Haematological Changes in Alcohol and Substance Use Disorders- An Overview

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Abstract

Alcohol and Substance use remains a worldwide social problem. There is an increasing awareness that alcoholics and substance abusers do show some haematological abnormalities (e.g., hemoglobin, white blood cells count, mean corpuscular volume, mean corpuscular haemoglobin concentration, red blood cells count, hematocrit). Consequences of these haematological abnormalities can result in serious medical complications. The aim of this paper is to present an overview of haematological changes in alcohol and substance use disorders. This may be beneficial for defining the homeostasis condition of the body, which leads to indications for treatment approaches.

Keywords

Alcohol, Substance use, Hematological changes

Introduction

Substance use disorders cause tremendous burden to health care systems and society world-wide. As per the World Drug Report (2019) [1], about 35 million people worldwide suffer from drug use disorders. Disorders due to illicit drug use accounted for 10.9% of the DALYs caused by mental and substance use disorders and alcohol use disorders accounted for 9.6% [2]. These drugs can be consumed either by inhalation, injection, or by ingestion. Alcohol and Substance use changes the body functions by influencing endogenous constituents of the bodies [3]. These substances, when cross the blood-brain barrier on ingestion, may affect the brain function either depress or stimulate its activity and temporarily alter the chemical milieu of the brain. Long-term use of these addictive substances leads to serious damage to the nervous system and internal organs. Moreover, illicit drug uses are commonly linked with aplastic anaemia, bone marrow repression and variety of systemic disorders [3]. Hence, early diagnosis of these disorders and identification of the complications they result in is important. Haematology is the branch of medicine that deals with blood, blood-forming organs and blood disorders. This article summarizes current information on the haematological changes that are observed in different substance use disorders and the utility of these changes in clinical assessment.

Overview of Substances

Alcohol

Alcohol is the most commonly used worldwide. Alcohol consumption is one of the leading causes of death. Chronic alcohol intake can interfere with various physiological, biochemical and metabolic processes of the blood cells and affect multiple organ systems. Alcohol use, especially in heavy drinkers, can cause different metabolic derangements. Haematological adverse effects of acute and chronic alcohol use result from both direct and indirect effects [4,5]. The direct consequences include toxicity to the blood-forming organs (viz. bone marrow); the blood cell precursors; and the mature Red Blood Cells (RBC’s), White Blood Cells (WBC’s), and platelets, resulting in fewer than-normal or non-functional mature blood cells.

