The Effect of Drugs of Abuse and Alcohol Can Lead to Ocular Disorders: A Systematic Meta-Analysis

Rodiah Rahmawaty Lubis¹*, Anna Mira Lubis², Hamzah Sulaiman Lubis³, Yuliani Mardiati Lubis⁴

¹Department of Ophthalmology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia
²Division of Hematology and Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia
³Department of Surgical Oncology, Haji Mina Hospital, Medan, Indonesia
⁴Department of Otorhinolaryngology-Head and Neck Surgery, Faculty of Medicine, Universitas Prima Indonesia, Medan, Indonesia

Address Correspondence to Rodiah Rahmawaty Lubis, rahma.lubis@yahoo.com

Received 27 July, 2020; Revised 11 September, 2020; Accepted 18 September, 2020

Copyright © 2020 Rodiah Rahmawaty Lubis, et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Background & Aim: The effect of those drugs and alcohol on the ocular can range from mild to severe that can cause visual loss or even blindness. The effects of drug and alcohol abuse remain unclear and were studied in this meta-analysis.

Methods: Prospective studies that randomised heavier alcohol consumption to either were included. The primary outcome was odds ratio (OR) with a 95% confidence level risk of early AMD. Methodological quantitative was assessed using STATA software.

Results: Patients with more than three drinks per day were classified in the highest category in all studies. The six studies reported an increased risk of early AMD in relation to heavy alcohol consumption, but only in one study found it to be statistically significant. There was a borderline heterogeneity between studies (p 0.698; <50%); therefore the results are presented in the form of a fixed effect.

Conclusion: Heavy alcohol consumption more than three times the standard drink per day is associated with an increased risk of early Age-related macular degeneration (AMD). Although this relationship appears to be independent and is thought to be related to smoking as a confounding effect in this meta-analysis.

Keywords

Heavy alcohol consumption, AMD, Drug and alcohol abuse

1. Introduction

Drug abuse is rife in our society. Many cases in which people fall to death due to use drugs a lot without awareness of its hidden danger. Drug abuse or better known as drug abuse is use of a drug in amounts or by different methods for any purpose which are harmful to the individual or others. The effect of drug and alcohol abuse may lead to ocular and non-ocular manifestation.

The effect of those drugs on the ocular can range from mild to severe that can cause visual loss or even blindness. It depend on the dose, routes of administration such as enteral or oral ingestion, and parenteral such as nasal inhalation, intravenous injection, or topical application. Injection drug use can result in a variety of severe ocular conditions. Hematogenous dissemination of various fungi and bacteria may produce endophthalmitis with resultant severe visual loss [1–3]. Some study related the alcohol consumption to ocular manifestation. Decreased tear production, tear film instability may trigger the signs and symptoms of dry eye syndrome were describe following ethanol ingestion. Early cataract formation, significant degeneration of the ocular surface epithelium, glaucoma, age-related macular degeneration, open globe injury, etc may also happened due to heavy consumers of alcohol [4–7].

Thiamin deficiency due to severe malnutrition seen in chronic alcoholics patients and caused Wernicke’s encephalopathy. The classic clinical triad of Wernicke’s encephalopathy is ophthalmoplegia, ataxia, and confusion. Nystagmus is one of the extra ocular motility disturbances [8].

Other drugs abuse most often associated with ocular manifestation are amphetamines, barbiturates, benzodiazepines, cannabis, cocain, hallucinogens, methaqualone and opioids. Corneal damage and pupillary
mydriasis, retinal vascular diseases were reported as ocular side effect of the use of topical anesthetics, cocaine and methamphetamine [9–11].

Hallucinations are often a favourable effect of various drugs of abuse. Sympathomimetics effect causing not only vascular occlusive and hemorrhagic disease within the eye, but also ischemic stroke and intracerebral and subarachnoid haemorrhaga. Those affect are mostly occur in the use of cocaine and methamphetamine [12].

