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Congenital adrenal hyperplasia: Bariatric surgery as a path to parenthood

Allison Landa
DeFiore and Company, USA

Congenital adrenal hyperplasia sufferers are at heightened risk for obesity, which in turn can preclude a successful pregnancy and childbirth. When Allison Landa was diagnosed with CAH at the age of 30, she was told she would likely never be able to give birth. However, following bariatric surgery in 2014, Landa's substantial weight loss gave way to an unplanned pregnancy that resulted in the birth of her son, Baz. Landa offers a personal perspective as both patient and advocate for fellow CAH sufferers. Bariatric surgery may be considered a successful gateway to parenthood with regards to CAH sufferers previously considered infertile.

allison@allisonlanda.com

Stem cell therapy of polycystic ovary syndrome

Ayman Al-Hendy
University of Illinois at Chicago, USA

Polycystic Ovary Syndrome (PCOS) is the most common metabolic disorder affecting 5-20% of reproductive age women. The clinical manifestations of PCOS include hyperandrogenism and ovulatory dysfunction. In addition the majority of affected women exhibit reduced postprandial thermogenesis. Brown Adipose Tissue (BAT) is important in the dissipation of energy in the form of heat and changes in BAT could explain the reduction of postprandial thermogenesis found in women with PCOS. Most PCOS treatment approaches aim to reverse such metabolic challenges with lifestyle (exercise and diet) modifications or the use insulin-sensitizing medicines but with limited success. Several recent studies emphasized the importance of ovarian chronic inflammation in driving higher androgen production by ovarian theca cells which in turn drives most of the metabolic PCOS-related aberrations. Human bone marrow Mesenchymal Stem Cells (hMSCs) possesses robust anti-inflammatory properties. We hypothesized that ovarian injection of hMSCs will effectively inhibit chronic inflammation, reduce ovarian androgen output and improve metabolic abnormalities in PCOS patients. In this pre-clinical study, we investigated the effect of ovarian injection of hMSCs on serum androgen levels, on the activation of BAT and on the induction of browning in the white fat of a PCOS mouse model. We anticipated that that the engraftment of hMSCs in the ovaries of this PCOS mouse model will reduce hyperandrogenemia and promote energy expenditure through white fat tissue browning leading to correction of metabolic dysfunctions. To test our hypothesis, we established a drug-induced PCOS animal model by implanting Letrozole (LET) pellet subcutaneously in the neck area (5 mg/pellet, 90 days release) of C57BL6 female mice at the pre-sexual age of 3 weeks. Mice were randomly assigned to one of three groups: (1) Placebo control (untreated), (2) LET group (untreated) and (3) LET group (treated with hMSCs). The mice weight-gain induced by LET treatment was monitored weekly. Human hMSCs were collected from a healthy female donor by flow cytometry using standard surface markers. After 4 weeks of Letrozole treatment, hMSCs (250,000 cells/ovary) were injected into both ovaries using limited laparotomy. The control mice received sham surgery and were injected with PBS. To study the impact of hMSCs on the metabolic criteria of PCOS, we evaluated energy expenditure in hMSCs treated versus control animals by monitoring metabolic parameters such as O2 volume, CO2 volume, Respiratory Exchange Ratio (RER), heat production, food intake and motility. Furthermore, gonadal fat tissues collected after 8 weeks of treatment were examined by H&E staining and immune-histochemistry for UCP-1 (Uncoupled Protein-1) and PD-L1 markers for brown fat. The analysis of fat mRNA markers (UCP-1, Prdm-16 and PGC-1a) was done by Q-RT-PCR. Our results show that the engraftment of hMSCs for 8 weeks following PCOS induction with letrozole (LTZ), was able to significantly reduce the circulating levels of androgen in treated PCOS mice (<20 ng/dl) versus PCOS-untreated group (28.1±4.3, $P<0.05$). Furthermore, indirect calorimetry in open-circuit Oxymax chambers demonstrated significantly increased heat production in PCOS mice engrafted with hMSCs compared to PCOS placebo-treated control group ($P<0.05$). Additionally, the expression of UCP-1 was significantly increased in the white gonadal fat from hMSCs-treated group versus placebo control both at mRNA and protein levels ($P<0.005$). We conclude that stem cell therapy might potentially be a novel tool for effective treatment of PCOS women.

aalhendy@UIC.EDU