Alcohol’s indirect effects include metabolic or physiological alterations resulting in liver disease and nutritional deficiencies such as folate deficiencies that...
impaired the production and function of various blood cells [4-6]. Folate deficiency also has an important role in the pathogenesis and progression of alcohol-related liver disease [7]. Moreover, Liver damage secondary to alcohol abuse also impacts red blood cells and the hemostatic mechanisms. These direct and indirect effects of alcohol can result in serious medical complications among alcohol abusers. For instance, anaemia resulting from diminished RBC production and impaired RBC metabolism and function causes fatigue, shortness of breath, light headedness, and even reduced mental capacity and abnormal heartbeats in alcoholics. It has been found that alcohol interferes with the production and function of white blood cells. The number of WBC’s decreases (especially neutrophils) which increases the risk of serious infection. Also, the platelet (PLT) production gets impaired resulting in interference with blood clotting. This may lead to symptoms ranging from nose bleeding to bleeding in the brain (i.e., hemorrhagic stroke). Finally, alcohol-induced abnormalities in the plasma proteins, required for blood clotting can lead to the formation of blood clots (i.e., thrombosis) [4]. Evidence is there to suggest that alcohol abuse can cause bone marrow suppression, or ethanol has cytotoxic effects. These includes myelosuppression that is accompanying with slight reduction in all blood cells, blood loss from gastrointestinal tract, malnutrition etc [8]. Among the mechanisms explored for the effect of alcohol is the formation of adducts by acetaldehyde with cellular proteins [9]. These altered proteins have been postulated to evoke an immune reaction as evidenced by the presence of IgM and IgG antibodies against them. Studies suggest that consumption of alcohol causes changes of Complete Blood Counts (CBC). A study from India shows significant reductions of haemoglobin, RBC, WBC, haematocrit and significant elevations in MCV and MCH among alcoholics [10]. Another study from, India, compared the changes in the complete blood count in 30 young male subjects between 20-40 years of age group who consumed two to three units of alcohol on a daily basis with abstainers of the same age group [11]. The findings suggest that drinking of alcohol even for a short or moderate duration can affect various hematological parameters like platelet count and Mean Corpuscular Volume (MCV). Furthermore, another study from North India examined the haematological profile of alcohol dependent subjects [12]. The results showed an increase in erythrocyte Mean Cell Volume (MCV), Mean Corpuscular Haemoglobin (MCH), and a decreased mean value of RBC, total leucocyte and platelet counts, particularly among those with higher amount of alcohol consumption. In another study from South India the haematological parameters were examined in male alcoholics. The results were in line with the earlier report which suggested that the MCV was increased in the patients with alcohol dependence either co-morbid with tobacco dependence or without, compared to normal subjects [13]. Recently, a cross-sectional study has been published in which comparison of haematological parameters between alcoholics and non-alcoholics were done. The findings indicated that mean RBC count, mean MCH, MCHC were normal among the non-alcoholic group and decreased among moderate alcoholics and more so with severe alcoholics and a similar type of result was also seen with total count and platelet count [14]. A study from Japan attempted to characterise the change in the white blood cell counts with varying alcohol consumption levels as it has been seen that lower number of white blood cells has been associated with a decreased risk for chronic heart disease [15]. The common abnormalities that are associated with alcohol abuse with respect to duration of alcohol abuse and the quantity of alcohol consumed are anaemia, leucopenia and thrombocytopenia [8]. Several studies have tried to explain the mechanism through which alcohol causes these changes in blood parameters. Anemia may be caused by a patient’s poor nutritional status coupled with poorer access to health care. This resulted in chronic infections causing anemia of chronic disease, through blood loss from gastrointestinal bleedings, through splenic sequestration and destruction of cells in hyper-splenic from portal hypertension [16,17]. The findings suggest that the development of megaloblastic haematoipoiesis in alcoholics is due to the induction of folate deficiency. Besides folate depletion, direct toxic effect of alcohol on erythropoietic precursors is reflected by the presence of normal plasma and erythrocyte folate levels in several patients with megaloblastic change. Another important effect of alcohol is in haematopoiesis in the marrow. Ringed side oblasts are seen in the marrow and the marrow might be hypoplastic or even aplastic [18]. A finding that precedes anaemia is macrocytosis, the mechanism of which is not known [19]. This result in cell sizes ranging from 100-110 falls this finding has to be differentiated from megaloblastic anaemia in which cell sizes generally exceed that seen in alcohol use. The poor immunity to infections in alcohol dependent subjects may be the result of both the decrease in neutrophil number as well as faulty functioning [20]. The decreased counts may be caused due to marrow hypoplasia or hypersplenism. The effects on the blood platelets are similar with effect on both thrombocyte formation as well as functioning. The platelet count rarely falls below 10,000/mm³ Abstaining from alcohol results in a rebound thrombocytosis in the first two weeks, counts may reach up to 600,000/mm³ [21]. Alcohol use has also been clearly observed with increased iron stores specially in the liver resulting in an iron overload state [22]. This adds to the oxidative stress that plays a part in the development of hepatic cirrhosis.

