

**Letter to Editor.**  
**Depression and Cytokines – a different perspective**

Cemil Celik, Taner Oznur, Barbaros Ozdemir

Department of Psychiatry, Gulhane Medical Faculty, Ankara, Turkey

In a recent issue of *Psychiatria Polska*, we read with great interest the article by Wilkowska [1] entitled “Increased plasma pro-inflammatory cytokine concentrations after myocardial infarction and the presence of depression during next 6-months” in which the authors discussed the role of inflammatory reaction and autoimmune processes present in myocardial infarction (MI) and depression. They found increased levels of pro-inflammatory cytokines IL-17a, IL-6, TNF- $\alpha$  and IL-12p70 in the entire group of patients after MI compared to age-matched controls. This study is well designed, however, we would like to make some comments with respect to the authors’ interpretations of pro-inflammatory cytokines levels.

Pro-inflammatory cytokines are mostly secreted by macrophages and T-cells to stimulate immune response against inflammatory agents. Otherwise, some of them, such as IL-6, are myokines secreted by muscle cells as a result of muscle contraction. Serum IL-6 level is elevated both in response to muscle contraction and inflammation [2]. The intensity and duration of muscle contraction determines the magnitude of increase in plasma pro-inflammatory cytokines such as IL-6 in the exercise [3]. Although IL-6 acts as a pro-inflammatory cytokine when secreted by monocytes or macrophages [3], it creates an anti-inflammatory response in the vigorous exercise [2]. In the exercise, IL-6 causes the elevation in other pro-inflammatory cytokines levels and thus acts as an anti-inflammatory myokine. In their paper, the authors reported that levels of pro-inflammatory cytokines are elevated in patients. For these reasons physical activity degree, profession, serum sampling time and hospitalization of participants should be considered carefully. We suggest that these factors should be determined and stated in the paper.

Most women begin to experience emotional changes before and during menstruation period which is known as premenstrual syndrome (PMS) [4]. Symptoms of PMS include affective, physical, cognitive, and behavioral changes. Affective symptoms include irritability (a cardinal symptom), mood swings, anxiety and depression [5, 6]. These psychological symptoms not only occur in PMS, but also can be seen during and after menopause. Women may experience a wide range of feelings, from anxiety

and discomfort to release and relief, upon menopause [7, 8]. Consequently, levels of stress and depression shows fluctuations during menstrual cycle and menopausal period. In this study, the authors did not state menstrual status of female individuals which could cause falsely lower or higher stress and depression levels.

Therefore we think that it is highly important to examine these issues for reliable interpretation of the results. In conclusion, clarifying these concerns will certainly provide a clearer picture when interpreting levels of pro-inflammatory cytokines among participants.

## References

1. Wilkowska A, Pikuła M, Rynkiewicz A, Wdowczyk-Szulc J, Trzonkowski P, Landowski J. *Increased plasma pro-inflammatory cytokine concentrations after myocardial infarction and the presence of depression during next 6-months*. Psychiatr. Pol. 2015; 49(3): 455–464.
2. Petersen AM, Pedersen BK. *The anti-inflammatory effect of exercise*. J. Appl. Physiol. 2005; 98: 1154–1162.
3. Beiter T, Hoene M, Prenzler F, Mooren FC, Steinacker JM, Weigert C et al. *Exercise, skeletal muscle and inflammation: ARE-binding proteins as key regulators in inflammatory and adaptive networks*. Exerc. Immunol. Rev. 2015; 21: 42–57.
4. Yonkers KA, O'Brien PM, Eriksson E. *Premenstrual syndrome*. Lancet 2008; 371(9619): 1200–1210.
5. Rapkin AJ, Mikacich JA. *Premenstrual dysphoric disorder and severe premenstrual syndrome in adolescents*. Paediatr. Drugs 2013; 15(3): 191–202.
6. Gao X, Sun P, Qiao M, Wei S, Xue L, Zhang H. *Shu-Yu capsule, a Traditional Chinese Medicine formulation, attenuates premenstrual syndrome depression induced by chronic stress constraint*. Mol. Med. Rep. 2014; 10(6): 2942–2948.
7. Bromberger JT, Matthews KA, Schott LL, Brockwell S, Avis NE, Kravitz HM et al. *Depressive symptoms during the menopausal transition: the Study of Women's Health Across the Nation (SWAN)*. J. Affect. Disord. 2007; 103(1–3): 267–272.
8. Cohen LS, Soares CN, Vitonis AF, Otto MW, Harlow BL. *Risk for new onset of depression during the menopausal transition: the Harvard study of moods and cycles*. Arch. Gen. Psychiatry 2006; 63: 385–390.