traumatic brain injuries (multiple falls and a ski accident) complained of years of insatiable hunger leading to hyperphagia and over 20 pounds weight gain. With tremendous will-power, she avoided additional weight gain by adopting a strict meal-plan and increasing her water intake (10–12 liters a day) to relieve her hunger. She sipped so much water, that her sodium remained 123 - 133 mmol/L (ref: 135–146) with dilute urine. Initial tests revealed: IGF-1 315 ng/ml (52–328), FSH 77.5 mIU/ml (23–116.3), LH 24.3 mIU/ml (14.2–52.3), prolactin 17.1 ng.ml (10–54.7), estradiol 17 (<31), TSH 1.09mIU/ml (0.45–4.5), FT4 1.0 ng/dl(0.8–1.8), all within the normal limit for her age. Semaglutide 0.25mg/week was started and increased to 0.5mg/week. Within the first six months of treatment, she experienced 22 pounds of weight loss, hunger relief, less water sipping behavior, and more enjoyment of food. Her sodium rose to 137 mmol/L. **Case 2:** A 40-year-old female, s/p craniectomy and aneurysm clipping due to intracranial hemorrhage complicated by an ischemic stroke developed sudden, documented, 45-pound weight gain over thirteen months despite aggressive lifestyle modification attempts. Initial labs revealed: TSH 1.33 mIU/ml (0.45–4.5), FT4 1.22 ng/dl (0.8–1.8), midnight salivary cortisol 0.03 mcg/dl (<0.09), ruling out hypothyroidism and Cushing syndrome. Liraglutide 1.8mg/day was started and has resulted to date in 26 pounds (11.8% of maximum weight) by 9 months with an associated decrease in subjective hunger. **Conclusion:** Hyperphagia can be seen in brain injury, in response to some medications, and some genetic conditions, like Prader-Willi. The exact mechanisms are not clear am may be multifactorial. In the case of brain injury, proposed mechanisms include insatiable hunger due to ventromedial hypothalamic or brain stem dysfunction, or disinhibition and poor impulse control due to frontal lobe injury. GLP-1's may act on the causal mechanism for increased hunger, or it may result in clinical improvement through a parallel pathway. More studies are warranted to investigate the application of GLP-1's to hyperphagia.

Adipose Tissue, Appetite, and Obesity

NOVEL INSIGHTS FROM THE CLINIC INTO THE DEVELOPMENT OF METABOLIC DISEASE: CASE REPORTS

Association of NOS3 and TNF Genetic Polymorphisms With the Predisposition to Elevated Cholesterol, Retrospective Study

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Background: Endothelial nitric oxide synthetase (eNOS) encoded by NOS3 gene has an important role in modulating vascular endothelial function. TNFα gene is responsible for coding TNFα protein that plays a significant role in regulating body inflammation and lipid metabolism. Many studies reported an association between NOS3 and TNFα genetic polymorphisms and elevated total cholesterol (TC) level, low-density lipoprotein (LDL), triglyceride (TG). In this study, we investigated the association of NOS3 (G>T) rs1799983 and TNFα -308G>A rs1800629 genetic polymorphisms with TC level.

Methods: A random sample of 250 subjects with an elevated TC level (defined by TC level ≥ 200mg/dL) compared with 500 healthy subjects. Sample obtained from Palestinian adults who consented to genetic and biochemical testing. Subjects genotyped for NOS3 SNP (G > T) rs1799983 and TNFα -308G>A rs1800629 using ARMS PCR. TC level was obtained for all subjects. Logistic regression analysis adjusted for age and body mass index (BMI) was performed to test for association between NOS3 and TNFα genetic polymorphisms and TC level.

Results: NOS3 T allele was significantly more frequent in the elevated TC group, (odds ratio = 1.8, 95% CI =1.02–3.18) with likelihood ratio statistically significant (P = 0.004). Homozygous TNFα variant was more frequent in the elevated cholesterol group without a statistically significant association (P = 0.54).

Discussion: Many studies reported an association between NOS3 and TNFα genetic polymorphisms and elevated TC levels. Homozygous NOS3 variant was associated with a 1.8-fold increase in the risk of high TC after adjustment for age and BMI. TNFα polymorphism didn't show a statistically

significant association with having elevated TC levels. With the increasing popularity and availability of genetic testing, NOS3 can serve as a screening tool to identify people with high risk for elevated TC. Further studies are required to understand the exact role of NOS3 genetic polymorphism in cholesterol metabolism.

Conclusion: NOS3 genetic polymorphism had a statistically significant relationship with TC levels. These results support the association between NOS3 polymorphism and elevated TC.

Adipose Tissue, Appetite, and Obesity

NOVEL INSIGHTS FROM THE CLINIC INTO THE DEVELOPMENT OF METABOLIC DISEASE: CASE REPORTS

Effects of Glucagon-Like-Peptide-1 Analogue Treatment in Genetic Obesity

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Introduction: Obesity is highly prevalent, comes with serious health burden and is difficult to treat. In a minority, there is a genetic cause for the obesity. In these patients, therapy-resistant obesity is often observed despite intensive lifestyle treatment. Moreover, it is still unclear whether bariatric surgery is less successful in genetic obesity. Liraglutide is a Glucagon-Like-Peptide-1 (GLP-1) receptor agonist or GLP-1 analogue, showing positive effects on metabolic parameters, satiety and weight loss