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Effects of the Alcohol: A Review

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Abstract— *The alcohol beverages consumption by humanity is a common fact in a large number of cultures, for different purposes. Due to a high level of ethanol ingestion in many countries, and this relation about health and social problems, it is an issue which deserves special cautious. Alcohol metabolism can be made in three different ways. However, Enzymatic System of Alcohol Dehydrogenase (ADH) is considered the main one. This review will treat about nutritional aspects, which can cause undernutrition, vitamins and minerals deficits; endocrine-metabolic diseases, like diabetes mellitus and metabolic syndrome; Liver damage, such as steatosis, acute alcoholic hepatitis, a chronic alcoholic liver disease that causes cirrhosis and hepatic fibrosis, these manifestations can lead a hepatocarcinoma as well. Moreover, neurologic issues that can cause mood and behavior disorders, some examples of these problems are changes in synaptic transmission and neuronal excitability, anxiety and depression, attention deficit hyperactivity disorder, obsessions and compulsions, schizophrenic psychosis, affective disorders, insomnia, antisocial behavior, and suicide. It can also cause dependence with strong manifestations of abstinence.*

Keywords— ***alcohol, metabolism, hepatopathy, nervous system.***

I. INTRODUCTION

Evidence and historical accounts reveal that alcohol intake dated back to prehistory and was part of the culture of many ancient societies. For the Egyptians, wine and beer, for example, were partof their daily lives. As forGreek society, alcohol was a fundamental item amongst them, and its abstinence was highly rejected, just as in the Roman empire, where the alcoholic beverage was also present in several activities. The profile of alcohol consumption remains to this day in different populations and at different ages **(**Robinson and Adinoff, 2016**)**.

Currently, alcoholism is a health problem in Brazil and all over the world, as every year about 2.5 million people die from the use of this substance and 320,000of these people are between the ages of 15 and 29 **(**Pavlov et al, 2016**;**Pavlov et al, 2016**)**. The causes of death are related both to problems in the body andthe increased risk of accidents and fatal cases of violence. Reflections on alcohol use in health vary according to genetic and environmental factors and how this substance was consumed. It is estimated that today 20% of men and 10% of women consume alcohol abusively **(**Robinson and Adinoff, 2016**;**Miquel et al, 2016**;** Testino et al, 2016**;**Preuss et al, 2017;Orywal et al, 2017**)**.

Because of the numerous effects that alcohol can exert on the body, this study aims to review the relationship between alcohol consumption and its effects on the human body.

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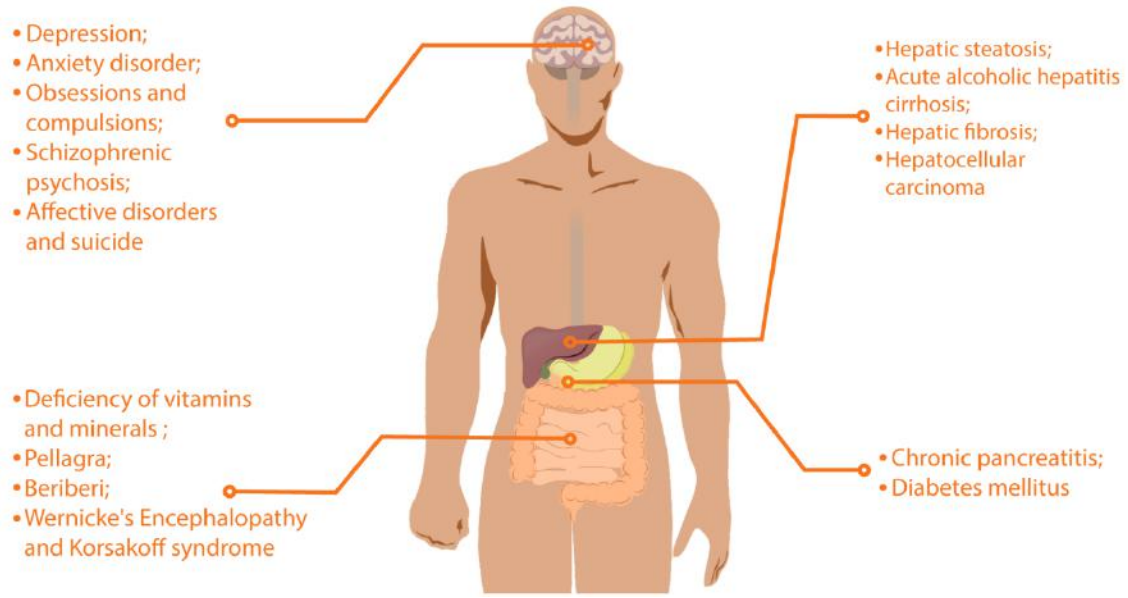

