Minerva Medica
EDIZIONI MINERVA MEDICA

Thrombosis following Covid-19 Vaccination: a possible role of alcohol consumption? A Suggestion from the Italian Society on Alcohol

Gianni TESTINO, Alice MATONE, Silvia GHIRINI, Rinaldo PELLICANO, Fabio CAPUTO, Emanuele SCAFATO

Minerva Medica 2021 Jun 18
DOI: 10.23736/S0026-4806.21.07670-9

Article type: Editorial

Article first published online: June 18, 2021
Manuscript accepted: June 1, 2021
Manuscript received: May 31, 2021

Thrombosis following Covid-19 Vaccination: a possible role of alcohol consumption? A Suggestion from the Italian Society on Alcohol

Gianni Testino[1,2], Alice Matone[3], Silvia Ghirini[3], Rinaldo Pellicano[4], Fabio Caputo[2,5], Emanuele Scafato[2,3] and the Executive Committee of the Italian Society on Alcohol (SIA)

[1]Unit of Addiction and Hepatology/Alcohological Regional Centre, ASL3 c/o IRCCS San Martino Hospital, Genova, Italy
[2]Italian Society on Alcohol, Bologna, Italy
[3]Italian National Institute on Health, Roma, Italy
[4]Unit of Gastroenterology, Molinette Hospital, Torino, Italy
[5]Unit of Internal Medicine, Cento Hospital (Ferrara) and University of Ferrara, Italy

Correspondence: Gianni Testino, SC Patologia delle Dipendenze ed Epatologia, Centro Alcologico Regionale; ASL3 c/o Padiglione 10, Ospedale Policlinico San Martino, Piazzale R. Benzi 10, 16132 Genova, Italy
gianni.testino@asl3.liguria.it

According to the European Medicines Agency (EMA), 30 cases of thromboembolic events (mainly venous) have been reported by March 10, 2021, among the approximately 5 million recipients of the Oxford-AstraZeneca Covid-19 vaccine in the European Economic Area. Moreover, EMA affirmed that "the number of thromboembolic events in vaccinated people is no higher than the number seen in the general population" [1]. Recently a Danish group have stated through preliminary data, that this association is coincidental[2].

The well-known predisposing conditions for venous thrombosis include: oral contraceptives consumption, pregnancy, puerperium, prothrombotic conditions, ear-nose-throat infections, central nervous system infections, other infections, central nervous system disorders, myeloproliferative disorders, cancers, inflammatory diseases (for example systemic lupus erythematosus and Behcet's disease), vasculitis, hyperlipidemia, diabetes mellitus, blood vessels abnormalities and alcohol consumption[3-5].

The Paul Ehrlich Institute reported cases of sinus or cerebral vein thrombosis (CVT) 4 to 16 days after Oxford-AstraZeneca Covid-19 vaccination[6].
CVT is recognized as a distinctive cause of cerebrovascular accident in the young. It results from the occlusion of a venous sinus-or cortical vein, that results in cortical venous infarction with petechial or overt hemorrhagic perivascular venous infarction[5,6].

The hypothesized pathogenesis for vaccination-associated cases of CVT provides the formation of antibodies against platelet antigens following a severe inflammatory and immune reaction.
Since thrombocytopenia is observed in these cases, it is supposed that which an immunological event should be the cause of the tendency to thrombosis[6].
It is known that alcohol consumption causes both an intense inflammatory reaction and an alteration of the immune system (both innate and acquired). Furthermore, this habit can be associated with

thrombocytopenia and disseminated intravascular coagulation. These phenomena are independent of the presence of any associated alcohol-related internal comorbidity (i.e. cirrhosis)[7,8].

The administration of alcohol to healthy volunteers induces an increase in thrombocyte aggregation. Hillbom et al. report that in alcohol addicts there is a 4-fold increase in platelet aggregation associated with thromboxane B2[19].

Zamir et al. reported a case of binge alcohol drinking as a possible cause of thrombotic thrombocytopenic purpura[10].

Experimentally, it has been shown that after infusion of a 5% alcohol solution there is a reduction of platelets in about 4-6 hours[11,12].

