PSYCHIATRIA ET NEUROLOGIA JAPONICA

Special Feature Article

Simulation of the Treatment and Treatment Goal for Alcohol Dependence Comorbid with Depression

Toshikazu SAITO
Psychiatry Institute, Hakuyukai Social Healthcare Corporation
Psychiatria et Neurologia Japonica 123: 494-499, 2021

Abstract

In the symposium, we showed an imaginary case with alcohol dependence comorbid with depression and discussed therapeutic goals and medications for those cases. It has been reported that the comorbidity rate of alcohol dependence with depression is high and comorbid alcohol dependence may negatively affect on the overall response of the treatment for depressive disorders. Abstinence had been the primary goal for patients with alcohol dependence comorbid with depression. However, not only abstinence but also a reduction in alcohol consumption has been reported to improve depressive symptom of those patients. We discussed brief intervention and pharmacotherapy as treatments for those patients.

Keywords : alcohol dependence, depression, comorbidity with alcohol dependence, diagnostic criteria, therapeutic approach and goal for alcohol dependence

Introduction

The topic of this article is alcoholism associated with depression. However, the first thing that must be discussed is the changing concept of alcohol-related problems and diagnostic

criteria. This is because changes in the concept and diagnostic criteria for alcohol dependence will lead to changes in the incidence and countermeasures against comorbid depression and other psychiatric disorders. In Japan, there is a large gap between the estimated number of alcoholics based on the World Health Organization's "ICD-10 Mental and Behavioral Disorders - Clinical Description and Diagnostic Guidelines" (ICD-10) 21) and the actual number of alcoholics 10)14). Furthermore, the American Psychiatric Association's "DSM-5 Diagnostic and Statistical Manual of Mental Disorders" (DSM-5) 3) proposed the term "alcohol use disorder" to encompass the concepts of alcohol dependence and abuse, clearly lowering the diagnostic threshold. Therefore, we will review the changes in the concept of alcohol-related problems and diagnostic criteria, present a hypothetical case of alcohol dependence and comorbid depression, and discuss the treatment of alcohol dependence and comorbid depression.

I. The Actual Situation of Alcoholics in Japan

The harmful effects of excessive alcohol consumption have been recognized as a problem in recent years, and with the enactment of the "Basic Law on Measures against Alcohol Health Disorders," efforts to combat problem drinking and alcohol dependence have been further strengthened. According to a 2013 national survey of adult drinking behavior, approximately 1.07 million people experienced alcohol dependence and met the criteria for alcohol dependence according to ICD-10 21), and approximately 580,000 people met the diagnostic criteria at the time of the survey. However, only about 80,000 responded that they were receiving treatment for alcohol dependence 14). According to a patient survey conducted by the Ministry of Health, Labour and Welfare in 2011, the total number of alcoholics was estimated to be 37,000. 10) It can be said that the majority of alcoholics are not correctly diagnosed, and as a result, are not receiving medical care. Until the late 1970s, the majority of alcoholics were said to be chronic alcoholics. Chronic alcoholism included all alcohol-related disorders, and in particular, endless drinking destroyed social and family life and led to a variety of tragedies. In addition, the image of the addict as an untouchable antisocial being has become firmly established among people due to his/her defiant and violent behavior in social and family

life, especially in medical situations. This image did not change even after the WHO abandoned the term "alcoholism" in 1977 and proposed the new concept of "alcohol dependence syndrome" 4). In other words, it is no exaggeration to say that only severe cases and those difficult to treat have been diagnosed as alcoholics in Japan due to the strong negative image of alcoholism. It is also likely that this strong negative image has led to an extremely narrow interpretation of the diagnostic criteria themselves. The WHO diagnostic criteria for alcohol dependence syndrome (ICD-10) is the fulfillment of three of the following six criteria 21): (1) intense desire or compulsion to drink (craving), (2) inability to abstain from alcohol (loss of control), (3) withdrawal symptoms, (4) increased tolerance, (5) taking most of the day to drink or recover from intoxication, neglecting recreational activities other than drinking (alcohol-centered lifestyle), (6) not abstaining from alcohol despite worsening mental and physical problems (loss of inhibitions against harmful drinking). For example, when a person runs out of alcohol, he or she goes out to buy more even in bad weather, drinks three or four drinks even when he or she intends to limit drinking to two drinks because heavy drinking will interfere with work the next day, or cannot stop drinking even when alcoholic liver or pancreatic disorders are indicated in a medical checkup and he or she is advised to stop drinking. If these factors are observed, the patient meets the diagnostic criteria for alcohol dependence syndrome in ICD-10 (1), (2), and (6), and can be diagnosed as an alcoholic. Unfortunately, however, even if the diagnostic items are met, most physicians do not diagnose alcohol dependence based on the impression that the patient "drinks too much" until now. On the other hand, it is necessary to pay attention not only to severe alcoholics whose conventional social and family life has been ruined and who suffer from serious organ damage, but also to mild alcoholics whose family and social life are maintained to a certain extent and whose organ damage is not serious. These mild alcoholics often hide behind various psychiatric disorders such as depression and anxiety disorders, and they often become a cause of refractory psychiatric disorders, such as prolongation of these disorders. Therefore, it is important not to overlook mild alcohol dependence hidden behind such psychiatric disorders.

