

Congenital Adrenal Hyperplasia: Consensus Guidelines and Beyond

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Despite recent guidelines from the Endocrine Society (1) and the Congenital Adrenal Hyperplasia Research, Education, and Support (CARES) Foundation (2,3), there remain many controversies in the diagnosis, management, and treatment of patients with congenital adrenal hyperplasia (CAH). Newborn screening (NBS) for 21-hydroxylase deficiency (21-OHD) is performed to avoid early salt-wasting crises, allow early diagnosis of simple-virilizing CAH in males, and reduce delay in sex assignment in severely virilized females. NBS programs are associated with a significant number of false-positive results most often due to infant illness and/or prematurity. Thus, it still remains unclear if the cost:benefit ratio is favorable. Genotyping individuals with CAH is fraught with error due to complexity of gene duplications, deletions, and rearrangements within chromosome 6p21.3.

To diagnose non-classic CAH (NCAH)/CAH after infancy, an early-morning serum 17-hydroxyprogesterone level is the screening test of choice in symptomatic individuals. If >200 ng/dL (6 nM), an adrenocorticotropic hormone stimulation is warranted to differentiate 21-OHD from other enzyme defects and to make the diagnosis in borderline cases. Genotyping in this situation may be helpful when results of the stimulation test are equivocal.

The glucocorticoid (GC) of choice for children is hydrocortisone (HC) in tablet form. For infants, tablets may be crushed, weighed, and mixed with a small amount of liquid and delivered immediately by medication syringe, rather than from bulk suspension preparations that deliver uneven doses. Prednisone and dexamethasone are sometimes useful in treating patients refractory to HC; however, routine chronic use of long-acting potent GCs in growing patients is not recommended. All treated patients should always wear or carry medical identification indicating adrenal insufficiency.

Patients should be regularly monitored for signs of GC excess, hyperandrogenism due to inadequate GC treatment, or hypertension from excess mineralocorticoid (MC) and/or sodium. Monitoring treatment should involve consistently timed hormone measurements. Endogenous adrenal steroid secretion should not be completely suppressed to avoid effects of overtreatment. There should also be regular

monitoring of height, weight, and physical examination; and bone age x-ray (after age 2 years).

Clinical or subclinical aldosterone deficiency is said to exist in all forms of 21-OHD. Patients with elevated plasma renin activity (PRA) or reduced aldosterone:PRA ratio (may) benefit from fludrocortisone (FC) therapy and adequate dietary Na. Sensitivity to MC's may vary over time with recovery from salt-wasting in some patients, probably secondary to extra-adrenal 21-hydroxylation.

All GC-treated patients should be monitored for iatrogenic Cushing syndrome, including height and weight in children, distribution of body fat, presence of pigmented striae, blood pressure, and plasma glucose. Since osteopenia and osteoporosis are rare in pediatric CAH patients, routine evaluation of bone mineral density is discouraged unless clinically indicated. Adrenal nodules have been identified more frequently in CAH patients than in general population; however, routine adrenal imaging is not recommended.

NCAH is not generally considered an absolute indication for GC or MC replacement. Children with NCAH should be treated when they have inappropriately early onset and rapid progression of pubarche and/or bone age. Adolescent females with overt virilization or erratic menses may also benefit. Asymptomatic individuals with NCAH need not be treated. Moreover, previously treated NCAH patients should be given the option of discontinuing therapy when their symptoms resolve.

The GC dosage should be increased in stressful situations such as febrile illness (>38.5 °C), gastroenteritis with dehydration, surgery with general anesthesia, and major trauma. Increased GC doses should not be given for mental and emotional stress, minor illness, and before physical exercise. Stress doses of GC should not be given to patients with NCAH unless their adrenal function is suboptimal or iatrogenically suppressed.

References

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