In conclusion, these new targets for glycemic control in GD led to less insulinization of the pregnant women, no differences between weight at birth of the newborns, a different distribution of the weight of birth according to Fenton curves (more newborns classified as appropriate for gestational age and less classified as small or large) and a reduction of neonatal morbidities.

Ref: (1) Almeida et al. Revista Portuguesa de Diabetes. 2017; 12 (1): 24-38

Adrenal

ADRENAL CASE REPORTS II

Repeat Unstimulated AVS with Aid of Plasma Metanephrines Identifies Unilateral Primary Aldosteronism When Initial AVS and Metomidate PET-CT Fails To.

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SUN-175

Repeat unstimulated AVS with aid of plasma metanephrines identifies unilateral primary aldosteronism when initial AVS and metomidate PET-CT fails to.

Introduction

Adrenal venous sampling (AVS) is the reference test for identifying unilateral primary aldosteronism (PA). However, in patients with corticol co-secreting adrenal nodules, elevated cortisol levels may affect the interpretation of aldosterone-cortisol (AC) ratios. ACTH-stimulation may further confound results. In such patients, the use of plasma metanephrines instead of cortisol as a correcting factor may be helpful.

Case Summary

A 54 year old lady presented with 8 years of hypertension and hypokalaemia (nadir 2.2mmol/L) while on amlodipine 10mg and valsartan 80mg daily. PA was confirmed by a post-saline infusion aldosterone 1075pmol/L. CT identified a 2.4cm right lipid rich adrenal adenoma. Serum cortisol post 1mg overnight dexa-suppression test was unsuppressed at 63nmol/L.

First AVS was done sequentially under ACTH stimulation and suggested lateralization to the right, with lateralization ratio (LR) 3.4. However, this was <4, and there were bilaterally low AC ratios compared to peripheral vein. Metomidate PET-CT scan then showed increased uptake over the nodule, but lower than the contralateral gland. In view of these findings, repeat AVS was done simultaneously without ACTH stimulation. Given the possibility of a co-secreting adenoma, plasma metanephrines were also measured. Second AVS showed right-sided lateralization (LR 11.8). Using metanephrines as a correction factor, the LR was even more elevated at 22.3, with contralateral suppression.

She underwent right adrenalectomy and was cured of hypertension and hypokalaemia at 6 months post surgery. Aldosterone renin ratio has normalized: aldosterone <4ng/dL, plasma renin activity 0.6ng/ml/hr.

Clinical Lessons

While ACTH stimulation helps to improve success rates of cannulation by increasing cortisol gradients, most studies show that it lowers LR. Furthermore, this would be concerning in patients with cortisol co-secreting adenomas. In this case, repeat AVS without ACTH demonstrated improved lateralization to the right. The use of metanephrine as a correcting factor appears to be a better indicator of right sided disease. However, while plasma metanephrines have been shown to be useful to indicate correct catheter placement, it has not been adopted as a correction factor for dilution yet. Finally, in addition to affecting AVS results, cortisol-cosecreting tumors may also affect 11C-Metomidate PET-CT imaging.

Conclusion

In patients with suspected cortisol co-secreting adenomas, unstimulated AVS and use of plasma metanephrines may help to identify unilateral PA even when conventional AVS and metomidate scans fail to. Further studies on using metanephrines as a correcting factor for lateralisation would be helpful.

Cardiovascular Endocrinology

PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE

Involvement of Sarco/Endoplasmic Reticulum Ca-ATPase (SERCA) in Membrane Progesterone Receptor Alpha (PAQR7)-Mediated Progesterone Induction of Vascular Smooth Muscle Relaxation

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SUN-559

Progesterone (P4) exerts multiple beneficial effects on the human cardiovascular system through its actions on vascular endothelial cells and also by acting directly on vascular smooth muscle cells (VSMCs). Membrane progesterone receptor alpha (mPRalpha) has been shown to mediate the rapid P4-induction of human VSMC relaxation through activation of MAPK, Akt/Pi3k and RhoA/ROCK signaling pathways and the resulting reduction of calcium influx through calcium channels. In this study, we demonstrate that treatment of cultured human VSMCs with P4 for 1-2 hours increases both the mRNA and protein expression of sarco/endoplasmic reticulum Ca-ATPase (SERCA), the major transporter of calcium from the cytosol into the sarcoplasmic reticulum (SR) during muscle relaxation. Knockdown of mPRalpha with siRNA completely blocked this stimulatory effect of P4 as well as that of OD 02-0, a mPR selective agonist, on SERCA protein expression. In contrast, expression levels of phospholamban (PLB), a SR protein that reversibly inhibits SERCA were downregulated by this P4 treatment, and mRNA expression of a channel that releases calcium from the SR, inositol triphosphate receptor (IP3R), was unaltered after treatment with P4. Moreover, treatments with P4 and OD 02-0, but not with R5020, a nuclear PR agonist, increased PLB phosphorylation, which would result in disinhibition of SERCA function. P4 and OD 02-0 significantly increased calcium levels...
in the SR detected with Fluo-5N, a specific SR calcium indicator, and caused VSMC relaxation. These effects were blocked by cyclopiazonic acid (CPA, a SERCA inhibitor), suggesting that SERCA plays a critical role in P4 induction of VSMC relaxation. Similarly, the effects of P4 and OD 02-0 on relaxation of umbilical artery rings measured with a myograph were significantly attenuated by CPA, which confirms the critical role of SERCA in the rapid action of P4 and 02-0 on vascular muscle relaxation. P4 has previously been shown to activate MAPK and Akt signaling pathways to induce VSMC relaxation. The P4- and OD 02-0-induced increases in calcium in the SR were blocked by MAPK and Akt/P3k signaling inhibitors, AZD6244 and wortmannin. Taken together, these results suggest that the direct, rapid effects of P4 on relaxation of VSMCs through mPRα involves regulation of the expression and function of the SR proteins SERCA and PLB through MAPK and Akt signaling pathways.