2. Methods

The meta-analysis randomized controlled trials (RCTs) was performed according to the reporting guidelines implied by the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE).

2.1. Search strategy and study eligibility

We conducted a PubMed, google scholar, sciencedirect database search for articles published between January 2000 to May 2020. The search term used in PubMed, google scholar and sciencedirect included (“drug abuse (All Fields) and ocular (All Fields)”). The included entries have an abstract available, which has to be either in English. Furthermore, investigations had to be performed in humans (or human tissue) and not in animals. Titles and abstracts were scanned to select eligible articles in which the relationship between drug abuse and ocular disorders was studied without any restricting selection criteria. A search was also carried out on the ClinicalTrials.gov website to identify completed but unpublished studies. All searches are carried out independently and completed with discussion.

2.2. Data extraction and quality assessment

The data entered consists of: (1) Country; (2) Patient characteristics (3) Type of research carried out; (4) Treatment protocol (intervention and comparison, sample size); (5) Measured results and effects. If there is insufficient data in the article, we contact the first author or the author in accordance with the information needed, but if the article's author does not respond within 4 weeks an in-depth search of the available information data will be carried out.

2.3. Data synthesis and analysis

The results of the research shown are presented as a odds ratio (OR) with a 95% confidence level. Meta-analyzes were carried out to calculate the estimated effect of the relationship between drug abuse and ocular disorder. The heterogeneity of the meta-analysis is measured by calculating I². Fixed effect models are used when studies are conducted homogeneous meta-analyzes or with low heterogeneity. For studies with low heterogeneity, a fixed effect models was used.

3. Result

A total of 221 studies were published between 2010-2020 with keyword search, 3 journal in not english form, 212 articles relevant to keyword search, but only 6 articles randomized controlled trials that fit the inclusion and exclusion criteria (Figure 1).

Inclusion and exclusion criteria were defined in all research studies included in this meta-analysis study. Point estimates for alcohol consumption in six studies [13–18], comparing the highest versus lowest consumption categories for early AMD, were collected and presented graphically (Figure 2). Patients with more than three drinks per day were classified in the highest category in all studies. The six studies reported an increased risk of early AMD in relation to heavy alcohol consumption, but only in one study found it to be statistically significant. There was a borderline heterogeneity between studies (p 0.698; <50%); therefore the results are presented in the form of a fixed effect.

4. Discussion

Alcohol, generally in the form of ethyl alcohol or ethanol, has an important role in human civilization for at least 8000 years. In western culture, beer and wine were the main drinks in everyday life until the 19th century [6]. In some countries, alcohol is an easy drink to get so it tends to be misused [7]. Alcohol interferes with the regulation of excitation or inhibition in the brain, so consuming alcohol can resulting in disinhibition, ataxia and sedation [4–6]. Pharmacological effects of ethanol include its effects on the onset of disease, prenatal development, gastrointestinal, cardiovascular and central nervous system. Ethanol upsets the balance of excitation and inhibition of electrical transmission in the brain, which causes disinhibition, ataxia and sedation. Tolerance to ethanol begins after chronic use which is indicated, among others, by psychological disorders and activity when alcohol consumption is stopped suddenly [8].

The increased risk of AMD is associated with heavier alcohol consumption. Our systematic review cannot investigate the J-shaped relationship. However, we show that heavy alcohol consumption is associated with an increased risk of early AMD (OR, 1.47; 95% CI, 1.10-1.95) [19]. The results of all studies in this meta-analysis agree with the negative pathophysiological effects of heavy alcohol consumption. Photoductive damage from blue light in the oxygen-filled environment of the retina, rich in polyunsaturated fatty acids, which are very susceptible to oxidation, which is thought to play a role as a pathogenesis of AMD. Alcohol has also been shown to increase oxidative stress or modify mechanisms that protect against oxidative stress, 10,11 which can lead to AMD. In addition, because antioxidants can prevent the occurrence of AMD and it has been proven in several studies that patients with intermediate AMD treated with high-dose antioxidant supplements (vitamins C and E, zinc, and carotene) have a 28% reduction in the risk of developing advanced AMD compared to placebo (OR, 0.72; 99% CI, 0.52-0.98) and heavy drinkers have lower serum antioxidant levels.
Identifying literature in Google Scholar and Pubmed (n = 221) → Excluded research (n = 212)

