Research Article

Determination of Interleukin- 13 and Interleukin 27 on Schizophrenic serums

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Abstract: There is increasing evidence suggesting that cytokines abnormalities are involved in the pathogenesis of schizophrenic disorders. The aim of this study was to evaluate the serum levels of interleukin-27 (IL-27) and interleukin-13 (IL-13) in patients with schizophrenia compare to healthy control subjects. In present study the serum IL-27 and IL-13 levels of 38 schizophrenic patients and 32 age and sex matched healthy control subjects using a sandwich ELISA assay was measured. It was found that IL-13 serum level were increased significantly in schizophrenic patients compare to healthy control group (4.32 ± 0.94 vs 2.04 ± 0.17, $p < 0.01$) and a significant increase in female patients (5.2 ± 5.1) and the healthy females ($2.05 \pm .21$) ($p < 0.01$) has found. There was also reported a significant increased in IL-13 on male patients (3.63 ± 2.51) and healthy males ($2.03 \pm .144$) with ($p < 0.01$). The findings also have been shown that there is a significant difference between the serum level of interleukin-27 of the patient (171) and healthy) group (231) ($p < 0.05$). By this study, it can conclude that there is a significant decrease between IL-27 in male schizophrenic patients compare to healthy controls. However a significant increase was found between IL-13 schizophrenic patients when compare with healthy control. A non-significant difference was reported in male and female in IL-13 schizophrenic patients.
Keywords: schizophrenic patients, interleukin-27, interleukin-1

INTRODUCTION

Schizophrenia is a chronic and the most complex mental disease with a prevalence of approximately 1% of the world population. The disease incidence in men begins in late adolescence or any time in life [1].

It seems that cytokines abnormalities are involved in the pathogenesis of schizophrenia [2]. It has been hypothesized that schizophrenia may be accompanied by an activation of inflammatory response system, which could be related to the pathophysiology of the illness [3] .

Immunological mechanisms have been proposed to be the underlying pathological factor for the disorder of the neurotransmitter systems. It has been shown that cytokines such as IL-1, IL-2, and IL-6 influence the dopaminergic and serotonergic neurotransmission [4].

Most cytokines which have been studied in schizophrenia more focus on cytokines such as interferon (IFN), interleukin-2, interleukin-6 and tumor necrosis factor (TNF) [5]. Increased levels of pro inflammatory cytokines such as IL-1, IL-6, IL-18 and tumor necrosis factor (TNF) have been reported in schizophrenic patients. Several studies have shown that serum levels of IL-12 and IFN- alpha decreased and IL-4 and IL-10 sera levels are increased in schizophrenia [6].

But serum levels of inflammatory markers IL-27 and IL-13 in schizophrenic subjects have not been reported yet. IL-13 was first described in 1989 as the P600, a protein expressed by activated TH2 in mouse cells and was cloned in 1993[7-8].

A cytokine gene cluster on chromosome 5 (5q31), encoded IL-13 and also including the gene coding for IL-3, IL-4, IL-5, IL-9 [9]. The effects of IL-13 induces through two receptors consisting of IL-13R alpha 1 and IL-13R alpha2 on the cell surface which activate intracellular STAT6 and ERK 1/2 MAPK pathway [10]. IL-27 is produced predominantly by macrophages and by endothelial cells [11]. The main role of IL-27 is induction of Th1-cell proliferation and inhibits Th-17cell differentiation by STAT1. IL-27 plays a role in the immune pathology of various diseases due to uncontrolled inflammatory response [12]. In addition, IL-27 may prevent excessive inflammation in autoimmune diseases [13].

The aim of this study was to examine the serum levels of interleukin-27 (IL-27) and interleukin-13 (IL-13) in patients with schizophrenia compare to healthy control subjects.

MATERIALS AND METHODS

This study was carried out in 2013 on Behravan psychiatric hospital for women and Iran psychiatric hospital for men in the city of Yasuj which was under supervision of state welfare organization of Yasuj, Iran. Control samples were carried out in Blood

Transfusion Organization Yasuj. In the present study 38 schizophrenic patients (21 men and 17 women) and 32 healthy control subjects (20 men and 12 women) was registered. All patients were diagnosed in the basis of the structured clinical interview (DSM-IV) criteria for schizophrenia (American psychiatric association). Studied in patients under the supervision of a psychiatrist and schizophrenia symptoms in a questionnaire for each patient were recorded.

