Glucocorticoid replacement regimen 3.1 We recommend glucocorticoid therapy in all patients with confirmed PAI. (1| ⊗ ⊗)

Glucocorticoid underreplacement 3.2 In patients with PAI, we recommend ongoing monitoring of glucocorticoid replacement using clinical assessment including body weight, postural blood pressure, energy levels, signs of frank glucocorticoid excess. (2| ⊗ ⊗ ⊗) We suggest against using Cushingoid signs as a marker of glucocorticoid excess. (2| ⊗ ⊗ ⊗) We suggest against the use of Cushingoid signs in the diagnosis of Cushing's disease. (2| ⊗ ⊗ ⊗)

Glucocorticoid underreplacement 3.3 As an alternative to hydrocortisone, we suggest using prednisolone (3–5 mg/d), administered orally once or twice daily, especially in patients with reduced compliance. (2| ⊗ ⊗ ⊗) We suggest against using dexamethasone for the treatment of PAI because of risk of Cushingoid side effects due to dose insufficiency. (2| ⊗ ⊗ ⊗)

Glucocorticoid replacement regimen 3.4 We suggest against using dexamethasone for the treatment of PAI because of risk of Cushingoid side effects due to dose insufficiency. (2| ⊗ ⊗ ⊗)

Glucocorticoid replacement regimen 3.5 We suggest monitoring glucocorticoid replacement using clinical assessment including body weight, postural blood pressure, energy levels, signs of frank glucocorticoid excess. (2| ⊗ ⊗ ⊗) We suggest against using Cushingoid signs as a marker of glucocorticoid excess. (2| ⊗ ⊗ ⊗) We suggest against the use of Cushingoid signs in the diagnosis of Cushing's disease. (2| ⊗ ⊗ ⊗)

Glucocorticoid replacement regimen 3.6 We suggest against using prednisolone (3–5 mg/d) in early morning as a single daily dose. (2| ⊗ ⊗ ⊗) We suggest against using prednisolone (3–5 mg/d) in early morning as a single daily dose. (2| ⊗ ⊗ ⊗)

Glucocorticoid replacement regimen 3.7 We recommend using prednisolone (3–5 mg/d) in early morning as a single daily dose. (2| ⊗ ⊗ ⊗) We suggest against using prednisolone (3–5 mg/d) in early morning as a single daily dose. (2| ⊗ ⊗ ⊗)

Mineralocorticoid replacement in PAI 3.8 We recommend that all patients with confirmed aldosterone deficiency receive mineralocorticoid replacement with fludrocortisone (starting dose, 50–100 μg in the morning). (2| ⊗ ⊗ ⊗) We suggest against using dexamethasone for the treatment of PAI because of risk of Cushingoid side effects due to dose insufficiency. (2| ⊗ ⊗ ⊗)

Mineralocorticoid replacement in PAI 3.9 We recommend that all patients with confirmed aldosterone deficiency receive mineralocorticoid replacement with fludrocortisone (starting dose, 50–100 μg in the morning). (2| ⊗ ⊗ ⊗) We suggest against using dexamethasone for the treatment of PAI because of risk of Cushingoid side effects due to dose insufficiency. (2| ⊗ ⊗ ⊗)

Mineralocorticoid replacement in PAI 3.10 If blood pressure remains uncontrolled, we suggest initiating antihypertensive treatment and continuing fludrocortisone. (2| ⊗ ⊗ ⊗) We suggest against using dexamethasone for the treatment of PAI because of risk of Cushingoid side effects due to dose insufficiency. (2| ⊗ ⊗ ⊗)

Mineralocorticoid replacement in PAI 3.11 We suggest a trial of dehydroepiandrosterone (DHEA) replacement in women with PAI. (2| ⊗ ⊗ ⊗) We suggest against using dexamethasone for the treatment of PAI because of risk of Cushingoid side effects due to dose insufficiency. (2| ⊗ ⊗ ⊗)

Mineralocorticoid replacement in PAI 3.12 We suggest against using dexamethasone for the treatment of PAI because of risk of Cushingoid side effects due to dose insufficiency. (2| ⊗ ⊗ ⊗) We suggest against using dexamethasone for the treatment of PAI because of risk of Cushingoid side effects due to dose insufficiency. (2| ⊗ ⊗ ⊗)
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4.1 We recommend that patients with suspected adrenal crisis should be treated with an immediate parenteral injection of 100 mg (50–100 mg/m²) of hydrocortisone, followed by appropriate fluid resuscitation and 200 mg (50–100 mg/m²) for children of hydrocortisone/24 hours (via continuous or q6 hr bolus injection), age- and body surface-appropriate dosing in required in children (see Table 3). (2⊕⊕)

