World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:11, No:02, 2017

Serum Concentration of the CCL7 Chemokine in Diabetic Pregnant Women during Pregnancy until the Postpartum Period

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Abstract : Introduction: Women with previous gestational diabetes mellitus (GDM) were significantly more likely to have urinary incontinence (UI) and pelvic floor muscle dysfunction compared to non-diabetic women two years after a cesarean section. Additional results demonstrated that induced diabetes causes detrimental effects on pregnant rat urethral muscle. These results indicate the need for exploration of the mechanistic role of a recovery factor in female UI. Chemokine ligand 7 (CCL7) was significantly over expressed in rat serum, urethral and vaginal tissues immediately following induction of stress UI in a rat model simulating birth trauma. CCL7 over expression has shown potency for stimulating targeted stem cell migration and provide a translational link (clinical measurement) which further provide opportunities for treatment. The aim of this study was to investigate the CCL7 levels profile in diabetic pregnant women with urinary incontinence during pregnancy over the first year postpartum. Methods: This study was conducted in the Perinatal Diabetes Research Center of the Botucatu Medical School/UNESP, and was approved by the Research Ethics Committee of the Institution (CAAE: 20639813.0.0000.5411). The diagnosis of GDM was established between 24th and 28th gestational weeks, by the 75 g-OGTT test according to ADA's criteria. Urinary incontinence was defined according to the International Continence Society and the CCL7 levels was measured by ELISA (R&D Systems, Catalog Number DCC700). Two hundred twelve women were classified into four study groups: normoglycemic continent (NC), normoglycemic incontinent (NI), diabetic continent (DC) and diabetic incontinent (DI). They were evaluated at six-time-points: 12-18, 24-28 and 34-38 gestational weeks, 24-48 hours, 6 weeks and 6-12 months postpartum. Results: At 12-18 weeks, it was possible to consider only two groups, continent and incontinent, because at this early gestational period has not yet been the diagnosis of GDM. The group with GDM and UI (DI group) showed lower levels of CCL7 in all time points during pregnancy and postpartum, compared to normoglycemic groups (NC and NI), indicating that these women have not recovered from child birth induced UI during the 6-12 months postpartum compared to their controls, and that the progression of UI and/or lack of recovery throughout the first postpartum year can be related with lower levels of CCL7. Instead, serum CCL7 was significantly increased in the NC group. Taken together, these findings of overexpression of CCL7 in the NC group and decreased levels in the DI group, could confirm that diabetes delays the recovery from child birth induced UI, and that CCL7 could potentially be used as a serum marker of injury. Conclusion: This study demonstrates lower levels of CCL7 in the DI group during pregnancy and postpartum and suggests that the progression of UI in diabetic women and/or lack of recovery throughout the first postpartum year can be related with low levels of CCL7. This provides a translational potential where CCL7 measurement could be used as a surrogate for injury after delivery. Successful controlled CCL7 mediated stem cell homing to the lower urinary tract could one day introduce the potential for non-operative treatment or prevention of stress urinary incontinence.

Keywords : CCL7, gestational diabetes, pregnancy, urinary incontinence
Conference Title : ICI 2017 : International Conference on Immunology
Conference Location : London, United Kingdom
Conference Dates : February 16-17, 2017