Screen search results (n = 9) → The study was excluded (n = 3)

Check the feasibility of full-text articles (n = 6)

Research included (n = 6)

**Figure 1:** PRISMA diagram.

**Figure 2:** Graph showing for rest plot odds ratio (OR) in age-related macular degeneration (AMD) with alcohol consumption category.
Although people often regard alcoholic drinks as stimulants, ethanol is basically a depressant of the central nervous system. As with other depressants such as barbiturates and benzodiazepines, consumption of moderate amounts of alcoholic beverages can cause anti-anxiety effects and cause loss of behavioral inhibition over a wide range of doses. Signs of intoxication in each individual varies, ranging from the effects of excitation and overflowing to uncontrolled mood changes and emotional turmoil that can be accompanied by violence. The peak concentration of ethanol in the blood can be reached within 30 minutes after ethanol ingestion in an empty stomach. The volume of distribution for ethanol is close to the total water in the body (0.5-0.7 l/kg). With an equivalent dose of alcohol orally, women have a higher peak concentration than men. This is because women have more total body water content [21].

5. Conclusion

Heavy alcohol consumption more than three times the standard drink per day is associated with an increased risk of early AMD. Although this relationship appears to be independent and is thought to be related to smoking as a confounding factor in this meta-analysis.

References

1. N. M. Bressler, Age-related macular degeneration is the leading cause of blindness, J Am Med Assoc 291 (2004), 1900–1901.
Editorial Board

DEPUTY EDITOR

Syed F. Ali
National Center for Toxicological Research
United States

Editorial and Advisory Board

Michael J. Kuhar
Emory University, United States

ASSOCIATE EDITORS

Emmanuel Onaivi
William Paterson University, United States

Emilio Ambrosio
National Distance Learning University, Spain

Jesus A. Angulo
City University of New York, United States

Eliot L. Gardner
Intramural Research Program of the National Instit
United States

Valentina G. Bashkatova
P. K. Anokhin Institute of Normal Physiology
Russia
Antonello Bonci
National Institute on Drug Abuse
United States

Herminia Alicia Brusco
University of Buenos Aires, Argentina

Jean Lud Cadet
National Institutes of Health
United States

Félix Carvalho
University of Porto, Portugal

Jian-Guo Chen
Huazhong University of Science and Technology, China

Marco Diana
University of Sassari, Italy

Peter R. Dodd
The University of Queensland, Australia

Katia Gysling
Pontificia Universidad Catolica de Chile
Chile

Glen R. Hanson
University of Utah, United States

Kazutaka Ikeda
Tokyo Metropolitan Institute of Medical Science
Japan

Raka Jain
All India Institute of Medical Sciences
India

Carlos A. Jiménez-Rivera
University of Puerto Rico, Puerto Rico

Peter W. Kalivas
The Medical University of South Carolina, United States

Hyoung-Chun Kim
Kangwon National University, South Korea
George F. Koob  
The Scripps Research Institute  
United States

Barbara Mason  
The Scripps Research Institute  
United States

John E. Mendelson  
California Pacific Medical Center Research Inst  
United States

