Mahdi Taher Sahib AL-Hadad et al /J. Pharm. Sci. & Res. Vol. 11(2), 2019, 402-405

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Effect of chronic toxoplasmosis on levels of some neurotransmitters (Dopamine, Adrenaline, and Noradrenaline) in human serum

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Abstract

Latent *Toxoplasma gondii* infection has been considered asymptomatic for many years, but results of recent studies have associated it with various neuropsychiatric problems, including Alzheimer's, Schizophrenia, Parkinson, Depression, Epilepsy. These chronic disease occur as a result of changes in the levels of hormones and neurotransmitters caused by parasitic infection in the host brain. A total of 45 blood samples of donors (33 men and 12 women) from AL-Najaf province, Iraq were tested for IgG anti-Toxoplasma antibodies by Elisa method and the results as follows 17 seropositive(12 male and 5 female) and 28 seronegative (21 male and 7 female). All samples were subjected to Elisa test to determine levels of three of neurotransmitters (Dopamine, Adrenaline, and Noradrenaline) in serum. The result show significantly (t test) higher serum levels of Adrenaline in patients with latent toxoplasmosis compared to controls ($p<0.05$). Both Dopamine and Noradrenaline hormones serum levels in patients showed a slight increase compared with control group, but statistically insignificant ($p>0.05$). Our findings suggest that chronic infection by *T. gondii* causes a change in some neurotransmitters and may be explained by the occurrence of certain neurological diseases in the incidence of latent toxoplasmosis.

Keywords: Latent toxoplasmosis, Neurotransmitters , Dopamine.

INTRODUCTION

Toxoplasma gondii is a protozoan parasite that is main or final host is cat but intermediate host is mammals and birds[1]. It is estimated that 30–50% of the world suffers from toxoplasmosis, the incidence of toxoplasma infection in younger peoples has decreased from 20 – 25% to 10% in the United states of American and several countries in Europa during the past fifteen years, at same time, the incidence increased from about 5% – more than 10% in some Asian countries [2]. In Iraq the seroprevalence of toxoplasmosis vary according to age, gender and region, they were ranging from 19-45% [3-7], *T. gondii* infection causes various neurological disease in host and alters neurological signaling pathways[8]. *Toxoplasma gondii* as chronic infection producing distinctive neuropsychiatric diseases and alterations in its intermediate hosts, (humans and rodents) [9]. Miscellaneous human diseases that correlated with chronic *T. gondii* infection, including Alzheimer's [10,11] schizophrenia [12-14] Parkinson[15-18] depression[19] epilepsy[20]. Its induce behavioral changes in human [21-23] and rodents [24], also a significant association between *T. gondii* infection and suicide attempts was reported[25]. Many studies correlated these symptoms with alterations in hormones concentrations in host, that include sex hormones[21,26-29]and neurotransmitters hormones[23,30]. One factor that pay to the vague changes and neurological disorder in human and animal is modulate of neurotransmitters levels during chronic toxoplasmosis such as dopamine [31]. In this paper we attempt to emphasis role of chronic toxoplasmosis in changes of three neurotransmitters levels in human serum.

MATERIALS AND METHODS

Forty-five samples (33 men and 12 women) of AL-Najaf province, Iraq aged 52.2±16.5 years were taken to investigate chronic toxoplasmosis using the Elisa method(IgG anti-Toxoplasma antibodies)(Calbiotech Inc.,). five ml of blood were withdrawn from each person. The serum was isolated in eppendorffs tubes and kept at -80°C until use. Serum concentrations of Three neurotransmitters (Dopamine, Adrenaline, and Noradrenaline) were measured using Elisa method (Elabscience biotechnology Co., Ltd) and the results were expressed at mean ± standard deviation for both the total experiment and the control group. Statistical analysis was used with a single-tailed t- test and a 5% probability level using Microsoft Excel 2010.

RESULTS

Table 1 shows the population characteristics of the samples under study. The levels of neurotransmitters (Dopamine, Adrenaline, and Noradrenaline) were monitored. The levels of hormones in case or patients group (seropositive IgG *Toxoplasma* antibodies persons) and in control group (seronegative IgG *Toxoplasma* antibodies persons) in human serum were presented in table (2). The result show significantly higher serum levels of Adrenaline in patients with latent toxoplasmosis compared to controls ($p<0.05$).Both Dopamine and Noradrenaline hormones serum levels in patients showed a slight increase compared with control group, but statistically insignificant ($p>0.05$).

Table 1: Demographic data in current study.

Categories	+ve IgG Toxoplasma	-ve IgG Toxoplasma	total
Samples	17(37.8%)	28(62.2)	45
Male	12	21	33
Female	5	7	12
Age (year mean ±sd)	52.3±17.5	52.2±16.2	52.2±16.5

Table 2: Dopamine, Adrenaline, and Noradrenaline hormones levels in seropositive IgG *Toxoplasma* antibodies and control group.