All members of the unit kg weight scale (Weighing scales made in Germany, capable of measuring up to 150 kg, with a precision of /01Kg) and height of the stature in meters Standing was measured in units of cm. BMI was calculated. Blood samples were collected in vacationer EDTA tubes between 6 to 10 a.m. and serums were isolated by centrifugation at 2500 rpm in 10 minutes. Serum samples were immediately frozen and stored at -80 °C until assay. The serum concentrations of IL-27 and IL-13 were determined using sandwich ELISA kits (Ebioscience, USA), in accordance with the manufacturer's instructions.Sensitivity to IL-27 and IL-13 9.5pg/ml and

0.7pg/ml respectively. An automated micro plate reader (Biotek , USA) set at 405 nm was used to measure the optical density. All laboratory procedures were done at the Laboratory Biochemistry from the University of Sistan and Baluchestan .

Statistics analysis

All results are expressed as mean ± standard deviation (SD). Statistical analysis was carried out by nonparametric tests Mann-Whitney and Wilcoxon .For analysis of data using Statistical Package for Social Sciences (SPSS) software version 13. Statistical significance was set at $P < 0.05$.

RESULTS

The participants of the present study were 38 patients, 21 males (55.3%) and 17 females (44.7%), who suffered from schizophrenia, and the control group were 32 healthy participants, 20 males (62.5%) and 12 females (35.5%). The characteristics of the participants (age, smoking, and body mass index) are presented in Table 1.

Table 1. Participant demographic in schizophrenic patients and healthy control

Parameters	Patient(n=38)		Control (n=32)		Sig.
	Female (17)	**Male (21)**	**Female(12)**	**Male(20)**	
Age	42.06±9.397	41.10±10.73	35.17±11.296	33.85±9.78	0.041
BMI	25.2±5.4	24.19±3.41	24.5±2.35	26.45±3.1	0.261
No Smoking	13	9	12	12	
Age class	20-30 : 8 30-40: 7 40-50: 4 50-65: 1	20-30 : 4 30-40: 3 40-50: 4 50-65: 1	20-30 : 4 30-40: 4 40-50: 7 50-65: 6	20-30 : 1 30-40: 5 40-50: 7 50-65: 4	0.653

The age range of the participants is 21 to 62. The statistical results show that there is a significant difference between the experimental and control groups in the age range (p<.05). The obtained results of the table indicate that the rate of smoking among patients is more than control group and the non-parametric test of Mann-Whitney has shown that there is no significant difference between the patient participants and the control ones.

The body mass index has not a significant difference among the groups. Although the proportion of the body mass index in men of the control group is more than the rest of the groups, but a significant difference between the healthy and patient participants was found. The age classification of the participants showed that most people are within the age range of 40-

50. The patients within the age range of 40-50 have the most frequency, while the healthy people within the age range of 20-30 have prominent ratio. Generally, there was no significant difference between the healthy and patient groups from in age parameter.

A significant increase in interleukin 13 level in patient group in male and female was reported compare to control groups (p<0.01) (Figure 1).

The findings also show that there is a significant increase in the serum level of interleukin-27 of the female patient (227) compare to healthy (180) groups (p<.001).However , a significant decrease in serum level of interleukin-27 in patient males was seen (115) compare to control (282) (P,0.001)(Figure 2 and Table 2) .

Table 2. Concentration of IL-13 and IL-27 on Schizophrenic patients and healthy control

