

New Therapies in Diabetes Management

Chair: *Andrea Daly*

Pre-clinical Development of a Biomaterial-based Microparticle Vaccine for Prevention of Type 1 Diabetes

Jamal Lewis

Current paradigms for diabetes treatment are inadequate at responding accurately to short-term homeostatic imbalances and cannot prevent chronic diabetes-related complications. Predictably, novel approaches to re-establish homeostatic conditions in patients afflicted by Type 1 diabetes mellitus (T1DM) are now under intense investigation. Notably, the *ex vivo* generation and injection of tolerance-promoting dendritic cells (DCs) is being pursued in clinical trials for applications in T1DM. While instructive, exogenously-conditioned cellular-based vaccines for T1DM treatment have numerous limitations. Dissemination of exogenously delivered DCs is inefficient, and treatment involves a personalized medicine approach involving the generation of cultured DCs, which amounts to high production and treatment costs that prohibit widespread application. To circumvent these limitations, we are developing a multifunctional, synthetic microparticle-encapsulating vaccine that can be easily administered with simultaneous and continuous delivery using controlled-release materials (poly lactide-co-glycolide) for the *in vivo* conditioning of DCs and amelioration of T1DM. Moreover, these microparticle-based vaccines are engineered to target DCs, and provide both intracellular and extracellular delivery of immunomodulatory agents as well as antigen. Our ultimate goal is to develop a microparticle-based (MP) vaccine capable of reversal of T1DM in humans. To date, we have demonstrated (i) the ability of targeted microparticles to improve *in vivo* DC uptake and translocation, (ii) the effect of our non-targeted MP vaccine on bone marrow-derived DC phenotype and downstream effects on allogenic T-cells and (iii) the efficacy of the non-targeted MP vaccine to prevent diabetes onset in non-obese diabetic (NOD) mice. Current investigative work is focussed on exposing the cellular mechanisms behind the observed prevention in NOD mice, reversal of T1DM and evaluating the safety of this biomaterial formulation in rodent models (at OneVax, LLC) with an eye on full translation of this technology.

Optimizing Nutrition in Diabetes Care: Spotlight on Selected Micronutrients

Ava V Simpson

Diabetes is estimated to affect 7.9% of persons in the 15–74-year age range, with an additional 2.8% having impaired fasting glucose in the Jamaican population. This increase in prevalence is likely to increase the number of persons with kidney disease, as compelling evidence supports a direct relationship. Intensive management of blood glucose levels is predicted to be beneficial to patients in the early stages of kidney disease, and several nutrients are involved in achieving this control. Damage to the kidneys may be delayed or prevented by carefully managing the nutritional status of these patients. The heavy burden of these diseases on our healthcare budget and the debilitating effects force healthcare providers to examine different ways to help with managing these illnesses. Could we be overlooking the importance of medical nutrition therapy and getting the nutrient balance right? This review will explore five micronutrients where deficiencies may play a role in advancing the progression of kidney disease in patients with diabetes.

CARES SYMPOSIUM

Hypothyroidism and Hyperthyroidism in the Pregnant Patient

Michael Boyne

Thyroid disorders are common in nonpregnant women of childbearing age, and they can emerge during pregnancy. The diagnosis can be missed because of nonspecific symptoms. About 2–3% of women are hypothyroid and ~0.2% are hyperthyroid during pregnancy. Lack of treatment is associated with an increased risk of miscarriage, placental abruption, hypertensive disorders, heart failure and growth restriction. Appropriate management can improve these outcomes. High-risk women (*eg* women with a prior autoimmune disease, or a family history of thyroid disease) should be screened for thyroid disease. Hypothyroid

women should be followed closely in pregnancy as their levothyroxine requirements may increase by as much as 50%, and it is important to keep their serum thyroid-stimulating hormone level less than 2.5 mIU/L. Hyperthyroidism is mostly due to Graves' disease and should be preferentially treated with anti-thyroid medications. The goal is to maintain the serum free thyroxine level in the high-normal range so as to limit fetal exposure to the effects of the thionamides. Postpartum thyroiditis can also occur and may present as hyperthyroidism or hypothyroidism. Most women with thyroid disease can safely breastfeed even while on treatment.

Case 1: Neonatal Hypoglycaemia

Emma Greenway

We shall discuss the case of a four-day old male infant with hypoglycaemia – the approach to the acute evaluation and management, differentials to consider and long-term outcomes of recurrent hypoglycaemia.

Case 2: Pituitary and Pregnancy

Natalie Smith

Prolactinomas are the most common hormone-secreting pituitary tumours. They are usually the result of neoplastic transformation of anterior pituitary lactotrophs, resulting in excess synthesis and secretion of prolactin (pathologic hyperprolactinaemia). A prolactinoma can be classified as

a microprolactinoma (< 10 mm diameter) or a macroprolactinoma (> 10 mm diameter).

Menstrual irregularity and infertility are typical clinical features of hyperprolactinaemia in women during childbearing years. While hyperprolactinaemia can be responsible for a third of all cases of female infertility, with adequate management, the majority of such women are expected to achieve successful pregnancies.

Management of prolactinomas during the peripartum and postnatal period can present some unique challenges. Growth of these pituitary tumours (particularly macroadenomas) during pregnancy has been described and is often a concern for the managing physician. Bromocriptine, a dopamine agonist, has been the mainstay of treatment for some time; however, newer agents such as cabergoline and quinagolide have shown better tolerance than bromocriptine, with similar or greater efficacy. Surgery is reserved for dopamine agonist resistance or intolerance to dopamine agonist and few special circumstances, and is generally avoided during pregnancy. Deciding on the appropriate time to resume treatment of hyperprolactinaemia in the postpartum period or whether to resume dopamine agonists or other forms of treatment may also be difficult to determine.

This case study will review some issues in the management of hyperprolactinaemia during the perinatal and postpartum periods.