Fig.1: Manly effects of ethanol consumption. Issues neuropsychic related. Clinical branch of alcoholic liver disease. Gastrointestinal damages, vitamins, and nutrients absorption problems. Pancreas disturb and the relation with protein, sugar, and fat metabolism.

II. METHODS

This literature review was based on articles collected in the following platforms of bibliographic data: Pubmed, PMC, Medline, Lilacs, and Scielo. The selected articles were the ones published in the last three years, written in English, Portuguese, Spanish, and French. The retrospective search was restricted to indexed scientific articles describing research involving human and animals.

III. DISCUSSION

Alcohol Metabolization

Alcohol is absorbed by the gastrointestinal tract, and 2 to 10% of it suffer pulmonary and renal elimination; the rest is oxidized by the organism. There are three metabolic pathways for the ethanol: the Enzymatic System of Alcohol Dehydrogenase (ADH), whose enzymes are located in the cytosol of hepatocytes, the Microsomal Oxidation System of Ethanol (MEOS) and the Catalase in peroxisomes **(**Chi et al, 2016; Boye and Yang, 2016**)**.

Through the ADH system, alcohol is transformed into acetaldehyde that enters the mitochondria, and it is oxidized by an enzyme called Aldehyde Dehydrogenase (ALDH) being transformed into acetate originating Acetyl-CoA, used as a substrate for the synthesis of ATP. When there is excessive consumption – or when there is some change in metabolization– an accumulation of acetaldehyde occurs – toxic to the tissues **(**Wall, Luczak, and Hiller-Sturmhöfel, 2016**;** Matejcic, Gunter, and Ferrari, 2017**;** Dinis-Oliveira, 2016**;** Chang, Hsiao, and Chen, 2017**)**. ALDH2 is the main responsible for the oxidation of acetaldehyde in mitochondria **(**Nene et al, 2017**)**.

The microsomal ethanol oxidizing system (MEOS) oxidizes ethanol transforming into acetaldehyde by cytochrome P4502E1 or CYP2E1 (present in the endoplasmic reticulum of the liver and Catalase promotes oxidation with the aid of hydrogen peroxide**(**Chang, Hsiao, and Chen, 2017**;** Navarro and Navarro, 2013**)**.

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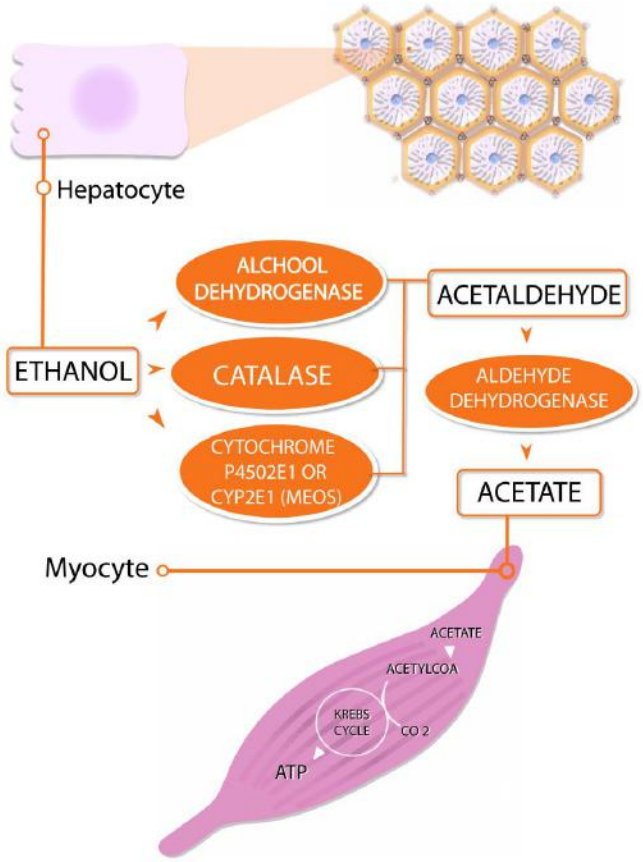

Fig.2: Ethanol metabolization, explaining the oxidation metabolism pathways, which are affected by Enzymatic System of Alcohol Dehydrogenase (ADH), whose enzymes are located in the cytosol of hepatocytes, the Microsomal Oxidation System of Ethanol (MEOS) and the Catalase in peroxisomes.