Ethanol induces changes in serotonin and catecholamine metabolism in association with alterations in cortisol levels. This leads to increase aggregation and platelet destruction. Other mechanisms are the following: accelerated degradation and apoptosis, direct toxicity, bone marrow changes (acetaldehyde can damage DNA in bone marrow cells)[13,14].
It has also been hypothesized that the cause of venus sinus thrombosis may be dehydration and resultant hyperviscosity due to hazardous/harmful alcohol consumption[13,14].
The relationship between alcohol, autoimmunity and platelet damage is contradictory, but proven. Mandyam et al. for istance found a direct effect of AUD on PECAM-1 (platelet endothelial cell adhesion molecule-1) and on oligodendrogenesis[15].
It is therefore clear that ethanol usually has a negative effect on platelet function. This results in coagulation disorders.

Three important epidemiological considerations should therefore be carefully considered:

- according to the new criteria in the Diagnostic and Statistical Manual of Mental Disorders 5th Edition, the prevalence of alcohol use disorders (AUDs) is 20-30% in men and 10-15% in women worldwide;
- thrombocytopenia with possible association with coagulation disorders occours in 3-43% -of -AUDs outpatients and in 14-81% of patients who require hospitalization[11];
- Covid-19 vaccination of the entire population is underway.

In light of the large numbers that characterize these three considerations, it is possible that thrombosis cases (especially in the brain) may occur in conjunction with vaccination in patients with hazardous / harmful alcohol consumption.

To date, the data relating to thrombose cases are not yet well known to the scientific community.
The statements of the institutional scientific authorities, reported by the media, inform us, however, that the cases occurred in young and healthy subjects (mainly females).

If these data will be confirmed, the files should be reviewed (although complicated) for any associated risk factors with particular attention to the use of alcohol.

However, it is possible that, in the event of such adverse events finding a direct link with the administration of the Covid-19 vaccine, alcohol consumption could favor its occurrence for the overexposed reasons. This possibility must also be a reason for study because of the widespread consumption of alcohol in society.

In the coming months, Covid-19 vaccines built with a similar technology to that of the Oxford-AstraZeneca vaccine will be used in Europe.

For this reason, in view of the high chance that an alcoholic patient will be vaccinated, it is advisable to suggest that alcohol consumption should be correctly assessed[16].
In fact, it is well known that alcohol consumption is underestimated by both patients and healthcare professionals.

The alcoholic anamnesis should be studied more in-depth.
It is, therefore, appropriate to identify the consumption of alcohol in clinical practice using simple and validated tests. CAGE (Cut-down, Annoyance, Guilty, Eye-opener) and AUDIT (Alcohol Use Disorders Identification Test) are among the best known ones. However, CAGE does not perform well at highlighting drinkers who consume risky amounts of alcohol but who are not dependent. Thus, CAGE can be used at a later stage as an in-depth study of suspected alcohol dependence.
In light of this, we recommend paying more attention to alcohol consumption by using AUDIT. The test's sensitivity and specificity (92% and 93%, respectively) are very high, this fact allows identifying patients affected by hazardous or harmful consumption who are not alcohol addicted.
AUDIT consists of ten questions. Each question provides a response mode on a 5-point scale: each response has a value from 0 to 4 points. If the score is equal to or less than 7 points, consumption is low risk; if it is between 8 and 15 points, consumption is risky; if it is between 16 and 19 points, consumption is harmful; if it is equal to or higher than 19 points, there is an addiction. Each of these phases must be addressed differently.
By risky consumption, we mean a level of consumption or a way of drinking that can cause damage in cases where these habits persist (men: 21-60 g / day; women: 11-40 g / day). By harmful consumption, we mean a diet that involves both physical and psychological damage (men > 60 g / day, women > 40 g / day. By binge drinking, we mean five or more units of alcohol in two hours for men and four units or more of alcohol in two hours for women) [16,17].

In conclusion, the Italian Society on Alcohol (SIA) advise the scientific community of review the cases available to date to better define the lifestyle, with particular emphasis to alcohol consumption, of patients with thrombotic phenomena in after the Oxford-AstraZeneca vaccine administration and to the operators currently operating in the vaccination activity to identify any possible presence of harmful / hazardous consumption in conjunction with the inclusion in the list to access vaccination. Considering that platelet levels usually stabilize about a week after alcohol consumption[11], as a precaution it is advisable to abstain from alcohol consumption for about 15 days.
In addition, the Community of researchers is advised to investigate the possible synergistic effect of alcohol and vaccines in promoting thrombocytopenia and coagulation disorders.

