

assays for digoxin (DLM). In 2018, we characterized a new candidate for the DLM, Ionotropin. It is a phosphocholine (PC) ester of a novel steroid with 23 carbon atoms. As Ionotropin shares structural features (a) with spironolactone (both have spiral lactones in the E-ring) and (b) with digoxin (E-ring lactone and 3 α -5 β configuration), we have proposed that Ionotropin may function as a potassium (K⁺) sparing diuretic. This suggestion is supported by the observations that [1] patients who cannot make Ionotropin (7-dehydrosterol reductase deficiency) are K⁺ wasting and [2] breast cyst fluids with high K⁺ levels also have high Ionotropin levels.

Hypothesis: During the 3rd trimester, fetal requirements for K⁺ reach a maximum, fetal blood pressure increases and aldosterone signaling is blocked. This blockage leads to fetal sodium (Na⁺) wasting and is essential for formation of amniotic fluid. These events are consistent with a normal role for an unknown endogenous K⁺ sparing hormone and would be the basis for a modest elevation of maternal DLM during the 3rd trimester. Our hypothesis is that if any of the functions were inadequate, then the fetal-placental unit would synthesize excess PC-spiral steroids; the woman would exhibit symptoms of K⁺ sparing hormone excess (hypertension and proteinuria) and would be diagnosed with pre-eclampsia.

Experimental Results: We have just reported a pilot study associating elevated PC esters of spiral steroids in women with pre-eclampsia. In brief, 12 of 19 women had elevated levels of at least one of the PC steroids (Z-score > 2) when compared to the levels in 20 pregnant women matched for gestational age and fetal sex. There are two basic mechanisms for this dichotomy: (a) there may be episodic secretion with of a DLM with a short half-life or (b) there may be two different underlying biochemical causes. In prior studies, there has been no indication of episodic secretion of DLM similar to that observed with glucocorticoids, Ionotropin or other PC spiral steroids.

Discussion: There are two basic types of K⁺ sparing diuretics. Type A: Spironolactone functions by regulating the NaK-ATPase. Type B: Triamterene functions by blocking synthesis of epithelial Na⁺ channels. Thus, Type A would have high levels of spiral steroids and Type B would have low levels of spiral steroids. Type A patients would be expected to have higher risk of long-term consequences when compared to the Type B patients.

Conclusion: The recognition of the division of pre-eclampsia into two separate diseases might be the key observation for developing Type-specific diagnosis and therapy. For example, a Type A patient might benefit from a low salt diet but that diet would not be expected to benefit a patient with Type B disease.

Adipose Tissue, Appetite, and Obesity

RARE CAUSES AND CONDITIONS OF OBESITY: PRADER WILLI SYNDROME, LIPODYSTROPHY

Iron Parameters in Patients with Partial Lipodystrophy and Impact of Metreleptin Therapy

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Introduction Intriguing rodent studies and epidemiological data suggest that iron metabolism and adipocytokines crosstalk to regulate glucose metabolism and fuel storage. Iron parameters have not been previously studied in patients with lipodystrophy whereas increased iron stores have been associated with type 2 diabetes. In this study, we sought to investigate the status of iron parameters in patients with partial lipodystrophy (PL) and to interrogate whether the adipocyte hormone leptin can modulate iron metabolism. **Methods** Serum samples of 19 patients with PL (age: 42, IQR: 34-57, M/F: 3/16) were used from an open-label study previously performed at the University of Michigan evaluating the efficacy of metreleptin in non-alcoholic steatohepatitis (NCT01679197) to measure ferritin, hepcidin, iron, and transferrin soluble receptor levels. High-sensitivity C-reactive protein (hs-CRP) levels were also determined as broader changes in inflammatory pathways may potentially impact circulating ferritin levels. Results were integrated into an existing database of metabolic parameters. Data are presented as median, IQR. **Results** At baseline, ferritin levels were positively correlated with fasting glucose ($r = 0.533$; $p = 0.023$) and HbA1c ($r = 0.510$; $p = 0.031$). During the 6 months of therapy period, HbA1c (9.2%, 7.3-10.3 vs. month-3: 8.6%, 7.7-9.6; $p = 0.099$; and month-6: 8.5%, 6.8-9.5; $p = 0.264$), triglyceride levels (346 mg/dL, 240-1771 vs. month-3: 346 mg/dl, 237-479; $p = 0.047$; and month-6: 295 mg/dl, 207-495; $p = 0.091$), and hepatic fat (12.7%, 9.8-20.6 vs. month-6: 8.9%, 7.0-11.0; $p = 0.031$) decreased. Reductions were observed in serum ferritin after metreleptin treatment (83.23 ng/mL, 76.43-178.97 vs. month-3: 73.79 ng/ml, 68.30-78.59; $p = 0.007$; and month-6: 61.03 ng/mL, 46.45-157.74; $p = 0.004$). There was a tendency for hepcidin and iron to be decreased, but this did not reach statistical significance. On the other hand, there were notable reductions in hs-CRP levels at 6 months compared to baseline (2.94 mg/L, 1.30-4.80 vs. 1.6 mg/L, 1.00-6.30; $p = 0.012$). Baseline leptin level was inversely correlated with percent reduction in hs-CRP at month-6 ($r = -0.685$; $p = 0.001$). Also, modest correlations were observed between changes in serum iron and triglycerides ($r = 0.491$, $p = 0.033$) and hepatic fat ($r = 0.412$, $p = 0.079$). **Conclusions** We observed a significant relationship between ferritin and glucose control in a group of patients with PL. Metreleptin therapy was associated with improvements in triglycerides and hepatic fat and there were also significant decreases in ferritin and hs-CRP levels. These results raise the possibility that metreleptin therapy influences iron metabolism. However, whether the decrease in ferritin indicates a decrease in iron stores or is mediated by an effect on inflammation remains unknown.

Thyroid

THYROID DISORDERS CASE REPORTS II

Atypical Presentation of Recurrent Cardiac Tamponade Following Pericardial Window in the Setting of Uncontrolled Hypothyroidism

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