Alcohol and Nutritional Aspects

Alcohol possesses a large number of calories (7.1kcal/g). Consequently, there is a possibility of accumulation of fat and – paradoxically – malnutrition, which may be considered primary or secondary. The primary one is characterized by a nutritional deficit at the expense of a hypercaloric diet, but lacking macronutrients and vitamins. The secondary one, however, is described as intestinal malabsorption due to tissue injury **(**Barbosa and Ferreira, 2017**;** Barve et al, 2017; Sluik et al, 2017**)**.

Malnutrition causes deficiency of vitamins and minerals, such as complex B, C, D and K, zinc, magnesium, and iron. This lack generates inefficiency of catabolic and anabolic pathways; oxidative stress; inflammatory processes; pellagra; beriberi; neurological lesions; mental confusion; ataxia; ophthalmoplegia and amnesia **(**Barve et al, 2017**;** Sluik et al, 2017**)**.

Besides that, among the diseases caused by malnutrition and hypovitaminosis related to chronic ethanol consumption, we can cite Wernicke's Encephalopathy, which is a consequence of B12 hypovitaminosis, consisting of a severe, but treatable, neurologic disease if diagnosed early. It is detected through a classic triad, consisting of nystagmus (rapid eye movements), ataxia (loss of motor coordination) and confusional state. However, only 1/3 of the patients have thisclinical triad clearly defined. Thus, caution should be taken while diagnosing this encephalopathy and extra attention to the presence of persistent memory, learning difficulties, and the classical triad **(**Fernandes et al, 2017**)**.

The failure in the treatment of vitamin B12 replacement causes death in up to 20% of the cases, or progresses to Korsakoff syndrome (which happens in the chronic phase of this hypovitaminosis causing irreversible sequelae) linked with anterograde amnesia (inability of the brain to form new memories); short-term memory loss; compensatory confabulation (fake memories) and preservation of long-term memories and certain cognitive abilities. The late diagnosis of this disease leads to death **(**Fernandes et al, 2017**;**Kahl and Hillemacher, 2016**)**.

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Alcohol and Diabetes mellitus (DM) and metabolic syndrome (MS)

A European cohort study that included 60,000 participants pointed out that there is either a direct or indirect relationship between ethanol consumption and Diabetes Mellitus (DM). For example, the consumption can increase body mass index (BMI) - recognized as an essential cause for the occurrence of insulin resistance and type 2 DM **(**Fernandes et al, 2017**)**.

In patients with DM, alcohol can act leading to two acute complications such as hypoglycemia, as a result of the inhibition of gluconeogenesis, which can lead to convulsion and death, if not identified and treated. The other acute complication that may occur is diabetic ketoacidosis, causing glycemic elevation and activation of the ketogenic pathway owing to the low insulin/glucagon ratio **(**Hermann et al, 2017**)**. This fact is of great significanceas a result of the high prevalence of alcohol use among young people. In a multicenter study with 29,000 patients, it was found that 10.8% of young patients with DM1 consumed alcohol, 19% of this number were individuals between 19 and 25 years of age. Teetotaler's group had a lower rate of diabetic ketoacidosis and lower glycated hemoglobin. It was also observed that young people who consumed ethanol had a greater pre-disposition to tobacco use and worse glycemic control **(**Szücs et al, 2017**)**.

The MS, defined by obesity, hypertension, dyslipidemia, and hyperglycemia, affects about 20 to 25% of the population. The association of alcohol with the MS is still controversial. The beneficial effect of alcohol can be explained by its action on lipid metabolism and blood coagulation since it is found a higher HDL-cand lower LDL-level as well as higher insulin sensitivity alcohol users in low doses compared to non-users.However, studies show an increased prevalence of MS in alcohol-dependent patients. This fact arises as a result of factors such as increased blood pressure, increased triglycerides/, increased abdominal circumference, and, therefore, an increased risk of DM2**(**Hermann et al, 2017**)**.