References

1) Wise J. Covid-19: European countries suspend use of Oxford-AstraZeneca vaccine after reports of blood clots. BMJ 2021; 372: n699
2) Ostergaard SD, Schmidt M, Horvàth-Puhò E, Thomsen RW, Sorensen HT. Thromboembolism and the Oxford-AstraZeneca Covid-19 vaccine: side effect or coincidence? The Lancet 2021; 397: 1441-3

3) Moulakakis KG, Sfyroeras G, Pavlidis P, Besias N, Maras D. Hypercoagulable state due to alcohol-paracetamol syndrome producing acute limb ischemia. Vasc Endovascular Surg 2007; 41: 362-5
4) Malarcher AM, Giles WH, Croft JB, Wozniak MA, Wityk RJ, Stolley PD et al. Alcohol intake, type of beverage, and the risk of cerebral infarction in young women. Stroke 2001; 32: 77-83
5) Singh H, Talapatra P, Ray S. Gupta V. A rare presentation of acute alcohol intoxication, subarachnoid haemorrhage and cortical venous sinus thrombosis. J Neurol Res 2012; 2: 62-4
6) Oldenburg J, Klamroth R, Langer F, Albisetti M, von Auer C, Ay C et al. Diagnosis and management of vaccine-related thrombosis following AstraZeneca Covid-19 vaccination: guidance statement from GTH. Hamostaseologie 2021; doi: 10.1055-a/1469-7481
7) Testino G, Pellicano R. Alcohol consumption in the Covid-19 era. Minerva Gastroenterol Dietol 2020; 66: 90-2
8) Bailey KL, Samuelson DR, Wyatt TA. Alcohol use disorder: a pre-existing condition for Covid-19? Alcohol 2021; 90: 11-7
9) Hillbom M, Kangasaho M, Lowbeer C, Kaste M, Muuronen A, Numminem H. Effects of ethanol on platelet function. Alcohol 1985; 2: 429-32
10) Zamir D, Polychuck I, Leibovitz I, Reitblat T, Ducach A, Lugazzy G. Thrombotic thrombocytopenic purpura due to alcohol binge drinking. Eur J Int Med 2004; 15: 262-3
11) Silczuk A, Habrat B. Alcohol-induced thrombocytopenia: current review. Alcohol 2020; 86: 9-16; Post RM, Desforges JF. Thrombocytopenic effect of ethanol infusion. Blood 1968; 31: 344-47
12) Post RM, Desforges JF. Thrombocytopenic effect of ethanol infusion. Blood 1968; 31: 344-47
13) Yokoyama A, Yokoyama T, Mizukami T, Matsui T, Kimura M, Matsushita S et al. Platelet counts and genetic polymorphisms of alcohol dehydrogenase-1B and aldehyde dehydrogenase-2 in Japanese alcoholic men. Alcohol Clin Exp Res 2017; 41: 171-8
14) Smith C, Gasparetto M, Jordan C, Pollyea DA, Vasiliou V. The effects of alcohol and aldehyde dehydrogenases on disorders of hematopoiesis. Advances in Experimental Medicine and Biology 2015; 815: 349-359
15) Mandyam CD, Villalpando EG, Steiner NL, Quach LW, Fannon MJ, Somkuwar SS. Platelet endothelial cell adhesion molecule-1 and oligodendrogenesis: significance in alcohol use disorders. Brain Sciences 2017; doi: 10.3390/brainshi7100131
16) Scafato E, Caputo F, Patussi V, Balbinot P, Addolorato G, Testino G. The undertratment of alcohol-related liver diseases among people with alcohol use disorder. Eur Rev Med Pharmacol Sci 2020; 24: 974-82
17) Testino G, Balbinot P, Pellicano R. Substances use disorders and liver injury: a concise review. Minerva Gastroenterol 202; doi: 10.23736/S2724-5985.21.02885-0

Authors contribution Section

Conflicts of interest. The author certifies that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors contributions. Conceptualization: Gianni Testino, Fabio Caputo, Emanuele Scafato; methodology: Gianni Testino, Alice Matone, Silvia Ghirini, Claudia Gandin, Emanuele Scafato, Rinaldo Pellicano; data collection: Gianni Testino, Emanuele Scafato; writing: Gianni Testino, Alice Matone; review and editing Rinaldo Pellicano

The author read and approved the final version of the manuscript.