Research Article   Open Access

Treatment of Alcohol Dependence in the Context of the COVID-19 Pandemic

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ABSTRACT

Objective: The literature on psychiatric disorders associated with the coronavirus pandemic is scarce. In publications, indicate increased alcohol misuse. However, there is not treatment of alcohol dependence in the context of the COVID-19 pandemic

Materials and Methods: This was a double-blind trial for patients diagnosed with DSM-5 for of alcohol dependence. Eligible 100 participants all men to meeting the DSM-5 criteria alcohol dependence.

Results: As shown by catamiasis (12 months), among the patients treated with IF, (50 people), 5 had short-term breakdowns associated with exposure to microsocial causes. Among the patients who received disulfiram (50 people), all had cases of relapse.

Conclusion: The clinical, neuroendocrine and immune data demonstrate the high efficacy of the use of interferon in alcoholics. The mechanisms of the drug action are under discussion

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Introduction

Alcohol is an addictive psychoactive substance that is a Group 1 carcinogen for humans and has a significant impact on the health of the population worldwide [1,2]. Harmful use of alcohol is broadly defined as "use of alcohol that causes detrimental effects on the health and social life of the drinker, the people around him and society as a whole, as well as creates patterns of alcohol use that are associated with an increased risk of adverse health effects" [3]. This definition refers to consequences that go beyond the clinical context and emphasizes that alcohol use is one of the leading risk factors for health deterioration, disability and death worldwide. It is emphasized that alcohol affects not only consumers, but also many third parties, including victims of road traffic accidents or violence, as well as children born with fetal alcohol spectrum disorders or parents with alcohol problems; alcohol consumption also increases health care costs and decreases labor productivity [4]. Alcohol consumption is responsible for more than 200 diseases and injuries according to the International Classification of Diseases, and at least 40 diseases and injuries are 100% associated with alcohol consumption. The burden of mortality attributable to alcohol consumption goes back to 2 broader categories: chronic noncommunicable diseases (NCDs; neurological disorders, cancer, cardiovascular disease and cirrhosis of the liver) and the group of acute, intentional and unintentional injuries [1,4,5,6].

Literature evidence suggests an increase in alcohol abuse during the COVID-19 pandemic and rising risks of alcohol and drug addiction in a lockdown situation [7,8]. Earlier we described Mental Disorders Caused by the COVID-19 Pandemic [9].

The main goal of this work is to develop therapy for alcohol dependence in the context of the COVID-19 pandemic.

Materials and Methods
All patients was examined

This was a double-blind trial for patients diagnosed with DSM-5 for of alcohol dependence. The patients gave their informed, written consent to participate. In accordance with the Helsinki Declaration of the World Medical Association "Recommendations for doctors engaged in biomedical research involving people", adopted by the 18th World Medical Assembly (Finland, 1964, revised in Japan in 1975, Italy-1983, Hong Kong-1989, the South African Republic-1996, Edinburgh-2000); The Constitution of the Republic of Azerbaijan, the Law "On Psychiatric Assistance" (adopted on 12.06.2001, with amendments and additions -11.11.2011, Decisions of the Cabinet of Ministers of the Republic of Azerbaijan No. 83, dated April 30, 2010 "On Approval of the Rules for Conducting Scientific, Preclinical and Clinical studies of medicines" are established. The conditions of the conducted researches corresponded to the generally accepted norms of morality, the requirements of ethical and legal norms, as well as

the rights, interests and personal dignity of the participants of the studies were observed.

a) Conducted research is adequate to the topic of research work.
b) There is no risk for the subject of research.
c) Participants in the study were informed about the goals, methods, expected benefits of the study and associated with risk and inconvenience in the study.
d) The subject's informed consent about participation in the research was received.

