

## The Effects of Antidepressants on the Lipids of the Blood Serum of the Men

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### ABSTRACT

All of us have experienced some sorts of sadness and grief for long or short terms of our lives, especially due to the loss of our life partner, family members, or the loss of our job, etc.; and all of us had been able to encounter such incidents of the life. However, when such sadness is too deep and long, it can lead to the depression disorder. In any given time, at least 15 to 20 percent of the adult society would show the symptoms and effects of the severe depression, and millions of people would be under the treatment of their depression worldwide. Fortunately, the treatment of this disorder is considerably easy due to the wide and new scientific studies and researches. Early diagnosis of the depression and prescribing newer medicines (like those medicines that directly target the chemical changes of the brain) can control the effects of the disorder or the hard periods of it. Moreover, apart from the effects of the antidepressants in treating the depression disorder, the side effects of such medicines on different systems of our physiology has been considered by the researchers. In this research we aim to study the effects of the antidepressant uses in male patients. In this research we have tested the male samples in 3 groups: the first group used fluoxetine for a period less than 6 months, and the second group used the same medicine for a period more than 6 months. The third group known as the control group contained healthy subjects who were quite normal in the studied factors of the research. The findings of the research imply that the comparison between the first group and the control group showed no significant change in the study factors except for triglyceride that was reduced in the first group. However, in comparison between the second group and the control group it was shown that the fluoxetine leads to the reduction of serum level of the cholesterol, triglyceride, HDL, VLDL, and the increase in the serum level of LDL.

**Key words:** Depression, Fluoxetine, Serum Lipids.

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### 1. INTRODUCTION

Depression is one of the most common psychological diagnoses whose characteristics include disgruntle with feelings of sadness, low self-confidence and lack of interest or pleasure in daily activities of any kind, as it is known as mental cold. The term depression was used by the American Psychological Association in 1980 as a set of symptoms for mood disorders. According to a poll conducted in Iran, approximately 34% of the participants were depressed [1]. Antidepressant can be classified in two general classes: medicinal and non-medicinal. Although the attending physician would prescribe a special sort of treatment including psychotherapy, antidepressant pills, or both, depending on the symptom of the disorder, the severity of the depression, and the environmental conditions. Anyone would suffer from the depression, but usually the women are more prone to the depression than the men because the women are being more stressed by their work place or house environment than the men. The depression can have a genetic and family base. If one of the parents is severely depressed, their children are prone to be depressed up to 8 times more than the normal children. In cases of severe depression, antidepressant medicines are the best way of their treatment. In this research we intended to study the effects of antidepressant medicine, in particular the fluoxetine one the HDL, LDL, TG, VLDL, and cholesterol of the men, and we aim to find an answer to the following questions in order to reach a better decision on the dose and duration of the fluoxetine use:

1. Does fluoxetine change the level of the lipids of blood serum (i.e. HDL, LDL, TG, VLDL, and cholesterol)?
2. Is there any significant relationship between the duration of this medicine use and the changes in the mentioned factors?

## 1.1. Depression

Depression is one of the most common psychological disorders, being described as the mental cold. Approximately 8% of the people have experienced periodical depression. The emergence of the depression increases with aging. All human beings sometimes feel fatigue, misery, and sadness. But such feelings disappear after one or two weeks and do not disrupt their life cycle. Such people usually can overcome these senses alone without the help of the others [4 and 7]. The sense of depression is considerably stronger and more undesirable than the usual short-term sadness and despair periods of the most people. Such a sense is usually longer and can be prolonged for several days, weeks, or even several months. Winston Churchill who was suffered from the depression himself called it as the *black dog* [14, 15].

### 1.1.1. Depression treatment

The attending physician would prescribe a special sort of treatment including psychotherapy, antidepressant pills, or both, depending on the symptoms of the disorder, the severity of the depression, and the environmental conditions, or helps the patient leave his/ her negative attitudes that can be the cause of the depression [16]. If the depression is very severe or it has been prolonged, the psychologist can prescribe antidepressant medicines. Most persons do not feel any improvement in their mood during the first 2 or 3 weeks, although some of their other problems may vanish in a more rapid rate [6]. The human brain is made of millions of the cells that convey the messages to each other using many chemical components known as the neurotransmitters. Two types of these neurotransmitters play an important role. These two types are serotonin and noradrenaline. The antidepressants increase the level of these two chemicals at the end parts of the nerve, and thus strengthen the performance of those parts of the brain that use serotonin and noradrenaline [17, 18].