Parameters	Patient(n=38)		Control (n=32)	
	Female (17)	Male (21)	Female(12)	Male(20)
IL-13 (pg/ml)	5.2±5.1	3.63±2.51	2.05±.21	2.03±.144
IL-27 (pg/ml)	227.45±250.25	115.88±54.3	180.73±56.91	282.8±263.42
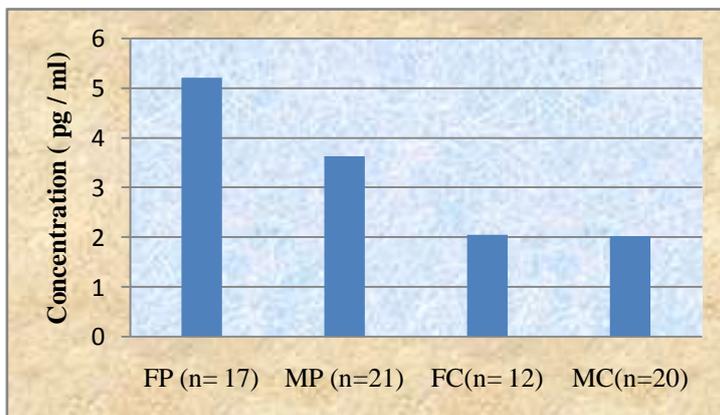
Figure 1 Concentration of IL-13 in schizophrenic patients and healthy control
FP= Female patient, MP = Male patient, FC= Female Control, MC= male Control
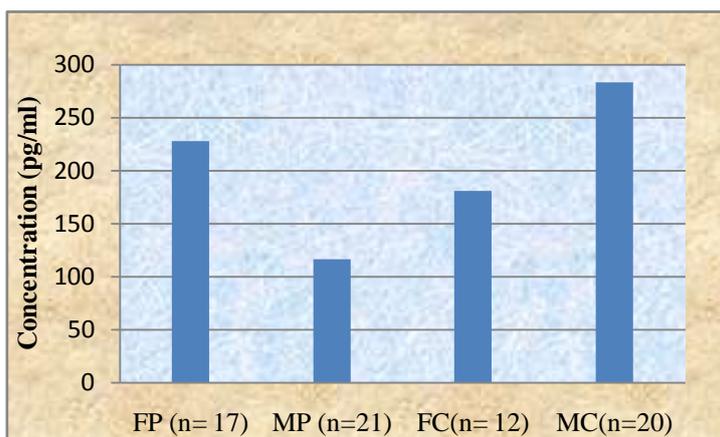

Figure 2 .Concentration of IL-27 in schizophrenic patients and healthy control
FP= Female patient, MP = Male patient, FC= Female Control, MC= male Control.

DISCUSSION

The main finding of present study was increased plasma levels of IL-13 in Schizophrenic patients in comparison with the healthy control group. IL-13 could control brain inflammation by inducing the death of LPS activated microglia in culture medium.

In vivo IL-13 expressed in microglia might contribute to the degeneration of microglia, in inflammation disease. Some study demonstrated a significant increase in the levels of IL-13 in the brain cortex was reported. IL-13 is expressed exclusively in activated microglia [14-15]. Several studies have shown that there is an imbalance between T helper 1 (Th1) cytokines and T helper 2 (Th2) cytokines in patients with schizophrenia.

IL-13 is a pleiotropic cytokine which could be essential in the regulation of the inflammatory and immune processes. It inhibits inflammatory cytokine synthesis and associate with IL-2 in regulating interferon-gamma production [14].Increase in IL-13 in present work in schizophrenia patient may be due to inflammatory cytokine synthesis.
It is hypothesized that IL-13 may play a role in schizophrenia by suppressing overactive Th1 system. IL-13 acts as a drug for the treatment of neurodegenerative diseases which associate with activation microglia. In present study decrease of IL-13 serum concentration in schizophrenia confirmed of suppressing overactive Th1 system. IL-27 plays key

roles in the innate and adaptive immune systems. It may be produce proliferation on naïve T cells.

L-27 is member of IL-12 cytokine family and it has property anti-inflammatory and pro inflammatory. IL-27 is required for Initial differentiation of TH0 to TH1 cells and begins producing IL-12. The immunosuppressive effects of IL-27 depend on prevention of the development of Th17 cells and induction of IL-10 production.

IL-27 may prevent excessive inflammation in autoimmune diseases [13].In present study decrease of IL-27 was reported in male patient who confirmed of inflammatory role of IL-27.According to some study IL27 significantly suppresses the inflammatory response induced by TH 1 cells, and decreased production IFN-γ [16].

Conclusion

The results reveal that the level of interleukin-13 in males and females and in interleukin-27 only female's patient is higher than the control.However in the level on interleukin-27 in males patients was low than control.

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