Diane B. Miller  
Centers for Disease Control and Prevention  
United States

Eric J. Nestler  
Mount Sinai School of Medicine  
United States

James P. O’Callaghan  
CDC/NIOSH  
United States

M. Foster Olive  
Arizona State University, United States

Merle G. Paule  
National Center for Toxicological Research  
United States

Sakire Pogun  
Ege University, Turkey

Marcus Rattray  
University of Reading, United Kingdom

Abel Santamaria  
National Institute of Neurology and Neurosurgery  
Mexico

Alois Saria  
Medical University Innsbruck, Austria

Susan Schenk  
Victoria University of Wellington, New Zealand
<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aristidis M. Tsatsakis</td>
<td>University of Crete, Greece</td>
<td>Greece</td>
</tr>
<tr>
<td>Yousef Tizabi</td>
<td>Howard University College of Medicine, United States</td>
<td>United States</td>
</tr>
<tr>
<td>George R. Uhl</td>
<td>National Institutes of Health</td>
<td>United States</td>
</tr>
<tr>
<td>Ming Xu</td>
<td>The University of Chicago, United States</td>
<td>United States</td>
</tr>
<tr>
<td>Kiyofumi Yamada</td>
<td>Nagoya University, Japan</td>
<td>Japan</td>
</tr>
</tbody>
</table>
Published Articles

Comparison of the Effectiveness of Allopurinol and Methylprednisolone in Reducing Reperfusion Injury in Coronary Artery Bypass Surgery
Heru Kurniawan, Aries Perdana, Anas Alatas and Akhyar Hamonangan Nasution
Volume (2020), Article ID 236102, 5 Pages
Published: October, 2020

Influence of Alcohol and Drug Consumption on Hepatitis C Treatment with Direct-Acting Antivirals
Jose Carlos Fernandez de Canete Camacho*, Jose Maria Moreno Planas and Natalia Garcia Sanchez
Volume (2020), Article ID 236101, 7 Pages
Published: September, 2020

Liquor Sophia as a New Branding to Improve Marketing Tourism in East Nusa Tenggara Indonesia
Suwandi Sumartias*, Emeralda Ayu Kusuma and Siska Armawati Sufa
Volume (2020), Article ID 236100, 3 Pages
Published: September, 2020

The Effect of Drugs of Abuse and Alcohol Can Lead to Ocular Disorders: A Systematic Meta-Analysis
Rodiah Rahmawaty Lubis*, Anna Mira Lubis, Hamzah Sulaiman Lubis, Yuliani Mardiati Lubis
Volume (2020), Article ID 236099, 3 Pages
Published: September, 2020

The National Policy of Drug Abuse Management in Schools in South Africa: Unknown and Unimplemented
Anthony Velaphi Mokwena, Kebogile Mokwena*, Hendry van der Heever and Mathildah Mokgatle
Volume (2020), Article ID 236098, 4 Pages
Published: September, 2020

Factors Related To Alcohol Consumption Among Motorcycle Riders In Chiang Rai Province, Thailand
Watcharapong ruankham and Narongsak noosorn*
Volume (2020), Article ID 236097, 5 Pages
DOI: 10.4303/jdar/236097
Published: July, 2020

Microbial Contamination In Laru (Local Community Beverage Alcohol of East Nusa Tenggara)
Apris A. Adu and Sarci M. Toy
Volume (2020), Article ID 236096, 2 Pages
DOI: 10.4303/jdar/236096
Published: July, 2020

Impact of a Substance Abuse Rehabilitation Program on the Locus of Control of the Service User, a South African Study
Lucy Fernandes* and Kebogile Mokwena
Volume (2020), Article ID 236095, 5 Pages
DOI: 10.4303/jdar/236095
Published: July, 2020

Alcohol Modulation of Amyloid Precursor Protein in Alzheimer’s Disease
Steven A. Masi, Madhavan P. Nair, Michael Vigorito, Tinchun Chu, and Sulie L. Chang*
Volume (2020), Article ID 236094, 11 Pages
DOI: 10.4303/jdar/236094
Published: July, 2020