**Tobacco**

Tobacco use remains a global public health problem. Each year, tobacco use is responsible for approximately
Cannabis also reduced [33]. It is still uncertain whether tobacco-
and dendritic cells in the alveolar parenchyma [32]. The ef-
flects components of innate immunity. It increases the
fect of release of catecholamines on WBCs or the in-
flammation caused by smoking in the respiratory tract.
The cessation of smoking for periods longer than one
year has shown reversal of increased WBC counts [25].
Although several studies have observed a positive as-
so associations between smoking and total white blood cell
counts, there have been some conflicting results for the
subpopulations [23,25,26]. Also, conflicting results have
been reported in the association between smoking and
thrombocytes and some red blood cell indices too [26-
29].

This causes the impaired oxygenation of tissues and
change in haematological parameters. Smoking also
has significant effects on immunity, some of which are
mediated through changes in the functioning of the T
lymphocytes. Smokers have decreased number of CD4+
ve t cells, while passive smoking increases the number
of naive CD4+ ve t cells in peripheral blood [30]. The
regulation of immune responses has been studied in
smokers with Chronic Obstructive Pulmonary Disease
through studying the changes in the sub-populations
of helper T cells. It has been found that smokers with
COPD have an increased number of Th17 cells, and that
smokers with and without COPD had increased number
of Th1 and Treg cells [31]. Smoking also adversely ef-
ects components of innate immunity. It increases the
numbers and alters the distribution of Langerhans cells
and dendritic cells in the alveolar parenchyma [32]. The
numbers of Natural Killer cells and the cytokines pro-
duced by them, such as INF-gamma and TNF alpha are
also reduced [33]. It is still uncertain whether tobacco
smoking causally influences the hematopoietic system.

Cannabis

There are a number of animal studies that looked
into changes in haematological parameters after expo-
sure to cannabis through different routes [34,35]. How-
ever, human studies are few and commonly have the
limitation of small sample sizes. The effect of cannabis
used through the smoking route on haematological pa-
rameters has been studied. Oseni, et al. [36] investigat-
ed the effect of marijuana smoking on haematological
parameters between smokers and non-smokers. The
findings suggest that the values observed for total leu-
cocytes, neutrophil, lymphocyte, monocyte and plate-
let counts, though in normal range, were marginally
lower in smokers, whereas values observed for PCV,
haemoglobin and eosinophil were marginally higher.
A published study from India [37] showed eosinophil
counts to be high in 6% of cases, and neutrophil count
abnormalities in 7.5% of subjects, which support pre-
vious studies on cannabis users [38]. The lymphocyte
counts showed a normal level while low mean relative
monocyte count was observed [36]. Another study from
Pakistan compared Hb concentration, RBC count, WBC
count and platelet count between cannabis smokers
and healthy controls. They found significant increase in
the leucocyte count of cannabis smokers as compared
to controls. Also, eosinophils and monocytes values
were significantly lower as compared to the control
group. The study results showed slightly lower haemo-
globin values in cannabis smoker group as compared to
control group which could be due to poor nutrition of
the smokers [39]. These findings suggest that cannabis
usage results in marked differences in some haema-
tological parameters which may lead to inflammation,
reduced immunity and ability to fight infections by users.
A study from Turkey investigated alterations of the he-
matologic cells in synthetic cannabinoid users [40]. They
found synthetic cannabinoid user group differed signifi-
cantly from a control group in terms of WBC, DLC, MPV,
MCH, MCV and RDW. The MPV and the percentage
of lymphocytes were lower in the group of synthetic can-
nabinoid users and the TLC, MCH, MC, RDW were high-
er compared to the control group. The findings suggest
that chronic use of synthetic cannabinoids can lead to
deterioration of hematopoietic cells. Thus, recovery of
subclinical haematological parameters should be con-
sidered in cannabis use disorder patients. The health
impact of cannabis-induced immunomodulation is still
unclear and additional studies are needed in this area.