Alcohol is still a significant cause of chronic pancreatitis, a progressive inflammatory disease of the pancreas, associated with damage in its cellular function and its anatomical structure, leading to DM **(**Tilg, Moschen, and Szabo, 2016**)**.

Alcohol and hepatopathy

Chronic alcohol use leads to a series of heterogeneous hepatic lesions, responsible for more than 2 million deaths annually **(**Rowe, 2017**)**. Among these deaths, liver cirrhosis is responsible for 1 million deaths/year. Liver cancer, the most severe complication of Alcoholic Hepatopathy (AH), causes about 800 thousand deaths. Among chronic diseases that reduce quality and life expectancy, the incidence of cirrhosis is only behind coronary heart disease, cerebrovascular disease, and chronic obstructive pulmonary disease **(**Zhang et al, 2017**)**. Hepatitis has an occurrence of 10 to 35% in chronic drinkers, and it is responsible for 1/3 of morbidity and mortality, being a fundamental factor in the development of Alcoholic Hepatopathy **(**Addolorato et al, 2007**)**. Also, AH is the second most frequent indication for liver transplant in Europe and North America, a total of about 20% to 30% of all liver transplants**(**Joshi et al, 2016**;** Marot et al, 2017**;** Chao, Waitzberg et al, 2016**)**.

Multisystemic effects are frequent in patients with a history of chronic alcohol consumption and the presence of AH. These comorbidities include malnutrition, hypovitaminosis, loss of bone density, sarcopenia, hemolytic anemia, peripheral and central neurological abnormalities, and nephropathy **(**Joshi et al, 2016**;** Childers and Ahn, 2016**)**.

The primary complications of this class of hepatopathy include hepatic steatosis; followed by acute alcoholic hepatitis and chronic alcoholic liver disease,causing cirrhosis and hepatic fibrosis **(**Chacko and Reinus, 2016**)**. Also, hepatocellular carcinoma, which occurs in 5% to 15% of patients with alcoholic cirrhosis, is considered to be the most severe complication of AH **(**Pavlov et al, 2016**)**.

Patients with AH are at the risk of developing fibrosis and liver cirrhosis, and this risk is higher when there is daily consumption of 20 to 40 g of ethanol for women and more than 80 g for men; in those whoseAlanine and Aspartate Aminotransferase serum levels are elevated and present as comorbidities hepatitis C and obesity **(**Pavlov et al, 2016**;** Lasebikan and Ayinde, 2017**)**.

Generally, patients with HA seek medical help when complications of cirrhosis appear **(**Pavlov et al, 2016**)**. The vicious cycle of injury and repair that occurs in the liver after ingestion of alcohol results in collagen deposition among structures of the portal triad and central vein, cirrhosis of this etiology is characterized by small regenerative (micronodular) nodules **(**Lasebikan, Ola, and Ayinde, 2017**)**.

Alcohol and the nervous system

Alcohol has a vital role in the pathogenesis of mental and behavioral disorders such as depression, attention deficit hyperactivity disorder (ADHD), anxiety disorder, irritation, obsessions and compulsions, phobia, difficulty in concentrating, schizophrenic psychosis, affective disorders, insomnia, antisocial behavior, and suicide. About the latter, itis related to severe intoxication

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by this substance and cases of depression and bipolar disorders caused by alcohol consumption inducing suicide. Studies carried out by Lucchese *et al*. and Becker *et al*(2017) showed that, in a group of alcohol and drug users, 37% of the individuals displayed a higher probability of developing mental disorders.The prevalence of pathologies, such as affective disorders in alcohol-dependent patients, is 23 percent. As for gender and age, the highest prevalence of mental disorders in alcohol and drug abusers is in women (mainly in mood and anxiety disorders)and patients under the age of 25**(**Preuss et al, 2017; Becker, Ehret and Kirsch, 2017; Lucchese et al, 2017**)**.

Ethanol is considered to be a depressant of the central nervous system by inhibiting glutaminergic (excitatory) pathways and stimulation of GAB Aergic (inhibitory) leading to relaxation modulated by the reward system.

