

tested, 1.1–2.1 ULN) and plasma and urine metanephrines (60% of cases tested, 1.1–33.7 ULN and 50% cases, 1.1–22 ULN, respectively). Severe systolic hypertension was more frequent in male patients <30 years of age and 41.6% were candidates to genetic testing due to the tumor characteristics or patient history. Surgery was performed in 55.6%, radiotherapy in 25.2% and 12.1% are under surveillance or pending surgery, 7.1% were lost to follow up. Only 5 cases with metastasis were documented in 1215 patient-years of follow-up. Treatment-related complications were reported in 14.7% and persistence in 32.2%.

Conclusions: despite the retrospective nature of the study and sub registry, we found more tumors than expected. The frequency of hormonal production was high, but it is likely related to patient selection bias (mostly symptomatic cases studied). Dopamine and metanephrines are useful in the evaluation of PGN. Endocrinologists should be aware of these common tumors and be part of the multidisciplinary team.

Adrenal

ADRENAL – CLINICAL RESEARCH STUDIES

Predictive Accuracy of Delta Cortisol on Recovery of Adrenal Function in Patients With Drug Induced Cushing's Syndrome With Secondary Adrenal Insufficiency

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There is a growing concern upon the finding of many drug induced Cushing's syndrome because of inadvertent use of glucocorticoids (GC) either prescribed or as alternative medicine in Myanmar. These patients are presenting with diversity of clinical problems ranging from hypertension, diabetes to acute adrenal crisis due to hypothalamic-pituitary-adrenal (HPA) axis suppression and secondary adrenal insufficiency (AI). The present study aimed to assess the delta cortisol (the degree of cortisol increments) during the first short Synacthen test (SST) as a factor predictive of adrenal function recovery in patients with drug induced Cushing's syndrome with secondary AI and to determine the proportion of patients who recovered from AI within six-month follow-up. This was a hospital based prospective analytical study that enrolled a total of 52 patients with drug induced Cushing's syndrome with secondary AI from January 2018 to June 2019. Secondary AI is defined by morning basal serum cortisol \leq 400 nmol/L with Synacthen stimulated peak cortisol level \leq 550 nmol/L and serum ACTH < 60 pg/ml. The follow-up SSTs were performed at three-month and six-month after first SST, and the patients with morning basal serum cortisol > 400 nmol/L (or) Synacthen stimulated peak serum cortisol > 550 nmol/L during follow-up SSTs are defined as recovered adrenal function group. In this study, a total of 52 patients were treated with modified regimen of physiological dose of prednisolone with tapering schedule or stress dose GC based on the basal serum cortisol levels up to six months. Among them, nearly half (n=25 / 48.1%) of the patients with drug induced Cushing's syndrome with secondary AI achieved normal adrenal function within six-month follow-up. It was found that mean values for delta

cortisol were not statistically significant between recovered and non-recovered groups, 118.6 nmol/L (SD 72.3) and 97.2 nmol/L (SD 64.2) respectively. The delta cortisol during the first SST could not predict strongly (AUC - 0.6, 95% CI - 0.44 to 0.76, $P=0.2$) the recovery of adrenal function in patients with drug induced Cushing's syndrome with secondary AI and it was inconsistent with previous studies. The older age of the patients, oral route of administration of drugs causing Cushing's syndrome and comorbid hypertension were found to be more significant in the non-recovered group. In conclusion, the present study did not support the evidence that the delta cortisol during the first SST could predict adrenal function recovery in patients with drug induced Cushing's syndrome with secondary AI.

Reference: (1) Baek *et al.*, 2016; Recovery of Adrenal Function in Patients with Glucocorticoids Induced Secondary AI. *Endocrinol Metab.* **31**, pp. 153–160. (2) Pofi *et al.*, 2018; The Short Synacthen Test Can Be Used to Predict Recovery of HPA Axis Function. *J Clin Endocrinol Metab.* **103**(8), pp. 3050–3059.

Adrenal

ADRENAL – CLINICAL RESEARCH STUDIES

Preoperative Amlodipine Is More Efficacious Than Prazosin in Preventing Intraoperative Haemodynamic Instability in Pheochromocytoma/Paraganglioma Patients: Interim Analysis of a Pilot Randomized Controlled Study

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Background: Preoperative blockade with α -blockers is recommended in patients with pheochromocytoma/paraganglioma (PPGL). The data on calcium channel blockade (CCB) in PPGL is scarce. We aim to compare the efficacy of CCB and α -blockers on intraoperative haemodynamic instability (HDI) in PPGL. **Methods:** In the interim analysis of this monocentric, pilot, open-label, randomized controlled trial, patients with solitary, secretory, and nonmetastatic PPGL were randomized to oral prazosin (maximum 30mg, n=9) or amlodipine (maximum 20mg, n=11). The primary outcomes were the episodes and duration of hypertension (SBP \geq 160mmHg) and hypotension (MAP<60mmHg) and duration of HDI (hypertension and/or hypotension) as a percentage of total surgical time (from induction of anaesthesia to skin closure). **Findings:** The median (IQR) episodes (2 [1–3] vs. 0 [0–1], p 0.002) and duration of hypertension (19 [14–42] min vs. 0 [0–3] min, p 0.001) and intraoperative HDI duration (22:85 \pm 18.4% vs 2:44 \pm 2.4%, CI 8:68-32:14%, p 0.002) were significantly higher in the prazosin arm than the amlodipine arm

whereas episodes and duration of hypotension did not differ between the two groups. There was no perioperative mortality whereas one patient had intraoperative ST depression on the electrocardiogram. The drug-related adverse effects were pedal edema (1 in amlodipine), dizziness (1 in prazosin), and tachycardia (6 in prazosin and 3 in amlodipine). **Interpretation:** Preoperative blockade with amlodipine was more efficacious than prazosin in preventing intraoperative HDI in PPGL. Larger studies that compare preoperative blockade with amlodipine and both competitive and noncompetitive α -blockers in PPGL patients of various biochemical phenotypes are warranted.