Opioids

Haematological parameters have been widely stud-
ied in population of opioid users. Most of these stud-
ies are cross-sectional in design. Literature reveals that
chronic use of opioids alters the blood homeostasis via
effects on the hematologic series [41]. Haghpanah, et
al. [42] reported that heroin addicts had significantly
increased neutrophil count (NEUn), Mean Corpuscular
Volume (MCV), and Hematocrit (HCT), while they had a
significant reduction in lymphocytes (LYMn) and mean
corpuscular hemoglobin concentration (MCHC). It is also
observed that they have an increase in terms of mean
platelet volume (MPV) [41]. Furthermore, decrease in
RBC lead to increase in MCV, hemoglobin (HGB), HCT,
Red Distribution Width (RDW) compared to the healthy
individuals [43]. It has been found in some studies that
haemoglobin, haematocrit, and platelet count were
comparable in a group of opioid users and a group of
healthy controls [44]. However, there was no differ-
ence in the parameters of people who were enrolled
in methadone maintenance programs when compared with those who were not in maintenance treatment programs. Another study, with a larger sample of 180 males who were referred for a 3 month treatment program, examined the haematological parameters of people who were dependent on heroin or opium for at least a period of two years and those who abstained for at least a period of 1 month [42]. The results showed no difference in the RBC among the groups of dependent, withdrawal or control population. The WBC was significantly increased in the dependent group compared to the controls. The neutrophil and monocyte counts showed a significant reduction whereas the lymphocyte count was significantly increased in the opioid dependent group compared to the controls. Haematocrit level showed a significant reduction whereas the lymphocyte count was significantly increased in the opioid dependent group compared to the controls. In inhalant-abusing adolescents living in Istanbul, Turkey [60]. The findings showed no significant relation between volatile abuse and haematological parameters. Published research from India shows low hemoglobin in 25% of inhalant users. Neutrophils, lymphocytes, eosinophils, and monocytes were elevated beyond normal in 10.8%, 6.5%, 15.2%, and 7.5%, respectively. There was no evidence of leukopenia. The study adds to the limited date available on the treatment-seeking inhalant users from Indian settings and additional studies need to done to examine the pattern of inhalant use in larger samples, across multiple sites in a prospective manner [61].

Inhalants

Inhalant abuse is on rise and is a serious drug problem worldwide, particularly in disadvantaged populations and among adolescents. Inhalants are volatile substances that produce chemical vapours that can be inhaled intentionally to induce a psychoactive, or mind-altering euphoric state. These substances have the potential to cause major physiological and neurological damage. The substances inhaled are often common household products that contain volatile solvents correction fluid, adhesive, paint thinner and nail polish remover. Some of the volatile substances in these products include toluene, chloroform, propane, acetone and many halogenated hydrocarbons. The diagnosis of inhalant abuse relies almost entirely on a thorough history and a high index of suspicion [55,56]. No specific laboratory tests confirm solvent inhalation. For inhalant intoxication treatment is generally supportive, because there are no reversal agents. Available research reports suggest that inhalant use may be associated with substantial haematological, renal, hepatic, and neurological morbidity and mortality [57-59]. Adverse effects of inhalants include aplastic anemia, bone marrow suppression, and leukaemia are among the haematological [57]. Long-term inhalant use can cause bone marrow suppression, leading to leukopenia, anemia, thrombocytopenia, and hemolysis [58,59]. Study from Turkey evaluated the haematological and biochemical changes in inhalant-abusing adolescents living in Istanbul, Turkey [60]. The findings showed no significant relation between volatile abuse and haematological parameters. Numerous clinical observations support the notion that substance abusers do show some haematological-
cal abnormalities (e.g., haemoglobin, white blood cells count, mean corpuscular volume, mean corpuscular haemoglobin concentration, red blood cells count, hematocrit) and that can lead to host tissues organ dysfunction. Routine haematology investigations may be beneficial for defining the homeostasis condition of the body, which may suggest to treatment approaches. There is a need to carry out further research work on various haematological and other health-related effects associated with illicit substance abuse. This may lead to a better understanding of the haematological effects in alcohol and substance abusers.

References