3.17 We recommend hydrocortisone stress dosing during the active phase of labor, similar to that used in major surgical stress. (1⊕⊕)

3.19 In children with PAI, we suggest avoiding synthetic, long-acting glucocorticoids (e.g., prednisolone, dexamethasone). (2⊕⊕)

3.20 We suggest patient education concerning glucocorticoid adjustments in stressful events and adrenal crisis prevention strategies including personal self-care and administration of emergency glucocorticoids. (3⊕⊕)

4.1 In pregnant women with PAI, we suggest using hydrocortisone over cortisone acetate, prednisolone, or prednisone (2⊕⊕). Inactivated in the placenta. (1⊕⊕)

3.15 In pregnant women with PAI, we suggest using hydrocortisone over cortisone acetate, prednisolone, or prednisone (2⊕⊕). We recommend sodium chloride supplements in the newborn period and up to the age of 12 months. (1⊕⊕)

4.2 If hydrocortisone is unavailable, we suggest prednisolone as an alternative. Dexamethasone is the least preferred alternative and should only be given if no other glucocorticoids are available. (2⊕⊕)

3.16 We suggest patient education concerning glucocorticoid adjustments in stressful events and adrenal crisis prevention strategies including personal self-care and administration of emergency glucocorticoids. (3⊕⊕)

4.3 For the prevention of adrenal crisis, we suggest adjusting glucocorticoid dose according to severity of illness or magnitude of the stressor. (2⊕⊕)

5.3 We suggest periodic screening for autoimmune diseases known to be more prevalent in PAI patients in whom autoimmune origin of PAI has not been excluded. The optimal frequency of screening is unclear; however, it can be done annually. These conditions include thyroid disease, diabetes mellitus, premature ovarian failure, celiac disease, and autoimmune gastritis with vitamin B12 deficiency. (2⊕⊕)

5.0 Additional monitoring requirement

5.1 We suggest that adults and children with PAI be seen by an endocrinologist or a healthcare provider with endocrine expertise at least annually. Infants should be seen at least every 3 to 4 months. (Ungraded best practice statement)

5.2 We suggest that PAI patients be evaluated for diabetes mellitus, premature ovarian failure, celiac disease, and autoimmune gastritis with vitamin B12 deficiency. (2⊕⊕)

5.4 We suggest patient education about increasing the dosage of glucocorticoids during intercurrent illness, fever, and stress. This education includes identification of precipitating symptoms and signs and how to act in impending adrenal crisis. (3⊕⊕)

5.5 We suggest genetic counseling for patients with PAI due to monogenic disorders. (Ungraded best practice statement)

5.6 We suggest that PAI patients be educated on how to use their glucocorticoid injection kit for emergency use. The optimal frequency of screening is unknown but can be done annually. (Ungraded best practice statement)

5.7 We suggest teaching or referring PAI patients to a trained pharmacist or guardian to provide emergency glucocorticoid instructions. (Ungraded best practice statement)

5.8 We suggest patient education concerning glucocorticoid adjustments in stressful events and adrenal crisis prevention strategies including personal self-care and administration of emergency glucocorticoids. (3⊕⊕)

5.9 We suggest that patients with PAI should be educated about increasing the dosage of glucocorticoids during intercurrent illness, fever, and stress. This education includes identification of precipitating symptoms and signs and how to act in impending adrenal crisis. (3⊕⊕)

5.10 We suggest genetic counseling for patients with PAI due to monogenic disorders. (Ungraded best practice statement)

5.11 We suggest teaching or referring PAI patients to a trained pharmacist or guardian to provide emergency glucocorticoid instructions. (Ungraded best practice statement)

5.12 We suggest patient education concerning glucocorticoid adjustments in stressful events and adrenal crisis prevention strategies including personal self-care and administration of emergency glucocorticoids. (3⊕⊕)

5.13 We suggest that PAI patients be educated on how to use their glucocorticoid injection kit for emergency use. The optimal frequency of screening is unknown but can be done annually. (Ungraded best practice statement)

5.14 We suggest teaching or referring PAI patients to a trained pharmacist or guardian to provide emergency glucocorticoid instructions. (Ungraded best practice statement)

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