of prednisolone (or equivalent doses) daily for longer than 4 weeks) admitted to hospital very unwell with confirmed or suspected COVID recommendations is to start on Hydrocortisone 100 mg per IV injection followed by continuous IV infusion of 200 mg hydrocortisone/24h (alternatively 50 mg every 6 h per intravenous or IM bolus injection). **Method:** Retrospect data collection on Patients admitted in May 2020 to Bedford Hospital with suspected or confirmed COVID 19 disease with adrenal insufficiency or on long term steroid use. Those patients should be started on Hydrocortisone 100 mg per IV injection followed by continuous IV infusion of 200 mg hydrocortisone/24h (alternatively 50 mg every 6 h per intravenous or IM bolus injection).
Results: In May 2020, 295 patients admitted under the medical team in Bedford Hospital with confirmed or suspected COVID-19. Only 12 patients met the inclusion criteria, one patient with a diagnosis of Addison disease and the remaining 11 patients on long term steroids. None of these patients were managed as per updated guidelines. 6 patients had less than the adequate dose, they were started on prednisolone 30-40mg. 4 patients dose of oral steroids was only doubled, 1 patient received the same dose of oral steroid and the only confirmed Addison had higher dose of hydrocortisone. Moreover, In June 2020, The RECOVERY Outcome trial results showed that Dexamethasone 6mg for 10 days reduces the death by one third in hospitalised patient with severe respiratory complications of COVID-19. Dexamethasone 6mg is 12 times the physiological required steroid dose, this is equivalent to 240mg hydrocortisone, which is adequate for steroid replacement in patients with adrenal insufficiency or suppression.
Conclusion: In view of these results and the outcome of the RECOVERY Trial, Local trust guidelines updated, indicated that any patient with Adrenal insufficiency or suppression including those on long term steroids very unwell admitted to the hospital should receive Dexamethasone if requiring oxygen or Hydrocortisone if not requiring oxygen. Recommendation of changes included teaching sessions delivered to doctors, posters on updated guidelines distributed in major areas in hospital and trust guidelines updated on the intranet.

Adrenal

ADRENAL – CLINICAL RESEARCH STUDIES

Changes in Adrenal and Gonadal Androgens After 14-Day Treatment With CRF1 Receptor Antagonist, Crinecerfont (NBI-74788), in Men With Classic 21-Hydroxylase Deficiency

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Background: Congenital adrenal hyperplasia due to classic 21-hydroxylase deficiency (21OHD) causes cortisol insufficiency and androgen excess. A phase 2 trial of crinecerfont, a CRF1 receptor antagonist, in 18 adults with 21OHD showed prominent decreases in ACTH, 17-hydroxyprogesterone, and androstenedione (A4), and in women, testosterone (T), after 14 days of treatment. In men with 21OHD, T derives from both adrenals and testes; in poor disease control, A4/T ratio is elevated due to disproportionately increased adrenal A4 production and decreased testicular T production. We sought to determine the impact of crinecerfont on both adrenal and gonadal androgen production in men with 21OHD in this phase 2 trial.
Methods: A4 and T data were analyzed for 7 men who completed 1 or more of 4 oral dosing regimens: Cohort 1, 50 mg QHS, n=4; Cohort 2, 100 mg QHS, n=2; Cohort 3, 100 mg QPM, n=5; and Cohort 4, 100 mg BID, n=3 (14 total treatment periods). Mean 0600-1000 4-hour morning window (M4hMW) and mean 24-hour (M24h) A4, T, and A4/T ratios were analyzed from serial serum samples at baseline and on day 15.
Results: Dose-dependent reductions in M4hMW A4 were observed [median (range)] in men, consistent with previously presented data in all subjects:Cohort 1: -21% (-84 to -12%);Cohort 2: -37% (-51% to -23%);Cohort 3: -43% (-85% to +140%);Cohort 4: -62% (-90% to -33%).
In contrast, M4hMW T showed inconsistent changes [median (range)]: Cohort 1: +18% (-40% to +82%);Cohort 2: -4% (-4.3% to -3.8%);Cohort 3: +9% (-11 to +24%);Cohort 4: +9% (-3% to +27%).
Thus, M4hMW A4/T ratios decreased with dose. Values at baseline, on day 15, and percent changes [median (range)] were, respectively:Cohort 1: 0.9 (0.3–2.6), 0.6 (0.1–2.1), -26% (-91% to +23%);Cohort 2: 5.0 (4.8–5.2), 3.3 (2.5–4.2), -35% (-49% to -20%);Cohort 3: 0.6 (0.1–6.9), 0.3 (0.1–2.7), -54% (-85% to +178%);Cohort 4: 3.9 (0.6–5.9), 0.4 (0.3–2.1), -65% (-92% to -31%).
M24h A4/T ratios similarly declined in all cohorts. Values at baseline, on day 15, and percent changes [median (range)] were, respectively:Cohort 1: 1.0 (0.3–2.3), 0.4 (0.1–1.9), -33% (-92% to +2%);Cohort 2: 4.3 (3.8–4.9), 2.7 (2.4–3.0), -36% (-51% to -22%);Cohort 3: 0.5 (0.1–4.7), 0.4 (0.1–2.4), -59% (-78% to +310%);Cohort 4: 3.2 (0.4–4.1), 0.4 (0.3–1.7), -58% (-89% to -31%).
Conclusions: Following crinecerfont therapy, A4 and A4/T decreased in a dose-dependent manner in men with 21OHD. In contrast to reductions in T observed in women with 21OHD, T did not change consistently and rose in some men. Preserved T values despite marked A4 reductions suggests testicular T production increased during crinecerfont therapy, perhaps due to release of gonadotropin suppression from adrenal-derived androgens. Long term studies are needed to determine if crinecerfont treatment improves additional measures of testicular function in men with 21OHD.
Reference: RJ Auchus, et al. *J Endocr Soc* 2020;4(Suppl 1):OR25-03.

Adrenal

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Changes in Clinical Presentation and Perioperative Management of Pheochromocytomas and