II. From DSM-5 Alcohol Dependence to Alcohol Use Disorder

DSM-5 3), published in 2014, provides diagnostic criteria for alcohol use disorder. In other words, the diagnostic criteria for alcohol use disorder are presented in the direction of integrating the concepts of abuse and dependence. In DSM-IV 2), alcohol use disorder was a superordinate concept of abuse and dependence. In DSM-5, however, three of the four diagnostic items for alcohol abuse, excluding "repetitive substance-related legal problems," seven diagnostic items for alcohol dependence syndrome, and "craving," which was found only in ICD-10, were added as diagnostic items. The diagnosis of alcohol use disorder is defined as mild if two to three of the 11 items are applicable, moderate if four to five items are applicable, and severe if six or more items are applicable. The inclusion of abuse in the diagnostic criteria has lowered the diagnostic threshold, but the number of items leading to a diagnosis has been further reduced from three to two. Therefore, most mild alcohol use disorders would not meet the diagnostic criteria for alcohol dependence in ICD-10. These mild alcohol use disorders are not often considered a disease in and of themselves. However, it should not be forgotten that these mild cases may be hidden behind other comorbid psychiatric disorders and have a negative impact on recovery from comorbid conditions, such as depression 20).

III. Depression Combined with Alcohol Dependence

A hypothetical case is presented. The case is as follows:

A 33-year-old woman, housewife, with a husband and a 3-year-old child. She developed depression after childbirth and has been receiving treatment at a psychiatric clinic. Her husband is very busy and she feels lonely, and with the added burden of childcare, her depression continues. Because drinking makes her feel better, she drinks 2/3 to 1 bottle of wine in between housework, neglecting her housework and childcare. Although her husband is unaware of this, she wants to reduce her drinking. However, she is unable to reduce it.

This patient has been drinking since her early twenties. She did not drink when she was pregnant with her child, but continued to drink almost every day except for that period. She did not have any drinking problems at that time, but around the time she developed depression after childbirth,

her alcohol consumption began to increase rapidly, and she drank from 2/3 to 1 bottle of wine. Recently, she has not been able to stop drinking until the bottle of wine is empty, but she is not as intoxicated as she used to be even though her drinking volume has increased. When she has only the leftover wine from the previous day, she sometimes sneaks out to a convenience store to buy a bottle of wine before her husband gets home at night. In such cases, she often thinks only of drinking and neglects her housework and childcare. Her husband comes home late and does not have dinner at home on weekdays, so she manages to get by, but she has not been able to reduce her drinking, although she would like to do her housework and childcare properly by reducing it. She has been suffering from depression for almost three years and has been receiving medication for depression, but the depression persists.

The patient's alcohol dependence was recognized as "craving" and "impaired control of alcohol consumption," two of the diagnostic criteria of ICD-10 Dependence Syndrome (F10.2), because the patient continues to drink heavily, mainly due to craving alcohol. "Tolerance" was also observed based on these heavy drinkers and changes in intoxication. Furthermore, "harmful use" was also observed, as the patient continued to drink while being aware that she was neglecting her housework and childcare because of it. Therefore, four of the six diagnostic criteria for alcohol dependence syndrome were met, and the patient was diagnosed as an alcoholic. However, the diagnosis of alcohol dependence is often overlooked in such cases. This is partly due to the fact that in this case, the patient's drinking problem was concealed from the public, there were no clear withdrawal symptoms or serious organ damage, and her speech and behavior were not violent. Although this is not considered a serious case, the fact that the patient has been attending a psychiatric clinic for depression for three years suggests that alcohol dependence due to excessive drinking had an influence on the course of her depression.

In a large-scale overseas survey, the complication rate of alcohol dependence among those who experienced major depression was as high as 40% 6). In addition, Matsumoto et al. 11) reported that drinking problems were found in 27.3% of depressed men and 15.9% of depressed women. However, as already mentioned, more than 90% of

alcoholics in Japan are outside the psychiatric care system. Therefore, the rate of depression comorbid with alcohol dependence is also underestimated. In addition, there may be many patients with alcohol use disorder that does not lead to alcohol dependence. If comorbid with depression, it is easy to imagine that the patient is suffering from prolonged depression, as in this case. When depression is comorbid with an alcohol problem (alcohol dependence), the prognosis of depression worsens (worsening of symptoms due to drinking, delay in recovery, decreased efficacy of antidepressants, and increased risk of relapse), social functioning deteriorates (increased divorce rate as a result of worsening relationship with spouse, increased frequency of visits to hospitals, and prolonged hospital stay), and the suicide risk increases 5)17)19). In addition, depressed patients with comorbid alcohol use disorders that do not lead to dependence (Alcohol Use Disorders Identification Test: AUDIT score of 12 or higher) have also been found to exhibit decreases in treatment responsiveness, remission rates, and efficacy of antidepressant medications 7)8).