Glutamate is a crucial excitatory neurotransmitter of the Central Nervous System (CNS), mediating 40% of glutaminergic synapses. Ethanol causes a reduction in NMDA Glutamate receptor activity and inhibition of the second messenger production (cyclic GMP)altering the synaptic function of this neurotransmitter and promotes CNS depression. In alcoholic patients, it occurs an up-regulation of NMDA receptors causing glutaminergic hyperactivity in the CNS during periods of abstinence that may lead to anxiety, delirium, and seizures **(**Preuss et al. 2017**;** Becker, Ehret and Kirsch, 2017**)**.

Gamma-aminobutyric acid (GABA) is the important in the balance of the CNS depressant pathway. Alcohol increases the action of this neurotransmitter, as it mimics its action on α-type GABAergic receptors. At the moment GABA connects to the receptor, there is an opening of the chlorine and ion channels and with consequent neuronal hyperpolarization. During chronic use of ethanol, it is believed that down-regulation of α-GABAergic receptors is generated, generating alcohol tolerance and greater difficulty in the action of this neurotransmitter **(**Preuss et al, 2017**;** Lucchese et al, 2017**)**.

The reward system belongs to the mesocorticolimbic circuit, where the production of pleasurable memories and stimuli occurs through the secretion of dopamine by receptors present therein **(**Lowenstein and Velazquez-Ulloa, 2018**)**. The mechanism with which alcohol interferes in the reward system is derived from interaction in other receptor and neurotransmitter chains such as GABA (inhibitory), Glutamate (N-methyl-D-aspartate), Opioid (pleasure and analgesia) and Serotonin (mood-bound, 5-HT) **(**Orywal et al, 2017**)**. In addition, alcohol metabolites elevate the spontaneous activity of the ventral tegmental area, substantia nigra, and nucleus accumbens (mesocorticolimbic circuit) – brain regions rich in dopamine **(**Naassila, 2018**)**.

It is believed that exposure to ethanol increases the expression of the tyrosine hydroxylase gene and its phosphorylation, which leads to greater dopamine synthesis since tyrosine is a precursor of this neurotransmitter. After chronic and continuous exposure to alcohol, it is possible to observe the degradation of the enzyme tyrosine hydroxylase with a reflex decrease, leading to a reduction in dopamine levels **(**Kawahata et al, 2017**)**.

Physiologically, the hypothalamus secretes corticotropin-releasing hormone (CRH) and vasopressin inducing the production of adrenocorticotropic hormone (ACTH) by the pituitary gland. As a result, there will be a secretion of cortisol through the adrenal cortex. Cortisol exerts an effect on its receptors at the systemic level. In the receptors of the Hypothalamus-Hypophysis-Adrenal axis cortisol leads to negative feedback for synthesis and release of CRH and ACTH. In individuals with major depressive disorder and alcohol users, this negative feedback regulation does not occur. In this way, an increase in the activation of the Hypothalamic-Hypophysis-Adrenal axis leads to hypercortisolism. This phenomenon occurs while the individual is still addicted and consume alcohol to stop the negative effects of abstinence, and not for simple pleasure **(**Rachdaoui and Sarkar, 2017**;** Blaine et al, 2016**)**.

The use of ethanol in adolescence may result in cognitive and psychic deficits in adulthood. This occurs because neurotoxicity causes an inflammatory process destroying white and gray matter during brain maturation in youth. In fact, the use of alcohol in this age group can cause worsening in school performance, since two ethyl alcohol poisonings in this period are capable of permanently altering the synaptic plasticity in the hippocampus, a cerebral region fundamental to the learning process and memory formation.

Chronic exposure to ethanol causes long-lasting changes in synaptic transmission and neuronal excitability – also known to have long-term synaptic plasticity. These modifications are defined as an increase/decrease or potentiation/depression of synaptic activity. These phenomena of plasticity are currently the best neurobiological substratum of learning and memorization mechanisms. The chronic effect of alcohol on this basis of memory processes induces the formation of a pathological memory, which partly elucidates the motive for alcoholics to present relapses even after long

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periods of abstinence or low exposure to the substance **(**Naassila, M. 2018**).**

IV. CONCLUSION

The consumption of alcoholic beverages has followed the history of humanity – deeply rooted in many cultures and part of countless people's lifestyle nowadays. Alcoholism is considered a public health problem not only in Brazil but all over the world. The systemic effects of ethanol consumption are countless and can lead to death. Therefore, alcoholic patients need a multidisciplinary team of professionals who take an individual approach so that all the disorders caused by this pathology can be identified so that they can have better clinical management, better prognosis, and improvement in their lives.

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