

scintigraphy showed increased tracer uptake at upper abdomen. Right adrenalectomy and partial nephrectomy were performed. The final pathological diagnosis was sympathetic paraganglioma, and angiomyolipoma which confirmed by immunohistochemical staining. We present here an unusual case of concurrent periadrenal paraganglioma and renal angiomyolipoma which was complicated by autonomous toxic multinodular goiter.

Neuroendocrinology and Pituitary

PITUITARY TUMORS II

Stimulation for Bilateral Inferior Petrosal Sinus Sampling May Be Unnecessary for Diagnosis of ACTH Dependent Cushing Syndrome.

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Introduction: Bilateral inferior petrosal sinus sampling (BIPSS) is the gold standard test to differentiate Cushing's disease (CD) and ectopic ACTH syndrome (EAS). Stimulation test for diagnosis may be unnecessary in some cases and the diagnostic yield of the stimulation test may be similar to the basal measurement. **Methods:** 34 adult patients referred for diagnosis of ACTH dependent Cushing syndrome. Basal samples for prolactin and ACTH were taken from bilateral inferior petrosal sinus and from peripheral vein. Stimulation test with desmopressin (32 subject) or CRH (2 subjects) was performed. Samples were taken at 0, 3, 5 and 10 minutes. To compare the percentage of diagnosis with each measurement the MacNemar test was done. **Results:** Right basal ACTH was 465 pg./ml (ICR 62-1250), ACTH at 3 minutes was 647 (ICR 227-2610), ACTH at 5 minutes was 1250 (ICR 245-1965), ACTH at 10 minutes was 230 (71-550). Left basal ACTH was 230 (71-550), at 3 minutes was 453 (ICR 116-1250), at 5 minutes was 431 (91-1250), at 10 minutes was 534 (140-1250). Median basal ACTH ratio was 13.8 (ICR 5.1-26), at 3 minutes was 34.5 (ICR 13-82), at 5 minutes was 30.6 (11.4-49.8), at 10 minutes was 18.5 (8.2-48.2). The higher ratio was at 3 minutes. Basal ACTH ratio was <2 in only 4 cases. 2 out of 4 cases had ratio >3 after stimulation test. CD was diagnosed with basal ratio in 88.6% of cases, and at 3, 5 and 10 minutes in 94.3% of cases. There was no difference in percentage of CD diagnosis at 3, 5 or 10 minutes ($p=1.0$). **Discussion:** Basal ACTH ratio was able to differentiate CD from ECS in most cases (88.6%). At least one additional sample with CRH or desmopressin stimuli identify 94.3% of CD cases with the higher increases at 3 minutes. Additional stimuli do not improve overall diagnosis, therefore, a basal ratio and additional stimulation test at 3 minutes is enough for CD diagnosis. This may decrease the cost of BIPSS and total duration of the procedure.

Neuroendocrinology and Pituitary

ADVANCES IN NEUROENDOCRINOLOGY

Extended Release Octreotide Pharmacokinetics in Healthy Subjects After Subcutaneous Injection of MTD201

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An open-label, randomised, single-dose Phase I study in healthy subjects evaluated octreotide pharmacokinetics after deep-intramuscular (IM) or subcutaneous (SC) injection of MTD201 (30mg). All subjects received Sandostatin[®] (100µg immediate release; SIR) by deep SC injection 24h before MTD201. MTD201 is manufactured by Q-Sphera[™] printing technology to minimize particle size variation and afford simpler reconstitution and less painful injection via a 21G needle. Plasma octreotide concentrations were measured over 63 days to ascertain the potential for a 6- to 8-week dosing interval. MTD201 is being developed as a next generation long-acting somatostatin analogue for maintenance management of acromegaly and neuroendocrine cancer patients. **Methods:** 28 healthy subjects were randomised to two groups. The reference product SIR (100µg) was injected SC, followed 24 hours later by MTD201 administered by either IM ($n=14$, 38mm 21G needle) or SC ($n=14$, 16mm 21G needle) injection. MTD201 was resuspended in WFI to give a final injection volume of 1.5mL. Plasma samples for determination of octreotide and serum samples for IGF-1 and GH levels were drawn pre-dose and over the 63-days post-dosing. Injection site reactions and AEs were recorded, scored and compared across groups. **Results:** MTD201 was very well tolerated by both groups with 3 mild TEAEs observed per group. Transient and mild injection site reactions were similar after all treatments. Upon MTD201 injection, a low initial burst of octreotide (<1ng/mL) was followed by a sustained period of release that extended beyond the final sampling point at Day 63. C_{max} values of 5.42ng/mL (SC) and 3.68ng/mL (IM) were within the plasma exposure range reported for marketed octreotide products. Octreotide bioavailability was 47% (IM) and 62% (SC) relative to SIR. Sustained suppression of IGF-1 concentration was achieved throughout the study period to similar levels for both groups. Octreotide PK profiles and overall exposures were similar between groups, indicating that these routes may be interchangeable in clinical use. **Conclusions:** MTD201 (30mg) by either IM or SC injection produced continuous octreotide release over a period of at least 63 days at levels predicted to maintain efficacious plasma concentrations at steady state with a dosing interval of up to 8 weeks. Reduced plasma IGF-1 concentrations were maintained throughout the study period. Unlike marketed octreotide depot products, MTD201 can be simply and rapidly reconstituted in WFI to give a stable suspension injectable via 21G needle in a 1.5mL volume. MTD201 can be developed as an easy to inject SC or IM depot for acromegaly and NETs, with an expected dose interval of 8 weeks, and confirmed patient-centric advantages.