Adrenal

ADRENAL – CLINICAL RESEARCH STUDIES

Prevalence of Suppressed Morning Serum Cortisol and Its Relationship With Cumulative Glucocorticoid Exposure in a Moderate-Severe Asthma Patient Cohort

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The extent to which inhaled glucocorticoid exposure (ICS) contributes to risk of adrenal insufficiency (AI) is not fully understood. The aim of this study was to establish the relative contribution of both oral (OCS) and inhaled (ICS) glucocorticoid exposure to risk of AI. 82 patients with severe asthma treated with fluticasone propionate (FP) who participated in a 32-week prospective randomised trial INCA SUN, (NCT02307669) were studied. Cumulative ICS exposure was calculated using a unique digital device, which creates an acoustic recording of inhaler adherence and technique. Analysis of this data provides an exact measure of the ICS dose received by each patient. Morning serum samples collected during the final study visit (week 32) were analysed for serum cortisol concentration (cortisol) using Roche Elecsys Cortisol II immunoassay. Participants were then stratified into three groups based on cortisol concentration to predict risk of AI; cortisol < 100nmol/l (high risk), 100–315 nmol/l (indeterminate risk) and > 315 nmol/l (low risk) based on locally derived reference ranges. 21% participants were classified as low risk, 18% as high risk and the remaining 61% at indeterminate risk of AI. Median morning cortisol in the low risk group was ten-fold higher than those in the high risk group (380 vs 38.5 nmol/l, p=0.001). OCS exposure was a significant predictor of risk of AI (OR 1.1 [1.03–1.17] per mg/kg increase in prednisolone exposure, p=0.004). Participants at high risk were more likely to be on maintenance OCS (33% vs 0%, p=0.015) and had a greater median cumulative OCS exposure over the study period (7.55 vs 0.66 mg/kg prednisolone, p=0.002). ICS exposure was also associated with risk of AI. Participants at high risk AI had a greater adherence to ICS therapy (78% vs 62%, p=0.049) and greater cumulative received

ICS dose over the study duration than those at low risk AI (178.2 vs 127.9 mg, p=0.036). ICS exposure remained a significant predictor of AI even when OCS exposure is controlled for (OR 2.49 [1.06–5.82] per 1mg/kg increase in FP exposure). Both the asthma control test (ACT) & asthma quality of life questionnaire (AQLQ) scores correlate with morning cortisol concentration (ACT r=0.2, p=0.068, AQLQ r=0.26, p=0.019). Interestingly, participants with cortisol < 100nmol/l reported worse asthma control (ACT score 16 vs 20, p=0.07) and a lower AQLQ score (4.1 vs 5.8, p=0.02) than the low risk group despite objectively better lung function (FEV1 90.6 vs 77.6% predicted). Our data suggests that both cumulative oral and inhaled glucocorticoid exposure contribute independently to cortisol suppression and risk of AI. The discrepancy between objective (FEV1) and more subjective measures of asthma control (ACT score) in the high risk group suggests that undiagnosed AI, as well as other non-airway co-morbidities, may contribute to the symptom burden experienced by these patients.

Adrenal

ADRENAL – CLINICAL RESEARCH STUDIES

Quality of Life and Its Determinants in Patients With Adrenal Insufficiency: A Survey Study From Three Tertiary Centers in the United States

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Context: Quality of life (QoL) is impaired in patients with chronic adrenal insufficiency (AI) despite standard glucocorticoid (GC) replacement therapy. Current evidence on the determinants of QoL is scarce and limited in very few European countries, and how it relates to AI subtypes remains underexplored.

Objective: We conducted the first survey study in patients with AI in the USA to determine the correlations between clinical parameters, adverse outcomes, patient education, socioeconomic factors, and QoL in different subtypes of AI.

Design, Setting and Participants: Cross-sectional survey study of 529 patients with AI between 2015 and 2020, at three tertiary centers in the USA.

Intervention: Patient-centered questionnaires.

Main Outcome Measures: QoL scores using Short-Form 36.

Results: Of 529 participants, 223 (42.2%) had primary AI (PAI), 190 (35.9%) had secondary AI (SAI), and 116 (21.9%) had glucocorticoid induced AI (GIAI). Median age at the time of survey was 58 years (IQR: 43–68), 342 (64.8%) were women and 483 (91.3%) were Caucasians. Median duration of AI was 6 years (IQR: 3–14.5), longest in patients with PAI (11 vs 4 years in SAI and GIAI, p=0.0001). Overall, Physical Composite Summary (PCS) score was lower than the Mental Composite Summary (MCS) (38.1±12.9 vs 46.5±11.8). Across the eight dimensions, each individual decade- and sex-adjusted Z-score (using the normative data of USA population) in patients with PAI was significantly