EVOLUTION OF ADRENAL FUNCTION AFTER ADRENALECTOMY IN CUSHING SYNDROME

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Background: ACTH-independent hypercortisolism accounts for approximately 15% of patients with Cushing syndrome (CS). It results from adrenocortical adenoma, bilateral macronodular and micronodular hyperplasia and adrenocortical carcinoma. First-line therapy in CS is the resection of the underlying tumor in all cases. After surgical cure of CS, most patients develop transient secondary adrenal insufficiency (SAI) due to central suppression of the hypothalamic-pituitary-adrenal axis resulting contralateral adrenal atrophy, with a variable time of recovery. Adrenal function testing can identify patients who may require glucocorticoid (GC) replacement.

This study is based on the review of 61 patients diagnosed with ACTH-independent CS in our clinical department between 2005-2015. Six patients with hypercortisolism resulting from adrenocortical carcinoma were excluded.

Of the 55 patients, 43 had adenomas and 12 had bilateral macronodular hyperplasia. The mean age was 52 years (range 26-76); 7 were male and 48 female. Tumor size ranged from 16-140 mm with a medium size of 39 mm. Subclinical Cushing (abnormal dexamethasone test only) was diagnosed in 29 cases and overt Cushing in 26 cases. Mixed GC and androgen secretion was found in 4 cases. Comorbidities at diagnosis included obesity, hypertension, diabetes mellitus, osteoporosis and depression.

Methods: 40 patients underwent unilateral adrenalectomy; 6 cases were excluded because of missing data. Postoperatively, we evaluated plasma cortisol levels at 08:00 a.m. and 4 hours and 24 hours after i.m. administration of 1 mg Synacthen depot (tetrasocactide). GC replacement was started for basal plasma cortisol <5 ug/dl, or a stimulated plasma cortisol <20 ug/dl. Follow up was performed at 3, 6, 9 months and 1 year or more in selected cases, in order to see the duration of GC replacement, morphological aspect of the contralateral adrenal and complications remission.

Results: From the remaining 34 patients, 18 developed SAI (15 with overt CS and 3 with subclinical CS), receiving GC therapy for a period of time that ranged from 3 to 18 months. There was no correlation between tumor size and the risk of developing SAI. The decision of ceasing therapy was based on a stimulated cortisol value ≥ 20 ug/dl, without any evidence of SAI symptoms after that. A longer period of substitution was required for those patients with atrophic contralateral adrenal at initial morphological evaluation. During this study there were performed 76 Synacthen tests: 81.5% showed correlation between the response at 4 hours and 24 hours and 18.5% were discordant.

Conclusions: Only about a half of the patients with autonomous secretion of GC developed postoperatively SAI. Cortisol response at 4 hours after 1 mg Synacthen depot administration proved to be as useful as the response at 24 hours for the decision of starting or ceasing the GC replacement therapy.