early GH (p = 0.004), and late GH (p = 0.037) improved significantly. Basal estradiol (p = 0.0002) and nocturnal urinary catecholamines, (p = 0.043) reduced, while testosterone (p = 0.014), testosterone:estradiol (T:E) ratio (p = 0.0005), freeT3 (p = 0.043), IGF-1 (p = 0.003), and cortisol awakening response (CAR) (p = 0.001) increased significantly. All basal parameters and early responses to ITT normalized, when compared to healthy athletes. Basal metabolic rate, fat oxidation, body fat, muscle mass, and hydration status had partial but non-significant improvements. Conclusion: After 12 weeks, athletes affected by actual OTS demonstrated substantial improvements, remarkably IGF-1, freeT3, CAR, testosterone, estradiol, testosterone:estradiol ratio, CK and catecholamines, and early cortisol, early prolactin, and overall GH responses to stimulations.

Adipose Tissue, Appetite, and Obesity

OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Novel Paradoxical Markers of Weight Loss: Is the Worse Actually the Better? a Retrospective Analysis of 1,567 Patients With Obesity With Successful Clinical Weight-Loss Approaches.

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MON-LB010

Background: Obesity is a chronic, multi-factorial, and relapsing disorder that has been reported to be a risk factor to more than 200 diseases, among which the majority is direct- or indirectly triggered by the metabolic abnormalities induced by excessive body fat. Indeed, patients with obesity tend to disclose multiple alterations of metabolic markers, which tend to improve with weight loss. Despite the multiple dysfunctions extensively in this population, only mandatory biochemical exams are usually ordered, likely due to limitations in cost and lack of cost-effectiveness, since the majority of the parameters typically altered in obesity does not drive therapeutic choices or influence in an individual-based evaluation. We developed a protocol for obesity treatment that includes a thorough analysis and follow up of the biochemical parameters of patients with obesity, including more than 50 parameters, for more precise diagnosis and response to treatments. Among these parameters, we identified unexpected changes, including some that would initially be related to increased cardiovascular risk or worse prognosis when in an usual context, but which could peculiarly indicate successfulness of weight loss, since these parameters tend to return to normal levels after a period in the new body weight. Our objective is to identify whether these paradoxical changes in biomarkers are linearly correlated with body weight loss, fat loss, mass loss, or whether they were related to the use of any anti-obesity drug. Methods: In a retrospective cohort of 1,567 patients that underwent a clinical weight loss treatment for obesity in a obesity center (Corpometria Institute, Brasilia, DF, Brazil), we performed a linear association analysis between body weight and body fat (air displacement plethysmography - Bod Pod, CosMed, USA) and 65 parameters, including hormonal, metabolic, inflammatory, and immunologic parameters. We also adjusted for the use of anti-obesity drugs.

Results: Homocysteine and triglycerides were identified to increase linearly according to the amount of weight loss (r = -0.77) and fat loss (r = -0.85), but not due to the use of any drug. Folic acid decrease was directly related to fat loss (r = 0.81). Additional findings include more significant decrease of ApoB, compared to LDLc, decreases of GGT, ALT, CRP, ESR, neutrophils, ferritin, fibrinogen, PTH, free T3, uric acid, a and temporary decrease of ApoA and HDLc, all related with body fat loss. Conclusions: Increase of homocysteine resulted from decreased folic acid metabolism, and increased triglycerides may be indirect markers of lipolysis, as no other plausible mechanism could explain these findings.

Reproductive Endocrinology

REPRODUCTIVE ENDOCRINOLOGY: REPRODUCTIVE FUNCTION AND DYSFUNCTION ON DEVELOPMENT

Cyclic Progesterone Therapy for Androgenic Polycystic Ovary Syndrome (PCOS) - A Systematic Review of the Literature

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MON-LB010

Women living with androgenic PCOS (WLWP) experience unpredictable oligomenorrhea and are at increased risk for endometrial cancer. Oral micronized progesterone (OMP) given cyclically (14 days/cycle or 4 weeks, Cyclic OMP), in luteal phase doses (300 mg at bedtime) as a “luteal phase replacement” therapy would be likely to effectively treat both. In addition, evidence suggests PCOS is causally related to rapid pulsing of GnRH and LH. OMP normalizes LH pulsatility if androgen levels are not elevated. Previous searches did not find progesterone therapy for PCOS. Our research question: Does the peer-reviewed literature provide evidence for prescribing cyclic progesterone therapy in PCOS? Literature search methods used Medline (Ovid) and PubMed for published articles. Our search terms were: “polycystic ovary syndrome”, “androgenic PCOS”, and, “micronized progesterone.” We sought publications with eligible women participants having androgenic PCOS, drug exposures (cyclic OMP, vaginal progesterone, and in varying doses and durations) and specific outcomes (biochemical or patient-reported data or both) in all languages. We excluded reviews and practice guidelines but searched bibliographies for missed citations. Results discovered 18 articles in combined Medline (n=6) and PubMed (12) searches. After excluding duplicates, articles on estradiol (E2) alone E2 alone with OMP therapy, five eligible articles remained. We read all in full detail.

