latitudes, is associated with a more frequent prevalence of vitamin D deficiency.
Objective: To determine if there are variances in 25-OH-VitaminD3 concentration throughout the season in school-aged children and their relationship with PTH, alkaline phosphatase (AP), and calcium, and its association with UVB radiation.
Methods: Cross-sectional study of 5–8 years old children without vitamin D supplementation. All subjects were recruited in Santiago de Chile (latitude 32°55' to 34°19' south) during different seasons of the year, and underwent a complete physical examination, measures of height, weight, and BMI, and biochemical analysis, including 25-OH-VitaminD3 (by liquid chromatography and tandem mass spectrometry), PTH, AP, and calcium. UVB radiation measures obtained from the Chilean Meteorological Service's database.
Results: A total of one hundred thirty-three children were recruited (summer = 41, autumn = 28, winter = 35, spring = 29). No differences in sex, age, height-SDS, and BMI-SDS were found between the groups.
25-OH-VitaminD3 mean difference was significative comparing summer with winter (9.6 ng/mL, p <0.0001), autumn (6.9 ng/mL, p <0.001), and spring (5.4 ng/mL, p <0.01). No difference was observed in calcium concentration. AP and PTH mean difference also was significative comparing summer with winter (AP -47.5 IU/L, p <0.01; PTH -11.1 pg/mL, p <0.0001), autumn (AP -54.7 IU/L, p <0.01; PTH -8.3 pg/mL, p <0.001) and spring (AP -49.9 IU/L, p <0.05; PTH -10.8 pg/mL, p <0.0001).
Vitamin D deficiency, insufficiency, and sufficiency status showed a seasonal variation (Pearson's $\chi 2$ (6) = 36.6, p <0.001). Sufficiency percentage was higher in summer (51.2%) compared with autumn (10.7%, Odd ratio= 8.7, 95% CI= 2.5 to 30.0, p=0.0007) and winter (8.6%, Odd ratio= 11.2, 95% CI= 3.2 to 38.0, p<0.0001)
25-OH-VitaminD3 showed an inverse correlation with PTH concentration (r= -0.383, R2= 0.15, p <0.0001), and in turn, PTH was directly correlated to AP (r= 0.240, R2= 0.06, p= 0.006). 25-OH-VitaminD3 concentration was directly related to the UV index (r= 0.531, R^2= 0.28, p <0.0001)
Conclusion: 25-OH-VitaminD3 concentration decrease significatively during autumn and specially during winter, associated to an increase in PTH and AP increase, but not a change in calcium concentration. During the darker months, the reduction of UVB radiation seems to be related to the decrease of 25-OH-VitaminD3 concentration, increasing the percentage of Vitamin D deficiency and insufficiency status.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

The WBC Differential in Relation to DKA Severity

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MON-638

Background: Diabetic ketoacidosis (DKA) is well-known to be associated with increased levels of inflammatory markers including cytokines. Interestingly, an elevated white blood count (WBC) has been associated with a higher prevalence of acute and chronic diabetes metabolic complications, including DKA, and micro- and macrovascular complications (Tong et al., 2004; Xu et al., 2013). However, very few studies have looked at the relationship between WBC differential and the severity of DKA. For instance, a study looking at platelet-to-lymphocyte ratio found it to be a significant predictor of mortality in DKA patients admitted to the intensive care unit (Liu et al., 2016).
Aim: The goal of the present study is to investigate the relationship between the WBC differential and the severity of DKA.
Method: This study was conducted at Dalhousie University-affiliated hospitals in Nova Scotia, Canada. Ethics approval was obtained. The medical records of 646 emergency visits for 338 patients between November 2015 to December 2018 with a provisional diagnosis of DKA were retrospectively reviewed. 84 records were excluded due to non-anion gap metabolic acidosis, and 66 were excluded due to radiological or microbiological evidence of infection (positive urine, stool or blood cultures, pneumonia, etc.). Only the first set of blood investigations were analyzed to avoid post-treatment changes in blood composition. WBC differential (neutrophils, basophils, eosinophils, immature granulocyte, lymphocytes, metamyelocytes, monocytes, and myelocytes) and severity of DKA based on pH value (mild: 7.25–7.30, moderate: 7.24-7.00, and severe: <7.00) were analyzed.
Result: A total of 496 visits for 277 patients were analyzed, with about 1:1.2 male-to-female ratio and median age of 36.5 years (range 18–90 years), with no significant differences in sex or age in relation to the severity of DKA (P-value= 0.68 and 0.16, respectively). Leukocytosis (WBC >11 x10(9)/L) was seen in 65% (n=314). 32% (n=158) had mild DKA, while 56% (n=273) and 1% (n=57) had moderate and severe DKA, respectively.
With increased severity of DKA, higher WBC count and hemoglobin levels were observed (P-value= 0.002 and 0.037, respectively). This is not unexpected due to hemoconcentration. However, monocytes, immature granulocytes, and basophils (percentage unit of the total WBC) increased with the severity of DKA (P-value: 0.004, <0.001, and <0.001, respectively). On the other hand, lymphocytes displayed an inverse relationship to DKA severity (P-value: 0.015). In contrast, eosinophils & neutrophils had no significant correlation to the DKA severity (P-value= 0.96, and 0.44, respectively).
Conclusion: The WBC differential (namely, monocytes, immature granulocytes, basophils, & lymphocytes) is associated with the severity of DKA. We propose that the WBC differential be further studied as a prognostic indicator in patients with DKA.

