.4 years, range 6–12 years) at diagnosis. The mean BA advancement at diagnosis and at 3 years of treatment was 3.2 ± 1.3 years (range 2.4–5.5 years) and 2.0 ± 0.35 years (range 1.5–2.5 years), respectively; the slowing of BA advancement was statistically insignificant (*P*-value 0.08). Four underwent GnRH stimulation test. The mean baseline and stimulated peak LH values were 0.4 ± 0.55 IU/L (range 0.1–1.23 IU/L) and 5.6 ± 0.52 IU/L (range 5.0–6.2 IU/L), respectively. All children received oral hydrocortisone (8–15 mg/m^2) and fludrocortisone. Depot leuprolide (initiated at 3.75 mg per month or 11.25 mg 3 monthly) was titrated according to LH values in follow-up. All children were followed up at 6 monthly intervals for at least 3 years. The mean height velocity (HV) and the mean unstimulated serum LH concentrations before and during 1st, 2nd, and 3rd years of therapy were 8.2 ± 0.5, 6.9 ± 1.7, 7.7 ± 1.0, and 7.6 ± 1.7 cm, and 1.4 ± 2.4, 0.21 ± 0.1, 1.4 ± 2.3, and 0.41 ± 0.1 IU/L, respectively. The improvement in mean predicted adult height (PAH) from the start to completion of 3 years of therapy was statistically significant (142.2 ± 6.3 cm vs 150.4 ± 4.2 cm, *P* value 0.04). Regression in testicular size and breast size was observed. The mean duration of follow up was 4.2 ± 1.6 years.

GnRHa therapy suppresses gonadotropin levels, stabilizes secondary sexual characteristics, and decreases rate of linear growth and BA maturation.[4] These effects were observed in our patients also. However, the treatment outcomes appear to be different as compared to patients treated in the developed countries.[4,5] Although our patients showed slowing down of BA advancement, the HV did not decrease significantly after GnRHa therapy in contrast with data from developed countries.[4,5] Additionally, the improvement in PAH barely reached statistical significance after 3 years of therapy. The lack of significant benefits of GnRHa therapy can be attributed to several factors peculiar to our setup such as delays in diagnosis of CAH due to lack of newborn screening, poor metabolic control, and late presentations with CPP.[2] The mean delay in seeking treatment exceeded 1 year in our patients that probably caused significant BA advancement. It is well-known that BA at initiation of GnRHa therapy is the most important factor that affects HV.[5] Delays in diagnosis and initiation of GnRHa therapy adversely affect height outcomes in CAH complicated by CPP in resource-limited setups.

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Conflicts of interest

There are no conflicts of interest.

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