Study the Effect of Amphetamine on the Immune System and Liver Function

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Abstract

Amphetamine is a chemical compound that was manufactured by the Romanians in the year 1887. This compound has a very strong effect on the nervous and psychological system and has negative effects on the nervous system as well as negative effects on the heart, liver, kidneys, and other organs of the body. Amphetamine is a good psychostimulant, but when misused it causes damage to dopamine and serotonin receptors, one of the most important negative effects that occur due to amphetamine is weak immunity and increased inflammation. Therefore, one of the biochemical parameters, which is an immunological and anti-inflammatory indicator, was chosen Lepoxin, whose results showed a decrease in the blood level of amphetamine abusers, in this research , sixty persons participated as a case study, compared to sixty others, were used as a control group. All samples were taken from Al-Fayhaa Hospital in Basra Governorate. The study focused on the immune factor represented by lipoxin, as well as liver enzymes AST, ALP, GGT and TSB. The concentrations were measured by ELISA technique for lipoxin and spectrometry for the rest of the biochemical parameters. The results of that search for liver enzymes and GGT, TSB showed that there was no significant difference between the amphetamine abusers and the control group, the reason is due to the period in which the people abused it, as well as to the concentration of the dose used. on the other hand, the results shows a significant decrease in lipoxin levels in case group as compare contol group . We conclude that the immune and inflammatory response to lipoxin is more sensitive than the response of liver enzymes, bilirubin and GGT. We recommend conducting a laboratory survey of drug users more accurately in terms of the concentration given and the period of use, taking into account the age and weight of the drug user.

1. Introduction

Lazar Edeleanu, a chemist from Romania, created amphetamines in 1887 from the Chinese chemical compound Ma-Huang. Amphetamines were used to treat inflammation, hay fever, and the common cold in the 1920s by widening the bronchial sacs of the lungs. When benzedrine inhalers were first released in 1932, they were a big hit as over-the-counter treatments. [1]

Amphetamine is a strong sympathomimetic and psychostimulant drug that has a profound effect on the body of the user and has negative neurological and physical effects. usage causes an increase in heart rate, blood pressure, body temperature, and alertness as well as a decrease in appetite. [2] Few researchers have looked at the effects of amphetamine on peripheral organs or the central nervous system because it affects altered neuronal function, addiction, and cellular destruction. Amphetamine is a commonly misused psychostimulant that causes lasting damage to dopamine and serotonin terminals. However, amphetamine exposure has also been linked to reports of liver and other organ damage. [3] According to the majority of studies, amphetamine increased AST, ALT, and ALP levels in the blood, or it induced immediate hyperthermic-dependent liver damage that persisted for at least 24 hours following drug administration. It also caused hepatotoxicity by triggering apoptosis and cell cycle arrest. [4] Abuse of amphetamines has a demonstrable impact on the brain and central nervous system, which results in toxicity and inflammation of the neurological system. This in turn has a detrimental impact on the immune system and the reaction of immunological parameters like interleukins in general and lipoxin. [5] the activity of the immunological markers lipoxin and interleukins in amphetamine users is inversely correlated with cognitive impairment. [6] The word "lipoxin" refers to the products of lipoxygenase interactions. The two primary lipid mediators produced in mammals are LXA4 and LXB4. [11] Given that the host defense and regulation of inflammation are significant in human immunological disorders, the discovery of four LXs may open up new possibilities for the therapy of chronic inflammatory diseases. [10] A unique class of arachidonic acid metabolites called lipoxins (LX) was just recently found in human leukocytes. The biological actions of lipoxins point to a potential for them to operate as mediators or regulators of inflammation. In the hamster cheek pouch and kidney, LXA 4 (5S, 6R, 15S-trihydroxy-7,9,13-trans-I 1-cis-eicosatetraenoic acid) increases leukocyte secretion, activates protein kinase C, and causes vasodilation. [11]. The first category of endogenous inflammatory braking signals to be discovered is called lipoxins (LXs). These molecules have the ability to inhibit the production of hazardous substances including ROS and pro-inflammatory cytokines, therefore aiding in the reduction of inflammation.