### 1.1.2. Antidepressant medicines

These medicines are known as neurotransmitters. To do its normal performance, the brain needs these neurotransmitters. Making these neurotransmitters accessible for the brain, these antidepressant medicines help the patients. Like any other medicines, antidepressant medicines may have some side effects for the user. Of course not all the antidepressant users encounter such side effects. The antidepressant medicines were introduced to the market in 1950s, and today, there are about 30 types of the antidepressant medicines that are classified in 4 groups [1, 2, and 3]:

- Tricyclic medicines;
- Mono Amino Oxidase Inhibitors (MAOIs);
- Selective Serotonin Reuptake Inhibitors (SSRIs); and
- Serotonin and Noradrenergic Reuptake Inhibitors (SNRIs)

Table 1. A list of the most important antidepressant drugs of different classes		
Class	Drug Trademark	Drug Name
Tricyclics	Tryptizol	Amitriptyline
	Anafranil	Clomipramin
	Prothiaden	Dosulpine
	Gamanil	Lofepamine
	Sinequan	Doxepine
	Tofranil	Imipramine
	Molipaxin	Trazodone
MAOIs	Allegron	Nortriptyline
	Nardil	Phenelzine
	Parnate	Tranlycypromine
SSRIs	Manerix	Moclobemide
	Prozac	Fluoxetine
	Seroxat	Paroxetine
	Cipramil	Citalopram
SNRIs	Lustral	Sertraline
	Edronax	Reboxetine
	Efxor	Venlafaxine

## 2. LITERATURE REVIEW

Melkersson, et al, (2000) studied the effects of fluoxetine on the serum level of triglyceride and HDL in the patients with severe social fear, fear of the crowded places, panic attacks, and depression. In this research in which

the fluoxetine doze was began with 20 mg per day and reached to 150 mg at the end of the 6 months, the level of triglyceride of the blood serum was decreased but the level of liver triglyceride was increased. Moreover, the serum level of the cholesterol and HDL was decreased as well [8].

In another research, Ehud Isacoff, et al, (2002) studied the effects of antidepressant medicines (fluoxetine) on the channels of the membrane potassium. In their study, they used Green Fluorescent Protein (GFP) to mark the membrane protein. They finally concluded that the fluoxetine leads to some changes in the combination of the membrane lipids during signal incidents, and these changes lead to the control of the potassium channels in turn [11].

On the other hand, Camila Guimaraes, et al, (2006) tested 35 fat patients for 90 days with the fluoxetine (20 mg per day), metformin and sibutramine. The results of their study showed that the fluoxetine leads to the reduction of the TG level (28.3%), reduction of the HDL level of the blood (12.8%), and the reduction of the serum level of cholesterol (25.8%). Other medicines had approximately the same amount of reductions in the mentioned factors [14].

In yet another research, ShimaJazayeri, et al, (2007) treated 40 depressed patients with fluoxetine (20 mg per day) in fasting conditions. The main goals of this study was to investigate the risks of the cardiac attacks of the depressed treatment with fluoxetine in the presence of omega-3 fatty acid and without omega-3 fatty acids after a period of 8 weeks, and to investigate the serum level of the cholesterol, HDL, and LDL. The results of this research showed that depression of the tested group had been reduced but the level of cholesterol had showed no significant change. Additionally, the serum level of LDL was increased in comparison to the HDL level, and the level of cortisol was decreased [10].

Sebastian Schneeweiss, et al, (2010) tested and studied 846 adult depressed patients with daily 20 mg of fluoxetine and daily 10 mg of citalopram. The results of Schneeweiss's study showed that these medicines increase the suicide thoughts and suicide activities, and the changes in the level of blood lipids showed a significant difference, so that the level of triglyceride and cholesterol was decreased while the level of the LDL of the blood was increased significantly [5].

Guillaume Pare, et al, (2010) studied 1795 persons who were using 20 mg of fluoxetine per day. After a period of 8 months, the researchers conclude that the level of the LDL of the blood serum had been increased while the level of the VLDL of the blood serum had been decreased [12].

