ABSTRACT

Cytokine Profiles Could a Priori Predict Response to SSRIs in Medication-Naïve Patients with Major Depressive Disorder

Amani Bashar Ahmed[1,2], Rahmeh Y. Natsheh[1], Oday M. Abushalbaq [1,3] , Hussain Y. Khdour [1,4], Mahmud A. Sehwail [1], Mohmmad M. Herzallah [1,4].

[1] *Palestinian Neuroscience Initiative, Al-Quds University, Jerusalem, Palestine.*

[2] *Faculty of Medicine, Al-Quds University, Jerusalem, Palestine.*

[3] *Department of Biological Sciences, Rutgers University, Newark, NJ, USA.*

[4] *Center for Molecular and Behavioral Neuroscience, Rutgers University, Newark, NJ, USA.*

Background: Major depressive disorder (MDD) is one of the most prevalent psychiatric disorders in Palestine. It manifests as symptoms of depressed mood and loss of interest in daily life activities. The "Cytokine Hypothesis of Depression" argues that MDD results from an imbalance between pro- and anti-inflammatory cytokines. Only 30% of patients with MDD respond to treatment with SSRI antidepressants.

Objectives: In this study, we investigate pro- and inflammatory cytokines as potential a priori predictors of response to SSRIs in patients with MDD.

Methods: We recruited eight medication-naïve patients with MDD and eight matched healthy controls. Patients with MDD were tested twice, at diagnosis, and 4-6 weeks after receiving SSRIs.
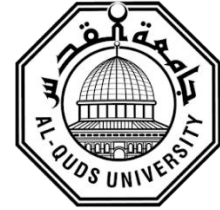
After treatment, patients with MDD were classified into responders (N=5) and non- responders (N=3). Healthy subjects were also tested twice with a 4–6-week gap. We collected peripheral blood samples from all participants both at test and retest. Using ELISA, plasma was assessed for IL-2, IL-6, IL-10, IFN-γ, and MIF levels.

Results: Compared to non-responders, responders showed higher medication-naïve levels of pro-inflammatory IFN-γ, MIF, and IL-2 and anti-inflammatory IL-10. However, the medication- naïve concentration of IL-6 was lower in responders compared to non-responders. After 4-6 weeks of receiving SSRIs, MIF levels were decreased in responders but not in non responders; IL-6 decreased in both groups; IFN-γ and IL-2 levels did not change in either of the groups. Cytokine levels in healthy controls did not show differences between test and retest. ROC analysis of the medication-naïve cytokine levels revealed that IFN-γ and IL-2 could identify responders, while IL-6 has better specificity for non-responders.

Conclusion: Our preliminary results indicate a clear difference in pathophysiology of SSRI-responsive and non-responsive MDD in the form of medication-naïve cytokine profiles. Potentially, cytokine diagnostic kits could be designed to evaluate patients with MDD before treatment to assess their potential for response.

Research Keywords: Cytokines, major depressive disorder, selective serotonin reuptake inhibitors, medication-naïve patients, ELISA.