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One of the most significant LXs, lipoxin A4 (LXA4), can bind to the LXA4 receptor (ALXR), a particular G-protein-coupled receptor (GPCR), in vivo. [12]
Methamphetamine (METH) is a commonly abused psychostimulant that permanently injures the liver and other organs. Studies have linked the drug's long-term dopamine and serotonin depletions, increased peripheral and brain ammonia, and liver damage from METH, emphasizing the importance of peripheral organ damage in mediating the drug's neurotoxicity. Despite these results, METH's hepatocellular damage has not been well studied in vivo. This is important because METH's hepatotoxicity appears to contribute to its well-known neurotoxicity. [14]
Lactate dehydrogenase, total protein, globulins, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), 5'-nucleotidase, conjugated (direct) and unconjugated (indirect) bilirubin, These tests can assist in locating the site of the liver damage, and the elevation pattern can assist in organizing a differential diagnosis. [13] Peptides transfer gamma-glutamyl groups to other amino acids. In contrast to alkaline phosphatase, which is prevalent in bone, it is plentiful in many other organs including the kidney, pancreas, intestine, prostate, testicles, spleen, heart, and brain, making it more selective for biliary disease. Serum While GGT from the kidney, urine, and pancreas differs from GGT from the liver enzyme in terms of electrophoretic mobility and lectin-affinity reaction, according to reports, obstructive liver disease causes an average 12-fold increase in GGT levels as opposed to a 3-fold increase in ALP levels, making GGT slightly more sensitive than ALP in this regard. Children's GGT activity levels may be a trustworthy indicator of bile duct injury. [15]

2. Subjects and Methods

1) Subjects

Patients

Sixty of the adducts aged (15-45 years) have participated in the current study. The samples were collected from (Al- Basrah Rehabilitation Centre for adduction in Al-Fayhaa Teaching Hospital in Basrah Governorate-Iraq), during the period from September 2022 to December 2022.

Controls

Sixty apparently healthy subjects were selected as a control group. Attended the outpatient clinical at Al-Fayhaa teaching hospital.
Using disposable needles and plastic syringes, five milliliters of venous blood samples from each patient and control were collected. The samples were moved into a fresh plain tube, the blood was allowed to coagulate for 15 minutes at room temperature, centrifuged for 5 minutes at 3000 rpm to separate the serum, and then the blood was moved into fresh disposable Eppendorf tubes. [7, 8, 9]

3. Methods

In this research, the lipoxin biomarker was used as a standard for inflammation and immunity, as the Elisa Kit used lipoxin from Sun long Company. (www.sunlongbiotech.com)(Catalogue Number: SL1086Hu) while the ALT, AST, ALP, in addition to bilirubin, and gamma-glutamyl transferase were measured by spectrophotometer according to biolabo's modus operandi.

4. Result and Discussion

Table (1): Distribution of the study sample according to the biochemical parameters:

Parameters		Amphetamine addicts n= 60 (mean ± SD)	Healthy Control n= 60 (mean ± SD)	P-value*
LFT	TSB (mg⁄dl)	0.6+ 0.52	0.7+ 0.35	p =0.86
	S.ALT (U/L)	19.12+ 9.9	18.88+ 10.7	p =0.915
	S.AST (U/L)	21.56+10.5	18.26+ 6.3	p =0.384
	S.ALP (U/L)	63.9+ 12.7	57.19+ 13.6	p =0.08
	S.GGT (U/L)	22.4+ 26.3	20.07+ 17.2	p =0.629
	Lipoxin	2.54+ 2.05	2.92+ 0.09	p =<0.001

Table 1 shows the liver enzyme, no significant differences were observed between cases of amphetamine addicts and controls in terms of ALT, AST, ALP, TSB, and GGT (p>0.05). Many types of research, or even most of the research that focused on the effect of addiction on the liver through its enzymes, confirm that the liver is negatively affected by drugs, as all kinds of drugs lead to damage to liver cells, as liver enzymes rise significantly as the period of abuse increases [16] This research does not agree with the current study, The research carried out by the scientists, (Lerman et al. 2018) clearly showed that the effect of liver enzymes, GGT and bilirubin is clear if the effector is from inside the liver, but if the effector is outside the liver, then the sensitivity of the liver enzymes towards the effect is gradual, as the scientists explained that the liver is greatly affected by amphetamine but it requires a certain period of time, so scientists found that the effects of liver enzymes varied when using drugs in general. [17] Others have proven that the rise in liver enzymes depends on the amount of dose given, and time period of abuse [18] The results of the search for liver enzymes in the aforementioned research show that the results of liver enzymes are not significant for new drug users, despite the influence of some other criteria such as happiness hormones and neurotransmitters, scientists have explained what is happening is that the neurotransmitters and happiness hormones are affected faster than the liver

is affected during the first periods of drug use. [19,20] The amount of narcotic substance that enters the body has a significant impact on the functioning of the liver, as research has shown that low concentrations of intoxicants and narcotics do not significantly affect liver enzymes over short periods of time. [19] The researches mentioned are completely identical to what was stated in the results of the current research.