The Effect of Thiamine Administration on Interleukin-6 (Il-6) Enzyme, Lactate and Sequential Organ Failure Assessment (SOFA) Score in Patients with Sepsis
Akhyar Hamonangan Nasution* and Riza Stya Yulianda
 DOI: 10.4303/jdar/236093
Published: July, 2020
Journal of Drug and Alcohol Research

Country: Egypt - SIR Ranking of Egypt
Subject Area and Category:
- Medicine
- Psychiatry and Mental Health
- Psychology
  - Clinical Psychology
Publisher: Ashdin Publishing
Publication type: Journals
ISSN: 20908342, 20908334
Coverage: 2015-2020

H Index: 6
Scope

The Journal of Drug and Alcohol Research (JDAR) is a scholarly open access, peer-reviewed, and fully refereed journal dedicated to publishing sound papers on advances in the field of drug, opiate, nicotine and alcohol abuse, both basic and clinical. The journal will consider papers from all sub-disciplines and aspects of drug abuse, dependence and addiction research. Manuscripts will be published online as soon as they are accepted, which will reduce the time of publication. Because there are no space limitations or favored topics, all papers, within the scope of the journal, judged to be sound by the reviewers, will be published.
Quartiles

The set of journals have been ranked according to their SJR and divided into four equal groups, four quartiles. Q1 (green) comprises the quarter of the journals with the highest values, Q2 (yellow) the second highest values, Q3 (orange) the third highest values and Q4 (red) the lowest values.

<table>
<thead>
<tr>
<th>Category</th>
<th>Year</th>
<th>Quartile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Psychology</td>
<td>2016</td>
<td>Q4</td>
</tr>
<tr>
<td>Clinical Psychology</td>
<td>2017</td>
<td>Q3</td>
</tr>
<tr>
<td>Clinical Psychology</td>
<td>2018</td>
<td>Q2</td>
</tr>
<tr>
<td>Clinical Psychology</td>
<td>2019</td>
<td>Q2</td>
</tr>
<tr>
<td>Psychiatry and Mental Health</td>
<td>2016</td>
<td>Q4</td>
</tr>
</tbody>
</table>

SJR

The SJR is a size-independent prestige indicator that ranks journals by their 'average prestige per article'. It is based on the idea that 'all citations are not created equal'. SJR is a measure of scientific influence of journals that accounts for both the number of citations received by a journal and the importance or prestige of the journals where such citations come from. It measures the scientific influence of the average article in a journal, it expresses how central to the global scientific discussion an average article of the journal is.

Citations per document

This indicator counts the number of citations received by documents from a journal and divides them by the total number of documents published in that journal. The chart shows the evolution of the average number of times documents published in a journal in the past two, three and four years have been cited in the current year. The two years line is equivalent to journal impact factor™ (Thomson Reuters) metric.

<table>
<thead>
<tr>
<th>Year</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cites / Doc. (4 years)</td>
<td>2015</td>
</tr>
<tr>
<td>Cites / Doc. (4 years)</td>
<td>2016</td>
</tr>
<tr>
<td>Cites / Doc. (4 years)</td>
<td>2017</td>
</tr>
<tr>
<td>Cites / Doc. (4 years)</td>
<td>2018</td>
</tr>
<tr>
<td>Cites / Doc. (4 years)</td>
<td>2019</td>
</tr>
<tr>
<td>Cites / Doc. (3 years)</td>
<td>2015</td>
</tr>
<tr>
<td>Cites / Doc. (3 years)</td>
<td>2016</td>
</tr>
<tr>
<td>Cites / Doc. (3 years)</td>
<td>2017</td>
</tr>
<tr>
<td>Cites / Doc. (3 years)</td>
<td>2018</td>
</tr>
<tr>
<td>Cites / Doc. (3 years)</td>
<td>2019</td>
</tr>
</tbody>
</table>

Total Cites

Evolution of the total number of citations and journal's self-citations received by a journal's published documents during the three previous years. Journal Self-citation is defined as the number of citation from a journal citing article to articles published by the same journal.