Diabetes Mellitus and Glucose Metabolism
DIABETES COMPLICATIONS II
Dulaglutide Commonly Known as Trulicity; An Anti-Diabetic Medication Causing Small Bowel Obstruction
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Bone and Mineral Metabolism
PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS
The Role of β-arrestin2 in Bone Catabolic Response to Hyperparathyroidism In Vivo
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MON-681
Introduction Small bowel obstruction is a common and life threatening surgical emergency. The general causes are intra and extra-intestinal mechanical obstruction, such as from post-operative adhesions, malignancy, hernias, Crohn’s disease, and volvulus. Less frequently neurologic, metabolic, and medications interfere with intestinal motility and lead to obstructive features. Here, we present a rare case of small intestinal obstruction caused by the anti-diabetic glucagon-like peptide 1 (GLP-1) agonist, Dulaglutide (Trulicity). Case A 52-year-old male with Diabetes Mellitus, presented with two weeks of severe nausea and vomiting, accompanied by four days of diffused abdominal pain. CT scan of the abdomen showed multiple mildly distended dilated loops of the proximal jejunum. The results lead to suspect the presence of fecal stasis with an apparent transition zone of a normal caliber bowel. This is strongly indicative of partial or evolving small bowel obstruction. The patient was treated with conservative management of bowel rest and NG tube per the surgery on board. However, patient deteriorated too quickly and the partial bowel obstruction lead to full obstruction and eventually taken for an emergent surgery. With careful investigation to identify underlying causes of small bowel obstruction revealed no mechanical, structural, or metabolic explanation. However, a review of patient’s medication list disclosed a daily consumption of Dulaglutide (Trulicity). The medication was started 3 weeks prior to admission. He started developing partial bowel obstruction symptoms within one week of starting the medications. Unfortunately, surgeon ended up performing a partial resection a small bowel due to severe ischemia. Patient improved clinically in four to five days and was discharged home with an alternative anti-diabetic medications. He follows up with us in the clinic and has no signs of bowel obstructions with the other anti-diabetic medications. Discussion: Dulaglutide (Trulicity) is associated with small bowel obstruction. The side effect is more common in males and in patients who are using the medication for less than one month. A total of 8 cases were reported in 2017 with majority of them requiring surgical intervention for the small bowel obstruction. In our patient, it also required a surgical intervention and was life threatening. Unfortunately, the actual mechanism Trulicity causing the small bowel obstruction is unknown; however the moderate side effect of Trulicity is constipation. In this case, our patient was not constipated. He had normal bowel movements on a regular basis. Also, he never had any history of abdominal surgeries which can cause adhesion and lead to small bowel obstruction. All the other caused of small bowel obstructions had been ruled out and finally concluded Trulicity was the culprit of this unfortunate case.

SAT-392
Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by elevated parathyroid hormone (PTH) levels and hypercalcemia caused by the overactive parathyroid glands, resulting in negative impacts on the skeleton including bone loss and increased bone fragility1. PTH binds and activates parathyroid hormone type 1 receptor (PTH1R) which primary couples to Gαs, leading to reduced signal termination and receptor internalization2. Previously, we have seen anabolic effects of hyperparathyroidism (cPTH) on trabecular bone in mice overexpressing Gαs3. We hypothesized that increased Gα protein levels in osteoblasts outcompete β-arr binding to PTH1R, leading to reduced signal termination and increased bone formation. To test this hypothesis, we are testing if the deletion of β-arr2 will also result in an anabolic response to cPTH in this study. The response of β-arr2 knockout (KO) mice to cPTH have yet to be documented. The hypothesis of this study is that β-arr2 KO mice treated with cPTH will exhibit anabolic effects on the trabecular bone. Nine-week-old wild-type (WT) C57BL/6 and β-arr2 KO mice were treated for 14 days with either rPTH1-34 (80ng/g/day) or saline (PBS) using micro-osmotic pumps to simulate hyperparathyroidism. There are 8 groups (n=10 per group) including both sexes, 2 genotypes (WT and KO), and 2 treatment groups (PTH and PBS). Two 30 mg/kg doses of 0.6% calcein green were administered subcutaneously to