Hormones	+ve IgG (test) Mean ± SD	-ve IgG (control) Mean ± SD	P value (t test)
Dopamine (pg/ml)	1567.709 ± 273.340	1462.116 ± 204.858	0.0736
Adrenaline (pg/ml)	265.8141 ± 189.790	169.2037 ± 101.314	0.0329
Noradrenaline (ng/ml)	3.878 ± 2.605	3.451 ± 1.956	0.282

DISCUSSION

Many may be unaware of the importance of toxoplasmosis and many consider it a secondary and transient disease, but recent studies have indicated that most psychiatric and neurological diseases affecting people are caused by the parasitic infection. The toxoplasma parasite is one of the most important parasites that manipulate its host, which contributes to the successful completion of its life cycle [32,33]. Studies have shown that mice infected with toxoplasmosis become not afraid of predators, cats, but rather become attracted to it [24,34]. *Toxoplasma* parasites manipulate more than thousand genes in a body of infected host[35, 36], ones have genes that encode the enzymes that make neurotransmitters most important gene that encodes a tyrosine hydroxylase enzyme which involved in the synthesis of dopamine [31]. Numerous studies have documented cases of chronic neurological diseases resulting from chronic exposure to toxoplasmosis, schizophrenia[12-14], dementia[10,11], epilepsy[20], depression[19] and Parkinson[15-18], and many cases of people trying to commit suicide [19,25] and people who commit traffic accidents[37]. *Toxoplasma gondii* also induce behavioral changes in man and animals, The one of important mechanism that confirmed by study of Prandovszky et al. [32] which provide interpretation for psychobehavioral changes in toxoplasmosis-infected humans is direct correlation between the number of infected dopaminergic cells in brain with *T. gondii* and the amount of dopamine released. The current study showed that there was no significant difference in the concentrations of dopamine and adrenaline between the group of chronic toxoplasma parasites and the control group, although there was a slight increase in concentration in the infected group from control group. The level of serum adrenaline in latent *T. gondii* infected human in the this trials was significantly higher than the control human. The changes recorded during this study in some neurotransmitters may result in neurons infection or as a result of an immune response to the infection. Melzer et al. [38] identified the presence of toxoplasma cysts in neurons solely and astrocytes cells are free from infection in brain of mice during chronic infection by using FITC-Dolichos biflorans dye with a confocal fluorescence microscope. Carbel et al. [39] pointed out that neurons are the main target cell of chronic *T. gondii* CNS infection and that the presence of bradyzoite stage limited in neurons during brain infection. There are several studies have shown that an increase in the concentration of dopamine in the brain of rodents, such as mice[30,32], also other studies have linked the increase in the concentration of brain dopamine with some neurological diseases such as schizophrenia in human. The both study of Juanah et al. [12] and Çelik et al. [40] were showed that there was a relationship between chronic infection with *Toxoplasma* and schizophrenia, these relationship was interpreted at the time by increasing the concentration of dopamine. In a previous study, the concentration of norepinephrine was found to be lower in the chronic infection of toxoplasmosis in rats, and this change in norepinephrine level did not give clear indications of the pathological condition of the rats [34]. In Toxoplasma-infected mice Ihara et al. [41] results demonstrated decrease in levels of norepinephrine in the cortex and amygdala. Zhou et al. [42] shown difference metabolites connected to changes in metabolism of some lipids and amino acid (phenylalanine, tyrosine, alanine, tryptophan, aspartate, and glutamate) during acute and chronic stage of *T. gondii* infection in mice.

In this study, a significant increase in the concentration of adrenaline was recorded in people with positive IgG antibodies to toxoplasma compared with negative antibodies (control group). One of the functions of adrenalin is to help induce the release of the prolactin hormone [43] . Dzitko et al. [44] explained that women who have a high concentration of prolactin have greater resistance to infection by *Toxoplasma gondii*. The adrenalin hormone is mainly extracted from the adrenal gland in the human body (80%) and the rest is produced within brain cells (20%)[45], Therefore, our interpretation of the increase in this concentration of people with chronic parasitic infection may have a significant impact of the parasite on the endocrine glands, including the adrenal gland. The adrenal gland is strongly affected by the occurrence of toxoplasmosis in marine mammals (*Stenella longirostris*) as it detects the tachyzoites and bradyzotes of the adrenal cortex[46].Other studies have shown that there are significant variations in levels of steroid hormones produced by the endocrine glands such as testosterone, prolactin and progesterone with chronic Toxoplasmosis[26-29]. Abdoli[47] explained that there are several factors that have been affected in the production of testosterone in toxoplasmosis infection and its consequences, which cause behavioural changes these factors are the strain of parasite, the severity of the infection and the specific variations of the host. In conclusion, changes in catecholamine levels in the incidence of toxoplasmosis gave an explanation of the mechanism by which nervous system diseases are linked to infection.

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