<table>
<thead>
<tr>
<th>Year</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self Cites</td>
<td>2015</td>
</tr>
<tr>
<td>Self Cites</td>
<td>2016</td>
</tr>
<tr>
<td>Self Cites</td>
<td>2017</td>
</tr>
<tr>
<td>External Cites per Doc</td>
<td>2015</td>
</tr>
<tr>
<td>External Cites per Doc</td>
<td>2016</td>
</tr>
<tr>
<td>External Cites per Doc</td>
<td>2017</td>
</tr>
<tr>
<td>External Cites per Doc</td>
<td>2018</td>
</tr>
<tr>
<td>External Cites per Doc</td>
<td>2019</td>
</tr>
</tbody>
</table>

External Cites per Doc

Evolution of the number of total citation per document and external citation per document (i.e. journal self-citation). International Collaboration accounts for the articles that have been produced by researchers from several countries.

<table>
<thead>
<tr>
<th>Year</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cites</td>
<td>2015</td>
</tr>
<tr>
<td>Cites</td>
<td>2016</td>
</tr>
<tr>
<td>Cites</td>
<td>2017</td>
</tr>
<tr>
<td>Cites</td>
<td>2018</td>
</tr>
<tr>
<td>Cites</td>
<td>2019</td>
</tr>
</tbody>
</table>

Cites

<table>
<thead>
<tr>
<th>Year</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cites</td>
<td>2015</td>
</tr>
<tr>
<td>Cites</td>
<td>2016</td>
</tr>
<tr>
<td>Cites</td>
<td>2017</td>
</tr>
<tr>
<td>Cites</td>
<td>2018</td>
</tr>
<tr>
<td>Cites</td>
<td>2019</td>
</tr>
</tbody>
</table>

% International Collaboration

<table>
<thead>
<tr>
<th>Year</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cites</td>
<td>2015</td>
</tr>
<tr>
<td>Cites</td>
<td>2016</td>
</tr>
<tr>
<td>Cites</td>
<td>2017</td>
</tr>
<tr>
<td>Cites</td>
<td>2018</td>
</tr>
<tr>
<td>Cites</td>
<td>2019</td>
</tr>
</tbody>
</table>

Cites / Doc
External citations are calculated by subtracting the number of self-citations from the total number of citations received by the journal's documents.

### Yearly International Collaboration

<table>
<thead>
<tr>
<th>Year</th>
<th>International Collaboration</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>14.29</td>
</tr>
<tr>
<td>2016</td>
<td>0.00</td>
</tr>
<tr>
<td>2017</td>
<td>0.00</td>
</tr>
<tr>
<td>2018</td>
<td>0.00</td>
</tr>
<tr>
<td>2019</td>
<td>0.00</td>
</tr>
</tbody>
</table>

### Yearly Cited Documents vs. Uncited Documents

<table>
<thead>
<tr>
<th>Year</th>
<th>Non-citable documents</th>
<th>Citable documents</th>
<th>Uncited documents</th>
<th>Cited documents</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2016</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>2017</td>
<td>0</td>
<td>4</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>2018</td>
<td>0</td>
<td>10</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>2019</td>
<td>0</td>
<td>15</td>
<td>15</td>
<td>0</td>
</tr>
</tbody>
</table>

### Yearly Citable Documents vs. Non-citable Documents

<table>
<thead>
<tr>
<th>Year</th>
<th>Non-citable documents</th>
<th>Citable documents</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2016</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2017</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2018</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2019</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
The users of Scimago Journal & Country Rank have the possibility to dialogue through comments linked to a specific journal. The purpose is to have a forum in which general doubts about the processes of publication in the journal, experiences and other issues derived from the publication of papers are resolved. For topics on particular articles, maintain the dialogue through the usual channels with your editor.
EST MODUS IN REBUS
Horatio (Satire 1,1,106)