MON-270

Background: The diagnosis of diabetes insipidus (DI) relies on indirect measurement of serum and urine sodium and osmolality. Since the diagnosis can only be made when an inappropriately dilute urine is paired with a significantly concentrated serum, the process is tedious for the clinician and uncomfortable for the patient. Copeptin is the C-terminal portion of the anti-diuretic hormone (ADH) prohormone which correlates with the less stable ADH, therefore providing a direct measurement of posterior pituitary response to hyperosmolar stress. (1,2)

Aim: This study aims to assess the diagnostic accuracy of copeptin in patients with central DI compared with subjects who underwent pituitary surgery without developing DI.

Methods: Serum samples from subjects with central DI, control subjects post pituitary surgery with no DI (NDI) and control subjects with SIADH were collected and analysed on the BRAHMS KRYPTOR copeptin assay. Groups were compared using unpaired T-test and Levene’s test for equal variance.

Results: 56 samples from 22 subjects (13 females, 9 males, mean age 53.9 ± 15.5 y.o.) were analysed. Two subjects had resolved DI (rDI) after copeptin analysis and were successfully weaned off DDAVP and reclassified as NDI. Of the DI subjects, 1 had acute and 5 had chronic DI. Copeptin was lower in DI compared to NDI group (p = 0.013), while serum sodium, osmolality, urine osmolality were similar. Copeptin did not differentiate between the SIADH and NDI groups. After exclusion of NDI samples with serum sodium ≤ 140 mmol/L, the area under the curve was 0.97 (95% CI 0.9 to 1.0), a copeptin cut-off of 2.9 pmol/L predicts DI with a sensitivity of 92% and a specificity of 90%.

Conclusion: Copeptin concentration of < 3.0 pmol/L concurrently with serum sodium concentration of > 140mmol/L predicted central DI when using post pituitary surgery subjects without DI as controls.

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Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Progesterone Receptor Membrane Component 1 Suppresses Lipid Accumulation and Lipotoxicity in Animal Model of Diabetic Cardiomyopathy (DCM).

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MON-672

Progesterone receptor membrane component 1 protects heart from lipotoxicity and suppresses diabetic cardiomyopathy (DCM).

Abstract: Diabetic cardiomyopathy (DCM) is one of the complications triggered by type II diabetes (T2D) (1). When free fatty acids (FFA) are abundant in insulin resistant pre-diabetic patients because of adipose lipolysis, FFA tends to move toward heart (2). Lipid accumulation can cause cardiac lipotoxicity and exacerbate DCM (3). In previous

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SAT-450

T3 inhibits thyrotropin-releasing hormone (TRH) synthesis in hypothalamic paraventricular nucleus (PVN). Although T3 receptor (TR) β2 is known to mediate the negative regulation of prepro-TRH gene, its molecular mechanism remains unknown. Our previous studies on the T3-dependent negative regulation of the thyrotropin β subunit (TSHβ) gene indicate the tethering mechanism, where T3-bound TRβ2 interferes with the function of the transcription factor GATA2, which is essential for TSHβ expression. Interestingly, the transcription factor Sim1, a determinant of PVN differentiation in hypothalamus, is reported to induce the expressions of TRβ2 and GATA2. Indeed, our immunohistochemistry revealed the expression of GATA2 in the TRH neuron of the rat PVN. According to the experimental report with transgenic mice, the DNA sequence from nt. -547 to nt. +84 is sufficient for the expression of the prepro-TRH gene in PVN. Using the CAT reporter gene harboring this region, we found that this promoter is activated by GATA2 approximately 6-fold in CV1 cells. The deletion and mutation analyses identified a functional GATA-responsive element (GATA-RE) between nt. -357 and nt. -352. When TRβ2 was co-expressed, T3 reduced GATA2-dependent promoter activity to approximately 30%. T3-dependent repression was maintained after the mutation of the putative negative T3 responsive element (site4).

Although the melanocortin 4 receptor signaling is known to stimulate the prepro-TRH promoter via protein kinase A pathway in the PVN, inhibition by T3 was dominant over the 8-bromo-cAMP-induced activation. We observed the in vivo recognition of GATA-RE by GATA2 using chromatin immunoprecipitation assay with CA77 cells, which express endogenous TRH. The electrophoretic mobility shift assay also demonstrated that GATA2 bound to oligonucleotide containing the GATA-RE. These results suggest that, as in the case of the TSHβ gene, GATA2 transactivates the prepro-TRH gene and that T3-bound TRβ2 interferes with its function, resulting in the negative regulation of this gene.

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