Finally, Nadeem Sarwar, et al, (2010) studied the level of the blood triglyceride (TG) with the use of SSRIs. In this research, 206 patients with the heart coronary problem were studied for 5 years. The researchers showed that the level of the serum triglyceride has been decreased significantly due to the use of SSRI antidepressant medicines like the fluoxetine [13].

### 3. METHODOLOGY OF THE TEST

Type of this study is application and will help many depressed patients, we had to select the samples whose duration of using fluoxetine can be studied. In referring to the Shiraz Psychiatric Hospital and the Hafez Mental Clinic of Shiraz, 42 men were identified at the age ranged from 22 to 48 years old who used fluoxetine. Then we designed the relevant form and the specifications of each patient were registered on the forms. Then 30 persons out of these patients who had used 20 mg of fluoxetine per day were selected as the samples. These patients were classified in two groups:

- First group: those patients whose use of the fluoxetine had been less than 6 months (15 patients)
- Second group: those patients whose use of the fluoxetine had been more than 6 months (15 patients)

We took 2 to 5 ml blood of the patients before eating the breakfast. The collected bloods were put in the flasks and transmitted to the laboratory of the Veterinary Medicine Faculty of Shiraz University. The centrifuge process was done for 20 minutes and then we undertook the process of separating serum bloods from the blood cells. The specifications of the samples were registered on the tubes and then we measured the level of the lipids of the serum blood (HDL, LDL, TG, VLDL, and cholesterol) by quantitative detection kit of Pars Azmoon company<sup>1</sup>. Besides, the third group had been selected from the men who had no use of fluoxetine and their level of the blood fats and sexual hormones was normal. We took the blood of these 15 men of the control group and prepared the relevant serum and then tested their level of serum lipids similar to the cases of the first and second group in order to compare the results of the first and second group with the results of this third control group.

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<sup>1</sup>- quantitative kit of HDL-C, quantitative diagnostic kit for LDL-C, total cholesterol reagent kit, triglyceride reagent kit, reagent 1 and reagent 2 of Pars Azmoon company.

**4. ANALYSIS OF THE RESULTS OF TESTING THE SAMPLES**

**4.1. Effects of the duration of fluoxetine use on the mean of cholesterol concentration**

Figure 1 shows that the cholesterol concentration is trivial in the group that has used fluoxetine for less than 6 months in comparison to the control group, and this trivial difference is not significant statistically ( $p>0.05$ ); but in the second group that had used fluoxetine for more than 6 months, the level of serum cholesterol was lower than the first and the control group and thus changes were statistically significant ( $p<0.05$ ).

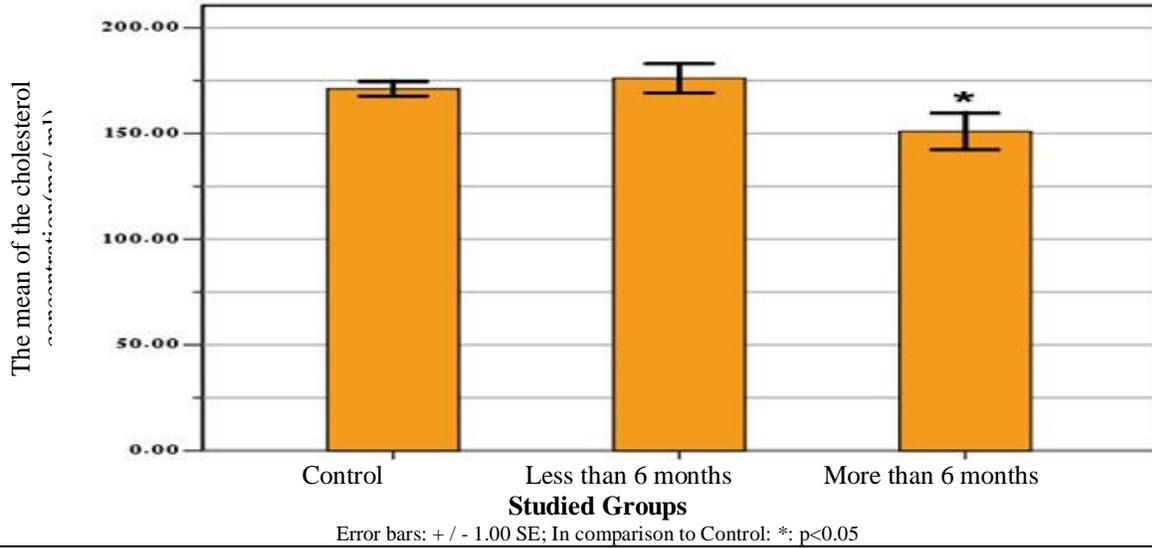


Figure 1. The comparison of the effect of usage duration of fluoxetine (20 mg per day) on the mean of the concentration of cholesterol serum