The decision of the Ethical Committee at the Azerbaijan Psychiatric Association on the article of NA Aliev, ZN Aliev "Treatment of alcohol dependence in the context of the COVID-19 pandemic" submitted for publication in psychiatric journals: in connection with compliance with its legislative requirements and regulatory documents is to approve the article by N.A. Aliyev, Z.N. Aliev "Mental disorders caused by the COVID-19 pandemic". The method of randomiza¬tion was given by lottery. Each patient was randomized to re¬ceive either human alpha interferon (50 patients) 500 mg three times per day for 6 weeks or matched placebo (48 patients) in a double-blind manner.

Patients were observed at the Mental Health Center of the Ministry of Health of the Republic of Azerbaijan. The study was conducted from January 01, 2020 to 01 of the January 2021 years. Also we excluded sexually active subjects with active or unstable epilepsy, other genetic syndromes or congenital infections associated with autistic-like syndromes, prematurity; subjects who have been treated within the previous 30 days by any medication known to have a clearly defined potential for toxicity or with any psychotropic drugs; subjects with clinically significant abnormalities in laboratory tests or physical examination; subjects with a history of hypersensitivity or serious side effects associated with the use any drugs A detailed clinical interview with parents by a clinical expert, accompanied by physical examination and blood analysis, was used to ensure that subjects did not meet any exclusion criteria. A structured clinical interview, for DSM-5 Axis I Disorder, Patient Edition, was used to diagnose alcohol dependence to DSM-5 [10]. Hundred patients all men whom we studied were under observation in Mental Health Center of the Ministry of Health of the Republic of Azerbaijan. The length of the washout was 2 weeks. Patients were washout from the all medications. Eligible participants were required to be between 18 and 65 years of age. We excluded serious medical conditions including with other psychiatric disorders (e.g. bipolar disorder II tipi, schizophrenia, patients judged to be at serious suicidal or homicidal risk, dependence of psychoactive drugs, somatic, neurological illness etc). Also we excluded unstable epilepsy, other genetic syndromes or congenital infections associated with autistic-like syndromes, prematurity; subjects who have been treated within the previous 30 days by any medication known to have a clearly defined potential for toxicity or with any psychotropic drugs; subjects with clinically significant abnormalities in laboratory tests or physical examination; subjects with a history of hypersensitivity or serious side effects associated with the drug use, and subjects who, during the previous 3 months, started new non- pharmacological procedures, such as diet, vitamins and psychosocial therapy. A detailed clinical interview with parents by a clinical expert, accompanied by physical examination and blood analysis, was used to ensure that subjects did not meet any exclusion criteria.

Patients clinically significant of abnormal laboratory or EEG findings were ineligible. Patients before the study had not used antidepressants, antipsychotics, anxiolytics, benzodiazepines.

Washout of all medicines was two weeks. In the context of the COVID-19 pandemic, for the treatment of alcohol dependence, we approached a new aspect, namely, we used interferon in the treatment of alcoholism. The examined patients were divided into 2 groups of 50 people each. Patients of group 1 took human alpha interferon (IF) for 30 days; group 2 received disulfiram 2 times a day (at 9 and 19 hours, 0.25 g per dose). In each nasal passage, 5 drops (0.25 ml) were instilled 2 times a day with an interval of at least 6 hours. Like disulfiram, IF was given to patients who were sober without hangover symptoms for 30 days.

Patients of the 2nd group received human leukocyte IF (produced by the Tbilisi Research Institute of Vaccines and Serums). The ampoule with the preparation was opened before use, 2 ml of distilled water at room temperature was poured into it. The contents were shaken until complete dissolution.

Human alpha interferon was instilled into each nasal passage 5 drops (0.25 ml) 2 times a day with an interval of at least 6 hours. Like disulfiram, IF was given to sober patients without hangover symptoms for 30 days.

Results
Clinical indicators were used to assess the results and mechanisms of therapeutic efficacy. As such, the duration of remission, the presence of alcoholic breakdowns during treatment, a change in the pathological craving for alcohol, and the clinical dynamics of the disease were selected.

In the approach to the clinical assessment of a symptom, syndrome and stage of alcoholism, we were mainly guided by the DSM-5 data [10].

