patients. In contrast, we found increased proportions of IFG and DM patients in SRL treated when compared to non-treated patients (euglycemic: 45%, IFG: 42%, DM: 13% vs. euglycemic: 70%, IFG: 22%, DM: 8%, respectively; p=0.006). In addition, SRL treatment increased the odds ratio of IFG and DM (OR 4.7; 95%CI 2.1-10.3). When considering the degree of response to SRL pre-surgical treatment, we found that poor responders displayed at the time of surgery glycemia diagnostic of DM; whereas, good responders displayed glycemia in the range of IFG (percent change in GH levels 50±35% vs 79±22%, respectively; p=0.05). Conclusions: Our findings show that the proportion of patients with acromegaly undergoing surgery with glycemic levels diagnostic of DM, is modest. Interestingly, pre-treatment with SRL represents an independent risk factor for high glucose levels. Moreover, among patients on SRL pre-treatment, the ones that respond poorly are the ones that at the time of surgery display glycemia diagnostic of DM. Our findings suggest that SRL pre-treatment may predispose to worsened glucose metabolism but selectively affecting those patients in whom biochemical control is not reached.

Reproductive Endocrinology
MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

The Testosterone-To-Estradiol Ratio, Rather Than Testosterone or Estradiol Alone, Is a More Precise Marker of Metabolic-Related Outcomes in Males: Insights From a Systematic Review.

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SAT-LB8
Background: Estradiol (E2) has been shown to exert beneficial effects on males, particularly for metabolic outcomes. However, these benefits tend to be more evident when accompanied by concurrent increase in testosterone (T) levels, when the increase of E2 is secondary to the increase of T. Opposite to its benefits in healthy males, when under metabolic and inflammatory diseases, E2 has been reported to be a marker of worse prognosis, once E2 is unproportionally high compared to testosterone in pathological conditions, which results in hypogonadism. The collective analysis of T and E2 shows that the balance between these two hormones determines whether increase in E2 levels is physiological or pathological, demonstrated by balanced T and E2, i.e., intact T:E ratio compared to healthy males, and disrupted balance between T and E2, with impaired T:E ratio, respectively. Hence, it seems that the dual relationship between E2 and health markers in males is based on the balance, or ratio, between T and E2. The objective of the present study is to propose a ratio between T and E2 (testosterone-to-estradiol ratio, or T:E ratio) as a better predictor of health outcomes than testosterone or estradiol alone, and to differentiate health from pathological states within this single marker, from a review of the literature. Methods: We systematically searched for articles using the following criteria: 1. Any of the combinations of the expressions “testosterone” (AND) “estradiol” (AND) “male(s)” (OR) “men” (OR) “masculine”, or “testosterone-to-estradiol” (OR) “testosterone:estradiol” (OR) “estradiol-to-testosterone ratio” (OR) “estradiol:testosterone” (AND) “male(s)” (OR) “men” (OR) “masculine”, to be present in the title and/or abstract; 2. Fully written in English; 3. Performed in humans; 4. Throughout the literature until Jan 30th 2020; and 5. Original researches. Results: We selected 39 articles, from which 27 were performed in healthy males, and 11 under metabolic or inflammatory conditions. Benefits of E2 in healthy males occurred irrespective of T for bone mass and quality, and anger levels. Benefits that were better identified when E2 and T were evaluated together include better libido, improved cognitive functions, improved well-being and other mood states, increased muscle mass, enhanced loss of fat mass, quality, increased basal metabolic rate, increased fat oxidation, and reduced cardiovascular markers, including reduced maximal intimal-media carotids thickness, when T:E ratio was > 13.7. In pathological states, increased estradiol was associated to increased risk of disease-specific complications, and worse quality of life, particularly when T:E was < 9.5. T:E ratio was also able to accurately identify healthy athletes from those affected by any sport-related metabolic conditions. Conclusion: Testosterone-to-estradiol (T:E) ratio is likely a more precise predictor of metabolic-related health outcomes in both healthy and pathological states, compared to testosterone or estradiol alone.

Tumor Biology
ENDOCRINE NEOPLASIA CASE REPORTS III

Concurrent Peri-Adrenal Paraganglioma and Renal Angiomyolipoma Complicated by Toxict Multinodular Goiter

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SAT-LB305
Concurrent Periadrenal Paraganglioma And Renal Angiomyolipoma Complicated By Toxic Multinodular Goiter

Abstract: A 40 years old woman presented with headache, palpitation and diaphoresis by the past 3 months, and then developed progressive dyspnea on exertion and chest pain 2 weeks ago. She also lost 5 kg of her body weight during the past 6 months. She ever had multinodular goiter and lobectomy was done 12 years ago, after that she lost to follow up. At meantime, toxic multinodular goiter was suspected and high level of free T4, T3, and suppressed thyrotropin were demonstrated. Furthermore, thyroid scan revealed heterogenous tracer uptake at her thyroid bed. Methimazole was started, however her blood pressure and heart rate were all uncontrolled. Phaeochromocytoma was suspected and markedly elevated of both urinary normetanephrine and metanephrine were confirmed. Computed tomogram revealed a huge, right supra-renal mass. In addition, hypodensity mass were found at upper pole of right kidney, and the results of 131I-Metaiodobenzylguanidine

doi: 10.1210/jendso/bvaa046 | Journal of the Endocrine Society | A1157
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 TUMORS II

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

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MON-LB51

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 simples 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.

SUN-LB47

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. Cmax 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.