**4.2. Effects of the duration of fluoxetine use on the mean of LDL concentration**

Figure 2 shows that the LDL concentration in the group that has used fluoxetine for less than 6 months in comparison to the control group, has not changed considerably and this difference is not significant statistically ( $p>0.05$ ); but in the second group that had used fluoxetine for more than 6 months, the level of serum LDL concentration has increased in comparison to the first and the control group and such an increase of the LDL level was statistically significant ( $p<0.05$ ).

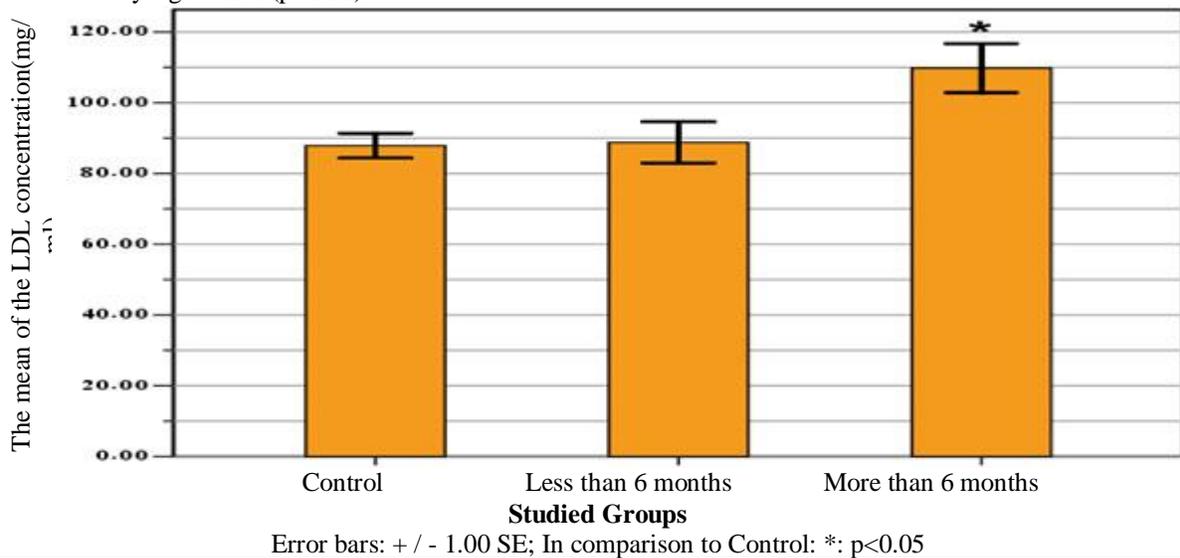


Figure 2. The comparison of the effect of usage duration of fluoxetine (20 mg per day) on the mean of the concentration of LDL serum

**4.3. Effects of the duration of fluoxetine use on the mean of HDL concentration**

Figure 3 shows that the HDL concentration in the group that has used fluoxetine for less than 6 months in comparison to the control group, has not changed considerably and this difference is not significant statistically ( $p>0.05$ ); but in the second group that had used fluoxetine for more than 6 months, the level of serum HDL concentration has been reduced in comparison to the first and the control group and such a reduction of the HDL level was statistically significant ( $p<0.05$ ).