The study showed that after treatment with disulfiram, patients experienced drowsiness, internal discomfort, and difficulty concentrating. In addition, they had a decreased mood tone, headaches, dizziness, heartbeat, complaints of sexual weakness, intense craving for alcohol, which manifested itself in repeated alcohol breakdowns during treatment, evasion from participation in labor, lack of criticism to their condition, ill will towards relatives and friends.

Follow-up observation (within 12 months) showed that among the patients who received disulfiram (50 people), no one was in remission during this time. After treatment, all patients, as a rule, resumed their alcohol intake during the first 3 months. It should be especially noted that patients treated with disulfiram experienced an increased attraction to alcohol, more than before the therapy with this drug. Alcoholization in these persons acquired a malignant character.

Observations of the patients receiving IF showed that in their clinical state opposite changes were observed in comparison with those treated with disulfiram. In patients of this group, alcoholic breakdowns were not noted ', the craving for alcohol was suppressed, active participation in labor processes, a friendly attitude towards relatives and friends, and a critical attitude to their condition prevailed; side effects from taking the drug were not observed. As shown by catamiasis (12 months), among the patients treated with IF, (50 people), 5 had short-term breakdowns associated with exposure to microsocial causes. Among the patients who received disulfiram (50 people), all cases of relapse were recorded.

It should be said that especially interesting results were found in the study of neuroendocrine and immune parameters before and after treatment with disulfiram and IF. A preliminary analysis showed that in terms of background (before treatment) biological indicators, patients in both groups did not differ statistically significantly. The legitimacy of comparing biological indicators in each of the studied groups after a course of appropriate treatment with the background parameters of the general group lies in the fact that, as indicated above, neurotransmitter, neurohormonal and ionological indicators did not differ statistically when compared with each other and with the general group.

Table 1: Changes in neuroendocrine and immune parameters in alcoholic patients before and after treatment with IF and in patients with disulfiram

Indicator	Healthy	Patients with alcoholism		
		before treatment	after treatment with IF	after treatment with disulfiram
DA, ng / ml	$220,0 \pm 14,0$	$98,0 \pm 10,0$ p1<0,001; p3<0,001	$200,0 \pm 8,0$ p2— nss	$100,0 \pm 8,0$ p2<0,001
C ng / ml	$44,5 \pm 6,3$	$382,0 \pm 12$ p1 <0,001; P3<0,001	$250,0 \pm 10,0$ p2<0,0!	$469,0 \pm 13,6$ p2<0,001
GABA, ng / ml	$45,8 \pm 6,8$	$70,6 \pm 5,9$ P1<0,001	$50,2 \pm 4,0$ P2—ND	$110,0 \pm 8,0$ P2<0,001
ACTH. ng / ml	$2,7 \pm 0,2$	$123,8 \pm 7,2$ P1 <0,001 P3<0,001	$76,0 \pm 8,4$ p2< 0,02	$155,4 \pm 8,6$ p2<0,001
PRL, ng / ml	$2,4 \pm 0,2$	$3,6 \pm 0,2$ p1<0,001 p3<0,001	$1,7 \pm 0,1$ p3<0,001	$5,8 \pm 0,2$ p2<0,001
STH, ng / ml	$2,4 \pm 0,2$	$1,1 \pm 0,1$ Pi<0,001	$2,0 \pm 0,1$ P2—nd	$0,5 \pm 0,1$ p2<0,001
cAMP, pmol / 1 10^{10}	$12,7 \pm 0,5$	$27,7 \pm 0,7$ p1 <0,001; p3<0,001	$14,0 \pm 0,5$	$36,5 \pm 1,8$
cGMP, pmol / 1 10^{10}	$4,5 \pm 0,3$	$2,0 \pm 0,3$ p1 <0,001; p3<0,001	$4,0 \pm 0,5$ P2— nss	$1,1 \pm 0,1$ p2<0,001
Lymphocytes %	$33,9 \pm 1,0$	$28,2 \pm 1,0$; p1 <0,001 P3—nd	$30,0 \pm 1,0$ p2<0,02	$20,07 \pm 0,8$ p2<0,001

Note: p1 statistically reliability between healthy and alcoholic patients before treatment; p2 - between healthy and alcoholic patients after treatment, p3 - between alcoholics before and after treatment, nss - not statistically significant.

