

Infliximab effect on immune response in endometriosis model rats sprague dawley

Abstract ID : 2487

Submitted by : syarief thaufik hidayat the 2017-01-30 16:35:03

Category : SEUD CONGRESS 2

Typology : Communication orale / Oral communication

Status : Validated

Authorisation to disclose : Yes/Oui

Infliximab Effect On Immune Response In Endometriosis Model Rats Sprague Dawley

Abstract

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INTRODUCTION: The tumor necrosis factor α (TNF- α) is a key cytokine in a variety of inflammatory processes, and it is likely that it has a role in the pathogenesis of endometriosis. Numerous researchers have shown that concentrations of TNF- α are elevated in the peritoneal fluid of patients with endometriosis and that its levels correlate with disease stage. The anti-inflammatory effects of TNF- α blocking by monoclonal antibodies (i.e., infliximab) have been demonstrated in vivo, in animal models and in humans. The clinical effectiveness of TNF- α blocking has been demonstrated in inflammatory conditions, but not in endometriosis. This association between endometriosis and increased cytokines opens the possibility for new proposals for clinical treatment, particularly using anti-cytokine therapies.

OBJECTIVES: To evaluate the effect of anti-TNF- α in the treatment of surgically induced endometrial implants in the peritoneum of rats.

MATERIAL AND METHODS: Experimental parallel group - pre-test and post-test design comparing anti-TNF- α drugs with placebo for pelvic peritoneal endometriosis.

Endometriosis was induced in 10 female Sprague Dawley rat, and randomized to Infliximab group (n=5) and placebo group. The peritoneal fluid and blood sample was collected from each group at the 15th day of peritoneal implantation, aliquoted and store at -80oC until as assayed. The Infliximab group received slow intraperitoneally injection of Infliximab (= 5mg/weight kg in human which diluted in 10 ml / weight kg rat of water for injection). The placebo group received slow intraperitoneally injection of 10 ml/weight kg in rat of water for injection. The procedure repeated every estrous cycle (at proestrus phase) for 5 times respectively. The second peritoneal fluid and blood sample was collected from each group, aliquoted and store at -80oC until assayed. The macrophage counting from isolated and cultured macrophage and immunocytochemical CD-68 staining confirmed the presence of abundant macrophages in peritoneal fluid.

TNF- α levels, IL-1 β levels, VEGF levels and sICAM-1 levels in aliquots of each peritoneal fluid and plasma sample were determined by an ELISA Quantikine R&D system kits following the manufacturer's protocols. The peritoneal fluid and plasma sample was evaluated in a duplicate assay. The detection limit were 5 pg/mL for TNF- α and IL-1 β , 2 pg/mL for sICAM-1 and 8.4 pg/mL for VEGF. Statistical analysis was performed using SPSS 17.0 with false discovery rate threshold of $p < 0.05$.

RESULTS : The activated macrophages was significantly reduced in Sprague Dawley rat endometriosis models treated with Infliximab compared to placebo. The peritoneal fluid level of TNF- α , IL-1 β , VEGF and sICAM-1 was significantly reduced in Sprague Dawley rat endometriosis models treated with Infliximab compared to placebo. The plasma levels of IL-1 β and sICAM-1 was significantly reduced in Sprague Dawley rat endometriosis models treated with Infliximab compared to placebo, but there was no significantly differences in plasma level of TNF- α and VEGF.

CONCLUSION : Inhibition of TNF- α Infliximab could represent a novel principle for the treatment of endometriosis.

Keywords : endometriosis , infliximab

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