MON-LB87

Introduction: Recombinant human TSH (rhTSH) is commonly used to prepare patients with differentiated thyroid cancer (DTC) for radioiodine (I-131) ablation after total thyroidectomy (TT). In adults, rhTSH is associated with equivalent oncologic efficacy and improved health-related quality of life in comparison to thyroid hormone withdrawal (THW). In this study, we aimed to measure disease-free survival after rhTSH stimulation vs. THW in pediatric patients with DTC. Methods: A prospective database was analyzed for pediatric patients under the age of 21 with DTC who underwent TT and I-131 ablation with rhTSH preparation at a single tertiary institution from 2012 through 2018. These patients were compared against historical controls prepared with THW. Tumor stage, I-131 treatment details, disease-free survival, structural recurrence, biochemical recurrence (defined as serum Tg > 2 at one year), and postoperative serum TSH, thyroglobulin (Tg) and Tg antibody levels were recorded. The log-rank test was used to compare groups, and time to recurrence was estimated by Kaplan-Meier analysis. Results: Seventeen patients who received rhTSH (mean age, 16.6±3.2 [SD] years) were compared to 28 historical controls prepared with THW. No differences were observed in RAI dose (mean 2.3±0.7 mCi/kg), tumor stage, or follow-up time (median [IQR] 2.6 [1.1-3.1] years) between groups. The THW group exhibited a nonsignificantly greater recurrence rate (14 [50%], 7 with biochemical recurrence and 7 with structural recurrence) than the rhTSH group (three [18%], 2 with biochemical recurrence and 1 with structural recurrence, p=0.2). A trend toward improved disease-free survival was identified in those treated with rhTSH compared to THW. Conclusion: In this cohort of pediatric patients with DTC, we observed a trend toward improved disease-free survival among those prepared with rhTSH compared to historical controls prepared with THW. Long-term follow up is needed to better characterize outcomes associated with rhTSH stimulation prior to I-131 ablation in the pediatric population.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Pulmonary Embolism in the Setting of Diabetic Ketoacidosis. an Under-Recognized Complication.
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MON-LB127

The relation between Diabetic Ketoacidosis and Venous Thromboembolism is important to appreciate for early recognition and management. 90 year old female with Type 2 DM was brought to the ER after a syncopal episode. Family reported the patient to be lethargic with a decreased appetite for one week. On arrival, patient had a blood pressure of 84/44 mmHg. Oxygen saturation was 89% at room air and improved to 93% on supplemental O2. Patient was afebrile with a respiratory rate of 16 and heart rate 89/minute. On exam, she was dehydrated with decreased skin turgor, dry oral mucosa. Labs revealed blood glucose of 621 mg/dL, Bicarbonate 16 mmol/L, B-Hydroxybutyrate 5.00 mmol/L, Anion Gap 21, pH of 7.26 on ABG. Urinalysis was suggestive of a urinary tract infection. After initiation of IV antibiotics and insulin, she was transferred to the intensive care unit. In the ICU, her blood pressure failed to improve with fluid resuscitation, ultimately requiring vasopressors. Due to hypotension with hypoxia, CT Chest was performed which revealed extensive bilateral PE. She was started on IV heparin infusion. Pro-Brain Natriuretic Peptide was elevated at 4,716 pg/mL. Echocardiogram confirmed right heart strain with severely dilated right ventricle, positive McConnell’s sign, systolic and diastolic septal flattening and an estimated RSP 67mmHg consistent with moderately severe pulmonary hypertension. Tissue plasminogen activator was recommended however given the patient’s age and functional status; family decided against systemic thrombolysis. Duplex ultrasound of her lower extremities also showed bilateral acute deep venous thrombosis. She was continued on intravenous anticoagulation and eventually was able to come off vasopressors. As the patient’s blood glucose levels improved and her anion gap closed, she was transitioned to basal/bolus insulin and transferred to the general medical floor. She was started on Apixaban and discharged home per family’s request after her code status was changed to DNR-Comfort Care Arrest.