It was found that compared with the control, patients with alcoholism showed a significant decrease in the level of DA, STH, cGMP. On the contrary, the content of GABA, ACTH, PRL, cAMP was higher than in the control. Under the influence of disulfiram, patients with alcoholism developed even more serious disorders in the neuroendocrine and immune systems. At the same time, the treatment of patients with IF promoted a tendency towards the normalization of neuroendocrine and immune values. Our Follow-up observation (catamnesus), was conducted from January 01, 2020 to January 01, 2021.

Discussion
Thus, it has been shown that, firstly, the treatment with disulfiram is inappropriate, and secondly, a new direction in the search for the means of the immune system is determined. At this stage of our understanding, it is difficult to give an exhaustive explanation of the anti-alcohol action of IF. When using this drug in mentally healthy people, an increase in mood tone (mania-like state), an exaggerated idea of their capabilities, ignorance of nutrition and daily regular physiological activities, and in some, refusal drinking [11]. This condition, in our opinion, partially corresponds to the symptomatology observed with hyperactivity of the dopaminergic and hypoactivity of the GABA- and serotonergic systems, which is confirmed by the results of this work.

A study on rats of the effect of IF and ethanol on the opioid system of the brain showed that when a 15% solution of ethanol is used for 14 months for drinking in animals, the binding affinity of labeled 3H-naloxone and 3H-enkephalin to the brain structures decreases. At the same time, if a-IF were administered to animals during the last 1.5 months of the experiment, then any changes in the affinity of opioid receptors were observed for only 24 hours after ethanol was discontinued. On the other hand, preliminary administration of α-IF into the cerebral ventricles or intraperitoneally increased the decrease in the methenkephalin content in the striatum caused by a single administration of ethanol and prevented the decrease in the β-endorphin content in the anterior pituitary gland caused by it [12].

Thus, interferon, firstly, is involved in neurotransmitter processes (dopamine, serotonin and GABAergic), and secondly, it affects the opioidergic system. The role of violations of these systems in the pathogenesis of alcoholism is now being actively studied [13,14].

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the normalization of neuroendocrine and immune values. Our Follow-up observation (catamnesus), was conducted from January 01, 2020 to January 01, 2021.

Regarding the causes of immunological changes under the influence of a-IF, it should be said that they are apparently associated with changes in intracellular cyclic nucleotides and, most likely, can be explained by the influence of a-IF on neuroendocrine regulation of immune function. The presence of an afferent connection between the immune and neuroendocrine systems confirms the validity of this approach.

The neurohormonal effects of a-IF, apparently, can be explained by the effect of the drug on the neurotransmitter and opioid systems. Another hypothetically possible way of the effect of IF on neurotransmitter and neurohormonal systems may be associated with the effect of the drug on the synthesis and secretion of immune cells of peptide hormones, which are modified post-translational products. In this regard, it is extremely important to present modified post-translational products. In this regard, a regulatory factor that controls the synthesis and secretion of peptide hormones by immunocompetent cells, which give a wide range of biological effects, including psychophysiological ones, is extremely important in the present and future studies of the neuroimmune link in the pathogenesis of alcoholism.

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Conclusion

A hypothetically possible pathway for the effect of IF on neurotransmitter and neurohormonal systems may be associated with the effect of the drug on the synthesis and secretion of immune cells of peptide hormones, which are modified post-translational products. In this regard, modified post-translational products are extremely important. In this regard, a regulatory factor that controls the synthesis and secretion of peptide hormones by immunocompetent cells, which give a wide range of biological effects, including psychophysiological, is extremely important in current and future studies of the neuroimmune link in the pathogenesis of alcoholism.

Acknowledgment

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