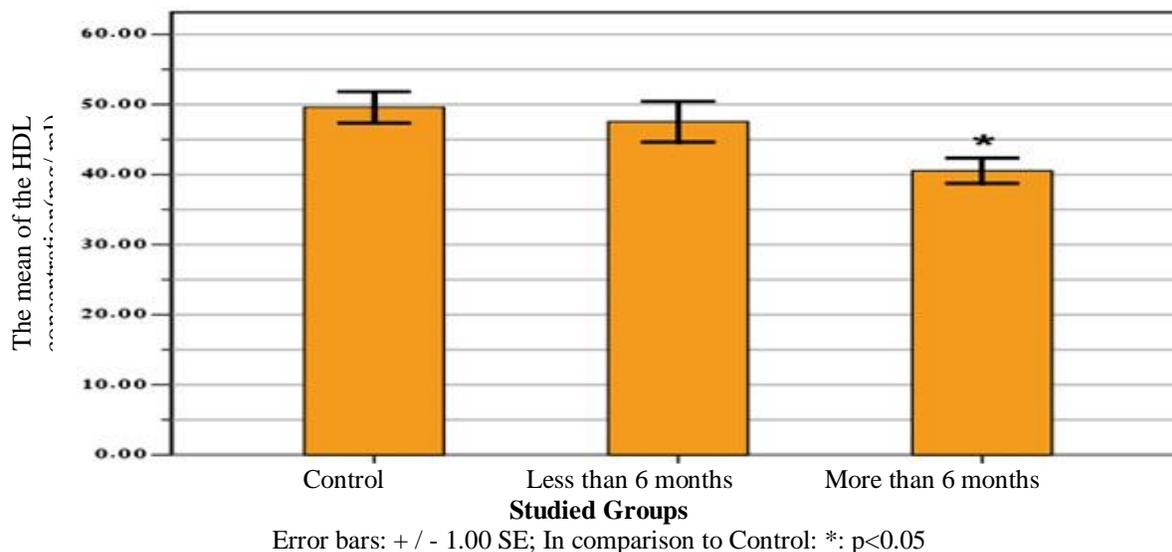


Figure 3. The comparison of the effects of usage duration of fluoxetine (20 mg per day) on the mean of the concentration of HDL serum

**4.4. The effects of the duration of fluoxetine use on the mean of triglyceride (TG) concentration**

Figure 4 shows that the TG concentration in the group that has used fluoxetine for less than 6 months in comparison to the control group, has changed considerably and this difference is significant statistically ( $p<0.05$ ); moreover, in the second group that had used fluoxetine for more than 6 months, the level of serum TG concentration has had more changes implying that the TG level has reduced and such a reduction was statistically significant ( $p<0.05$ ), thus the use of fluoxetine is effective on the serum level of the triglyceride.

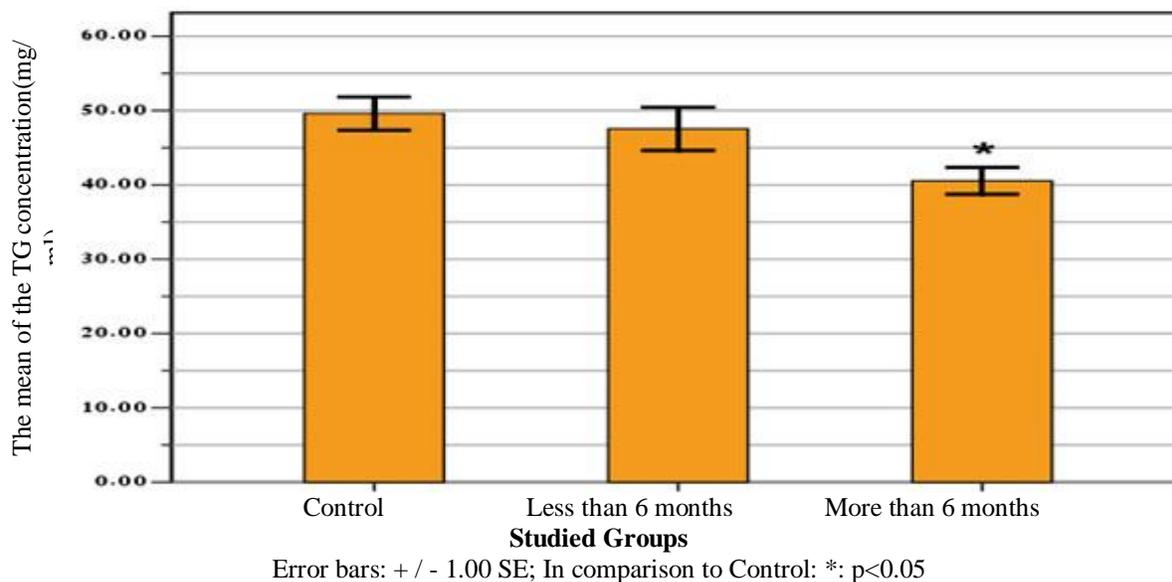


Figure 4. The comparison of the effects of usage duration of fluoxetine (20 mg per day) on the mean of the concentration of TG serum