Progesterone therapy was beneficial for WLWP as, even in sub-therapeutic doses (<300 mg at bedtime) and in cycles of too short durations (<14 days), it decreased luteinizing hormone (LH) and total testosterone levels. Vaginal progesterone (200 mg, b.i.d for 2 to 12 weeks) added to letrozole ovulation induction increased the pregnancy rate from 0 to 21%.

Although present data suggest Cyclic
OMP withdrawal predictively causes flow, we found no evidence it improved women’s cycle-related experiences nor decreased acne and hirsutism. Women-reported data on Cyclic OMP for improving androgenic PCOS cycle regularity, daily experiences and risks for endometrial cancer are needed.

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Adipose Tissue, Appetite, and Obesity
OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET
5-Year Data of an Aggressive Pharmacological Approach to Moderate and Morbid Obesity: Is Prevention of Bariatric Surgery Feasible in the Long Run?
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MON-LB101
Background: Maintenance of weight loss in patients that undergo weight loss interventions is highly challenging, irrespective of the type of approach to obesity (whether surgical, pharmacological, or non-pharmacological). We proposed a protocol of an aggressive clinical treatment for obesity aiming to prevent the need of bariatric surgery, in patients unwilling to undergo this procedure, by proposing a protocol that included the combination of different anti-obesity medications and non-pharmacological modalities, for longer duration, and with an active approach to prevent weight regain. Our initial 2-year data showed that 93% (40 of 43 patients) with moderate and morbid obesity were able to avoid the need of bariatric surgery, with concomitant improvements of the biochemical profile. However, whether these patients would maintain their successful rates after five years was uncertain. Our objective is to describe the efficacy and safety of a long term (5-year data) pharmacological and multi-modal treatment for moderate and severe obesity. Methods: The 40 patients that were successful in the two-year approach in our obesity center (Corporation Instituto, Brasilia, DF, Brazil) were enrolled. A long-term anti-obesity protocol was employed, with continuous or intermittent use of anti-obesity drugs, trisemtral body composition analysis, psychotherapy, visit to a nutritionist every four months, and both resistance and endurance exercises at least four times a week. Body weight (BW), total weight excess (TWE), body fat, markers of lipid and glucose metabolism, liver function, and inflammation were analyzed. Subjects that dropped out were considered as weight regain. Therapeutic success for the 5-year follow-up included as the maintenance of >20% loss of the initial BW loss, and no weight regain (or < 20% of the initial weight loss). Results: A total of 27 patients (67.5%) were able to maintain the body weight, seven dropped out, and six regained more than 20% of the initial weight loss. Of these, 21 (77.8%) had significant further increase of muscle mass and decrease of fat loss, while 17 (63.0%) had further weight loss (p < 0.05), compared to the 2-year data. Improvements on the biochemical profile persisted in all 27 patients, and had significant further improvements in 24 (88.9%) of these patients. Conclusion: The risk of weight regain five years after a weight loss treatment for obesity was significantly lower compared to previous literature, and comparable to the long-term outcomes of bariatric procedures. An aggressive, structured, and long-term clinical weight loss approach has been shown to be feasible, even for morbidly obese patients.

Neuroendocrinology and Pituitary
ADVANCES IN NEUROENDOCRINOLOGY
Steroid and Sex Specific Responses of Neural Stem Cells to Prenatal Dexamethasone versus Betamethasone Administration
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SUN-LB56
Synthetic glucocorticoids (sGCs) are widely administered to pregnant women for their anti-inflammatory, immunosuppressive and organ maturation properties. Worldwide, Dexamethasone (Dex) and Betamethasone (Beta) are the two most commonly administered prenatal sGCs to reduce morbidity and mortality associated with respiratory distress, intraventricular hemorrhage and necrotizing enterocolitis. Preterm administration of sGCs is associated with reduced birthweight and increased risk for hypertension, cardiovascular, metabolic, and neurological problems later in life. Adverse neurological outcome has been shown to depend on the type of sGCs used, the dose, timing of sGCs administration and sex. We have previously shown that the glucocorticoid receptor (GR) is expressed in the developing brain in stem and progenitor cells, neurons and glia from early developmental stages, and that prenatal Dex alters neural stem cell (NSC) biology and the developmental trajectory of the cerebral cortex, hypothalamus and adult behavior. To identify the molecular and cellular basis of the sex and steroid specific responses in the developing brain, we compared the consequence of Dex versus Beta exposure on embryonic cerebral cortical NSC biology. Murine NSC were isolated from the E14.5 cerebral cortex and exposed to 10-7 M Dex, 10-7 M Beta, or Vehicle for 4 or 24 hours and the immediate and long-term impact on transcription, proliferation and neuronal, glial and oligodendrocyte differentiation examined. Affymetrix complete genome transcriptional analyses reveal sex specific responses to Dex versus Beta within 4 hours. At >+/−1.5-fold change 548 genes were differentially regulated by Dex, 452 by Beta and 256 were altered by both Dex and Beta (P < 0.05). Distinct sex specific responses to Dex versus Beta were observed. At >+/−2-fold change 126 genes were significantly different in the Dex versus Beta female transcriptome, 146 in the male transcriptome with 18 genes unique to both male