As indicated by the results of the current research, lipoxin shows a significant decrease in people who abuse drugs, as the results of the research were in line with most of the research that focused its work on the relationship of lipoxin to infections and immune defenses, as most researches proved a low level of lipoxin in the blood in people with inflammation or immunity disorder [21], Many studies dealing with the study of lipoxin prove that it's level decline when the body was affected by inflammation or oxidative stress, where lipoxin stimulates prostacyclin, which is generated by endothelial cells, and stimulates nitric oxide, which is produced by vascular endothelial cells, which leads to rapid consumption of lipoxin.. [22], On the other hand, studies have shown that drug abuse exposes the user to inflammation and a lack of immunity [23], concluding from the above that the decrease in the level of lipoxin is a response to the occurrence of inflammation caused by drug abuse, which in turn causes a decrease in immunity and an increase in oxidative stress, which stimulates the body to consumption lipoxin for the purpose of increasing antioxidants, and this is consistent with the results of our current research. Lipoxins receptors are anti-inflammatory that are synthesized from LTA4 through metabolism, where they reduce the infiltration of white blood cells by adhesion to cells and remove phagocytes from cells and balance the production of cytokines from this we conclude that lipoxin remains at low levels during inflammation by virtue of the function it performs [26]. On the other hand, research that supports the current research results, where scientists have proven that a type of cytochrome (CYP4F3A) has a great affinity towards LXA4 AND LXB4 during the period of inflammation where the process of hydroxylation takes place [27]. Lipoxins (LX), a series of anti-inflammatory mediators, are short-lived endogenously produced nonclassic eicosanoids, whose appearance in inflammation signals the resolution of inflammation [24]. In another research carried out by (Bhatt, et al. 2017) in which they proved that the dissociation rate of LTA4 is many times greater than the dissociation rate of LTB4, and this confirms and supports the validity of the results of the current research [25].

Distribution of Lipoxin according to the duration of abuse with amphetamine addicts.

The distribution was demonstrated in table (2). The results of the present study revealed that the mean value of Lipoxine levels was not significant in amphetamine addicts with a duration of >1 year (1.73+1.91 µmol⁄l and 2.57+2.0 µmol⁄l) than those with a duration of < 1 year (1.64+0.32 µmol⁄l and 2.55+2.23 µmol⁄l) (p>0.05).

Table (2): Distribution of Lipoxine according to the duration of abuse with amphetamine.

Parameter		Lipoxin (Mean ±SD) (ng/l)	P-value*
Duration of abuse	≤ 1 year 26.6%	2.55±2.23	0.98
	>1years 73.4%	2.57±2.0	

As mentioned in the table above, there is no significant difference between lipoxin levels between the two periods, because the effect of amphetamine appears during a very short period [28].

Table (3): Distribution of Lipoxine of the study participants according to BMI

BMI (Kg/m2)	Lipoxin (Mean ± SD) (ng/l)		P-value*
	Amphetamine addicts n= 60	Healthy Control n= 60	
Normal weight 18.5-24.9	2.09+1.5	4.52+1.13	p =<0.001
Overweight 25-29.9	2.89+0.83	4.43+0.5	p =<0.001
Obese ≥30	2.8+2.61	4.0+1.65	p =<0.001

Table 3 demonstrate a significant change in all phase of BMI addict individuals as compared to the healthy group, In most research that takes into account the body mass index and the effect of drug abuse on that index, their results are mostly of significant variation, as body mass affects what the drug does to the body itself [29]. The reason for the discrepancy between the current research and other research that proves otherwise than the results of the current research is that the current research took samples randomly not taking into the concentration, period of the abuse, age of user, and type of abuse.

5. Conclusion

the immune and inflammatory response to lipoxin is more sensitive than the response of liver enzymes, bilirubin, and GGT. **Recommendation** We recommend focusing on the dose concentration of amphetamine for the user, the age and weight of the user, in addition, account for period of abuse during the initiation of the research.

6. Declaration

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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