#### 4.5. The effects of the duration of fluoxetine use on the mean of VLDL serum concentration

Figure 5 shows that the VLDL concentration in the group that has used fluoxetine for less than 6 months in comparison to the control group, has not changed considerably and this difference is not significant statistically ( $p>0.05$ ); but in the second group that had used fluoxetine for more than 6 months, the mean level of serum VLDL concentration has been reduced in comparison to the first and the control group and such a reduction of the VLDL level was statistically significant ( $p<0.05$ ).

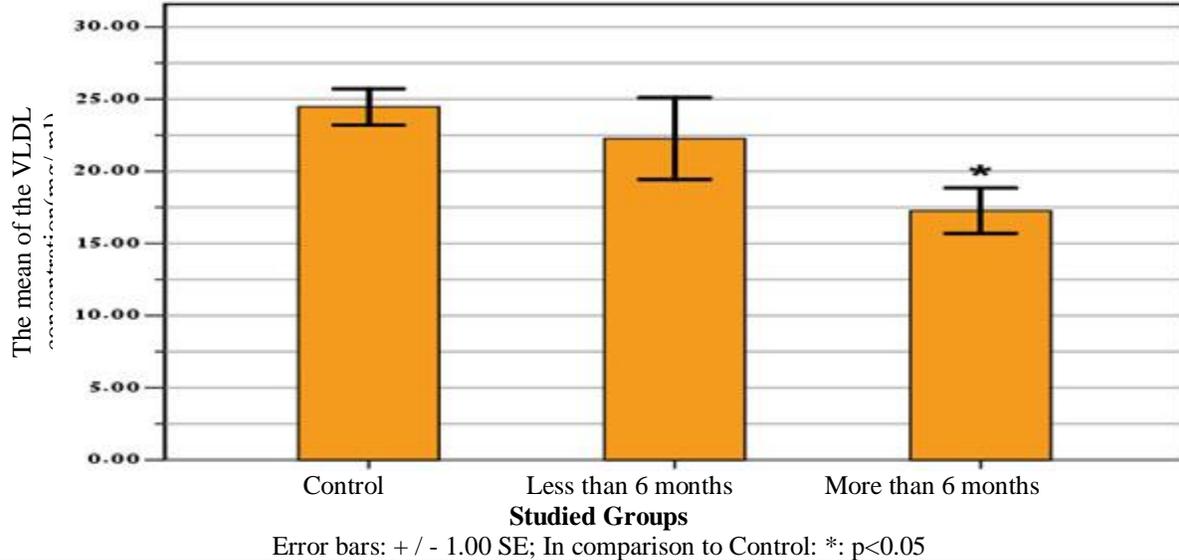


Figure 5. The comparison of the effects of usage duration of fluoxetine (20 mg per day) on the mean of the concentration of VLDL serum

## 5. GENERAL CONCLUSION

The results of this research showed that the use of fluoxetine for less than 6 months makes trivial and insignificant changes in the serum level of cholesterol, but longer fluoxetine use (i.e. longer than 6 months) reduced the serum level of the cholesterol. This result is consistent with the experiments of Camila Guimaraes, et al, (2006) who had studied the effects of the fluoxetine on the fat people. They had concluded that the use of fluoxetine will lead to the reduction of the serum level of the cholesterol and other lipid combinations [14]. Moreover, the obtained result is consistent with the experiments done by Melkersson, et al, (2000) who had studied the effects of fluoxetine on the patients with severe social fear, fear of the crowded places, panic attacks, and depression. In their research, they had found that the use of fluoxetine and its duration leads to the reduction of the serum level of the cholesterol [8]. On the other hand, our results is consistent with the results of Sebastian Schneeweiss, et al, (2010) who had tested and studied 846 adult depressed patients with daily 20 mg of fluoxetine, and concluded that the fluoxetine increases serum level of the cholesterol [5].