Adipose Tissue, Appetite, and Obesity

CNS, INFLAMMATORY, AND THERMOGENIC INFLUENCES OF BODY WEIGHT

G Protein $G_S\alpha$ in Muscle Is Essential for Survival During Cold Adaptation in the Absence of Thermogenesis of Brown Adipose Tissue

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OR04-06

Adaptive thermogenesis is important for the control of body temperature (Tb) and maintenance of body weight, and it is primarily regulated by sympathetically-driven brown adipose tissue (BAT). Studies indicate that muscle is also involved in thermogenic regulation. $G_s\alpha$ couples to ligands and receptors, including β-adrenergic receptors, to increase intracellular cAMP. Our previous studies have showed that mice with adipose-specific $G_s\alpha$ deficiency had inactive BAT and impaired cold tolerance. To determine whether $G_s\alpha$/cAMP signaling in skeletal muscle compensates for loss of BAT thermogenesis, we generated mice with $G_s\alpha$ deficiency in adipocyte tissue alone (AdipGsKO), in skeletal muscle alone (SkMGsKO) or in both (AdipSkMGsKO). Compared to control mice, AdipGsKO and SkMGsKO mice had normal body weight, while AdipSkMGsKO showed reduced body weight with normal food intake and energy expenditure. Both AdipGsKO and AdipSkMGsKO mice had elevated fasting glucose levels, but similar glucose tolerance to control or SkMGsKO mice. SkMGsKO mice displayed reduced insulin sensitivity. When acutely exposed to 6°C for 3 hours, AdipGsKO and AdipSkMGsKO mice rapidly decreased their Tb, indicating that they are sensitive to acute cold exposure, consistent with their inactive BAT. To assess adaptation to chronic cold, mice were exposed to gradually declining ambient temperature from 22°C to 6°C with a daily decrease of 2°C and were then kept at 6°C for 5 days. As expected, both AdipGsKO and AdipSkMGsKO mice failed to stimulate BAT UCP1 by cold adaptation. Unexpectedly, AdipGsKO mice maintained normal Tb similar to control and SkMGsKO mice. However, AdipSkMGsKO mice started to rapidly drop their Tb when ambient temperature declined to 14°C and 85% of SkMGsKO mice (11/13) died before the end of experiment. These results suggest that when there is a lack of BAT function, $G_s\alpha$/cAMP signaling in muscle plays an essential role for mice to survive in response to chronic cold challenge.

Neuroendocrinology and Pituitary

PITUITARY AND NEUROENDOCRINE CLINICAL TRIALS AND STUDIES

Serum Cell-Free Methylation-Based Signatures Distinguishes Pituitary Tumors According to Functional Status and from Other Neoplasia: A Liquid Biopsy Approach.

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OR32-03

Background: Several reports have indicated that distinct epigenomic patterns of pituitary tumors (PT), specifically DNA methylation, distinguish these tumor tissues according to their functionality and could be involved in their pathogenesis. Thus far, molecular diagnosis and classification criteria that guide clinical management of these tumors rely on the tissue profiling obtained by invasive surgical approaches (e.g. excision). However, increasing evidence confirmed that central nervous system (CNS) tumors release cell material into the circulation creating an opportunity for molecular profiling of these tumors using a blood-based liquid biopsy. Considering that 1) the pituitary portal system and the invasion of the cavernous system by PT may facilitate the spillage of tumor cell material into the bloodstream and 2) the stability, cell-specificity and reportedly the role of DNA methylation in PT, we hypothesized that liquid biopsy would be feasible to detect and define specific methylation-based signatures in the serum of patients harboring PT. **Methods and Findings:** We conducted analyses of the methylomes of paired serum circulating cell-free DNA (cfDNA) and tumor tissue from patients harboring PT (EPIC array) to identify serum-derived pituitary tumor-specific methylation-based signatures (sPTMet n=37) in a cohort comprised by 13 patients with pituitary macroadenomas (9 males; median age: 62; 9 Nonfunctioning/4functioning, 6 invasive/7noninvasive), 4 controls (non-tumor) and patients with other CNS tumors or conditions (114 gliomas, 6 meningiomas, 1 brain metastasis, 1 colloid cyst, 6 radiation necrosis). Unsupervised and supervised analysis indicated that the serum methylome from patients harboring PT was distinct from controls and other CNS diseases. Using the sPTMet as input into a machine learning algorithm, we generated a PT score that classified the serum of an independent cohort as PT or non-PT, with high accuracy. We identified serum-derived differentially methylated probes (DMP, n=3288) that distinguished PT according to their function (functioning and nonfunctioning). When overlapped with an independent cohort, these DMP also distinguished PT tissue according to their functional status. **Conclusion:** Our results showed the feasibility to identify PT-specific methylation signatures by profiling the methylome of serum cfDNA from patients with PT. These signatures distinguished PT from other CNS tumors and according to their subtypes. These results underpin the potential role of methylation profile and liquid biopsy as a noninvasive approach to assess clinically relevant molecular features. Potentially, tumor-specific serum-derived methylation signature may be used as a diagnostic, prognostic and surveillance tool as well to identify actionable molecular markers in patients with PT.

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID II

Reverse T_3 in Patients with Hypothyroidism, Helpful or a Waste of Time?

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SUN-410

Background: The normal thyroid secretes T_4 (an inactive precursor), T_3 (the active hormone) and reverse T_3,