Pulmonary embolism is a serious venous thromboembolic event that is rarely reported in association with DKA. Proposed mechanisms include some of the same mechanisms implicated in arterial thrombosis, namely abnormalities in coagulation factors, increased platelet aggregation, impaired fibrinolysis and endothelial injury due to hyperglycemia. Also, severe dehydration associated with DKA may contribute by virtue of increased red blood cell rigidity and increased blood viscosity establishing DKA as an underlying cause or contributing factor of pulmonary thromboembolism.1 Langevin C et al Presumed paradoxical embolus in a patient with diabetic ketoacidosis Int J Gen Med 2015;8:297–301 2015 Sep 18
2 Scordi Bello I et al Fatal Pulmonary Thromboembolism in Patients with Diabetic Ketoacidosis A Seven-Case Series and Review of the Literature Acad Forensic Pathol 2016;6(2):198–205

Bone and Mineral Metabolism

PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS

Design of the PaTH Forward Phase 2 Trial of TransCon PTH, a Long-Acting PTH, in Patients With Hypoparathyroidism
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hypoparathyroidism (HP) is caused by a deficiency in parathyroid hormone (PTH), which leads to hypocalcemia and hyperphosphatemia. Standard of care (SoC), i.e., large doses of calcium (Ca) and active vitamin D, worsens hypercalciuria and increases the serum Ca (sCa) x serum phosphate (sP) product. Studies have shown that continuous subcutaneous infusion of PTH(1-34) normalizes sCa, sP, serum magnesium, urine Ca (uCa) and bone turnover better than SoC or once- or twice-daily injections of PTH in HP patients. TransCon PTH, an investigational long-acting prodrug of PTH (1-34) transiently bound to an inert carrier via a linker, is under development as a potential once-daily replacement therapy for HP. Under physiological conditions, linker auto-cleavage occurs, releasing active PTH at a controlled rate with ~60 hour half-life. Phase 1 trial results demonstrated that once-daily TransCon PTH provided a flat, infusion like profile within the normal range of PTH 24 hours per day, increasing sCa while controlling uCa and decreasing sP, with no evidence of bone anabolic activity.

Phase 2 Design:
PaTH Forward is a global phase 2 trial evaluating the safety, tolerability, and efficacy of TransCon PTH in adult subjects with HP. Patients with HP treated with SoC were randomized at sites worldwide to daily TransCon PTH 15, 18 or 21 µg PTH(1-34) or daily blinded placebo via pen-injector for 4 weeks. The primary composite endpoint requires 1) normal albumin-adjusted sCa, and 2) normal Fractional Excretion of Ca (or ≥50% decrease from baseline), and 3) not taking active D, and 4) taking ≤1000 mg/d of Ca. After four weeks, all subjects enter an open-label extension period with the opportunity to receive TransCon PTH individually optimized to doses of 6 to 30 µg daily to evaluate long-term safety and efficacy. Other endpoints include the impact of treatment on patient experience, CaXp product, bone turnover markers, and bone mass by DXA and TBS to confirm the lack of anabolic effect.

Preliminary Results:
Approximately 55 subjects are expected to be randomized and dosed. Preliminary diary data on the initial 8 subjects completing 4 weeks of follow-up in the extension trial shows that all have discontinued SoC. Additional information will be presented at ENDO 2020. The Phase 2 trial is designed to inform the starting dose for a global pivotal phase 3 trial and evaluate TransCon PTH as a “true” PTH replacement therapy.

Diabetes Mellitus and Glucose Metabolism
METABOLIC INTERACTIONS IN DIABETES
In Experimental Peripheral Arterial Disease MIR29a Modulation Improves Perfusion Recovery and Muscle Function to a Greater Extent Than ADAM12 Augmentation in Mice With Type 2 Diabetes
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SUN-LB127
Diabetes Mellitus (DM) is a major risk factor for developing peripheral arterial disease (PAD) and individuals with DM have worse PAD outcomes but the molecular mechanisms involved are poorly understood. We previously identified a disintegrin and metalloproteinase gene 12 (ADAM12) as a key genetic modifier of post-ischemic perfusion recovery in experimental PAD that it is regulated by miR29a through direct interaction. In ischemic hind limbs non-diabetic mice, miR29a expression is downregulated and allows ADAM12 upregulation. However, in ischemic hind limbs of type 2