Besides, the results of this research showed that the use of fluoxetine for less than 6 months makes trivial and insignificant changes in the concentration of the LDL, but longer fluoxetine use (i.e. longer than 6 months) increases the concentration of the LDL. This result is consistent with the research of Puna, Singal, et al, (2005). These researchers had studied the effects of the fluoxetine to conclude that fluoxetine decreases the level of high density lipoprotein (HDL) and increases the level of low density lipoprotein (LDL) [15]. In another research, Sebastian Schneeweiss, et al, (2010) had studied adult depressed patients to investigate the effects of the fluoxetine use on the blood lipids of the patients. They had found that the daily use of 20 mg of fluoxetine leads to the increase of the serum level of the blood LDL [5]. Their result is consistent with the obtained results of the present research.

Moreover, we found that the use of fluoxetine and the duration of such a use are effective on the serum level of the HDL and it has been reduced in comparison to the control group. The level of the blood HDL shows more reduction with the increase of the duration of fluoxetine use. This result is completely consistent with the results of Soga, et al, (1998) who had studied the effects of fluoxetine use in postmenopausal women and had concluded that the serum level of HDL has been decreased and the serum level of the LDL has been increased in the subjected women. The findings of their research are completely consistent with our obtained result as well [9]. Additionally, our results are consistent with the researches of Camila Guimaraes, et al, (2006) who had studied the effects of

fluoxetine on the depressed fat patients. These researchers had reported that the fluoxetine leads to the reduction of the serum level of HDL [14].

The mean of the TG concentration in the group of the fluoxetine users who had used it for less than 6 months was lower than the control group. Moreover, in the group of fluoxetine users who used it for more than 6 months, the obtained changes in the TG concentration of the serum blood show a reduction of the level of TG. In other words, with the increase of the duration of the fluoxetine use, more sensible reduction of the serum level of the TG can be observed. This result is consistent with the researches of Camila Guimaraes (2006) who had tested 35 fat patients with the daily use of 20 mg of the fluoxetine and had concluded that the fluoxetine leads to the reduction of the TG level (28.3%), reduction of the HDL level of the blood (12.8%), and the reduction of the serum level of cholesterol (25.8%) [14]. Besides, our results is consistent with the findings of Melkersson, et al, (2000) who had studied the effects of fluoxetine use in the patients suffered from the fear. Their research had come to the conclusion that the use of fluoxetine reduces the serum level of the blood TG and increases the level of the liver TG [8]. Moreover, Sebastian Schneeweiss, et al, (2010) had studied depressed patients with daily 20 mg of fluoxetine. Their results showed that these the use of fluoxetine decreases the level of blood TG and cholesterol while increases the level of the LDL of the blood [5]. Once more, this result is completely consistent with the findings of our research.

Finally, in both groups (first group who used fluoxetine for less than 6 months and the second group who used fluoxetine for more than 6 months) some significant changes were observed in the VLDL concentration in comparison to the control group. These changes showed that the duration of using fluoxetine has an adverse relationship with the level of the blood VLDL, i.e. if the duration of the fluoxetine use was longer, the serum level of the VLDL was reduced, vice versa. The findings of this research are consistent with the findings of Guillaum, et al, (2010). They had studied the patients who were using 20 mg of fluoxetine per day. They found that the use of fluoxetine for a long term will have high effects on the level of the blood lipids. Specifically the found that the use of fluoxetine for more than 6 months will decrease theserum level of the VLDL of the blood and it will increase the serum level of the LDL of the blood [12].

In this research the quantitative effects of antidepressants on serum lipids levels have been and that these drugs, how and by what mechanism lipids decreases or increases in other studies are needed.

In sum, the obtained results of the studies and experiments show that: in comparing the first group with the control group, the studied factors have had no significant change, except for the TG level that was decreased ( $127\pm 1$  vs.  $172\pm 1$ ). But in comparing the second group with the control group, we found that the use of the fluoxetine causes the reduction of the serum level of the cholesterol ( $151\pm 1$  vs.  $171\pm 1$ ), TG ( $93\pm 1$  vs.  $172\pm 1$ ), HDL ( $40\pm 1$  vs.  $49\pm 1$ ), and VLDL ( $17\pm 1$  vs.  $24\pm 1$ ); and it causes the increase in the serum level of the LDL ( $109\pm 1$  vs.  $87\pm 1$ ). On the basis of the results of this research, the time- dependent use of fluoxetine is effective on the serum lipids, and more sensible changes will be observed on these factors with the extension of the time of using fluoxetine.

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