Traditionally, the goal of treatment for alcohol dependence has been abstinence from alcohol. However, this can be seen as a reflection of the fact that only severely ill or difficult-to-treat patients have received treatment. From now on, it will be important to treat mild (and some moderate) alcoholics who can maintain a reasonable family and social life and whose coexisting organ disorders are not severe. The treatment goal will be not only abstinence from alcohol, but also reduction of alcohol consumption. Alcoholism treatment guidelines in several countries already include the reduction of alcohol consumption as a treatment goal 12). The "New Guidelines for the Diagnosis and Treatment of Alcohol and Drug Use Disorders," published based on the work of the research group (Higuchi Group) of the Ministry of Health, Labour and Welfare of Japan 18), also state that "in cases of mild dependence and no clear complications, reduction of alcohol consumption may also be a goal unless the patient desires abstinence from alcohol or other circumstances necessitate abstinence from alcohol." The book further states that even in "cases of severe alcohol dependence, clear physical or mental complications, or serious family or social problems," where the goal of treatment should be abstinence, "if the patient refuses to abstain from

alcohol, the first step is to try to persuade him or her to do so, and one option is to start with the goal of reducing alcohol consumption and switch to abstinence if that does not work."

Brief intervention (BI) is considered to be effective as psychotherapy for reducing alcohol consumption 16)18). BI begins with an objective assessment of the patient's drinking problem and its extent using a screening test such as AUDIT, and feedback is given to the patient. Next, the patient is informed of the risks associated with continued drinking and advised on how to avoid these risks by reducing the amount of alcohol consumed. Counseling avoids confronting the drinking problem and does not address topics such as "denial" during the intervention. In fact, early intervention with "health" as a theme has resulted in relatively little denial or resistance from patients. After this approach, patients are asked to set specific goals for reducing their alcohol consumption that they can achieve with 70 to 80% effort. This technique uses interviewing methods such as motivational interviewing and coaching, and the key words in the intervention are "empathy," "encouragement," and "praise."

IV. Treatment of Alcohol Dependence with Comorbid Depression

1. Goal of treatment

The goal of treatment for alcoholics with psychiatric comorbidities such as depression has been considered to be abstinence, even in mild cases. As already mentioned, comorbid alcoholism is associated with a poorer prognosis for depression, worsened social functioning, and an increased risk of suicide. On the other hand, the "New Guidelines for the Diagnosis and Treatment of Alcohol and Drug Use Disorders" 18) state that even when there are clear psychological complications that should make abstinence from alcohol the goal of treatment, "If the patient does not respond to abstinence, first try to persuade him or her. If persuasion is unsuccessful, avoid dropping out of treatment because of it. One option is to start with the goal of reducing alcohol consumption and switch to abstinence if that does not work." In addition to avoiding dropout, the reduction of alcohol consumption must also be considered as a therapeutic tool for depression. Knox, J. et al. 9) interviewed 22,005 people in the U.S. (Wave 1), and conducted a similar survey three years later (Wave 2). The study subjects were classified into four groups according to their WHO drinking level, based on

their average alcohol consumption in the 12 months prior to the time of the study. The four groups were: low risk (average daily alcohol consumption of 1 to 40 g of pure alcohol), medium risk (41 to 60 g), high risk (61 to 100 g), and very high risk (101 g or more). The subjects were also examined for depressive and anxiety disorders according to DSM-IV. In the Wave 2 survey three years later, changes in the depressive/anxiety disorder status due to alterations in alcohol consumption were investigated in the same way as in Wave 1. The subjects were those who had a depressive/anxiety disorder in the Wave 1 survey and whose alcohol consumption classified them in the very high risk group. Of those whose alcohol consumption had not changed in Wave 2 after 3 years, 67.8% were classified as having a depressive/anxiety disorder. Of those whose alcohol consumption decreased from very high risk to high risk, from very high risk to medium risk, and from very high risk to low risk, subjects with depressive/anxiety disorder comprised 43.5, 37.6, and 51.5%, respectively. Thus, reduction of alcohol consumption improved the state of depressive/anxiety disorder 9). This report indicates that not only abstinence from alcohol but also reduction of alcohol consumption is effective in the treatment of depressive/anxiety disorder comorbid with alcohol dependence.

V. Pharmacotherapy

Antidepressants have been reported to be ineffective as part of treatment for depression comorbid with alcohol dependence. The efficacy of antidepressants has been examined in the past. Altintoprak, A.E. et al. 1) conducted a double-blind, placebo-controlled study of mirtazapine and amitriptyline for 8 weeks in patients with comorbid alcohol dependence and depression. Depression as measured by the Hamilton Depression Rating Scale (HDRS) and craving for alcohol as measured by the Alcohol Craving Questionnaire (ACQ) were also improved. They also reported that mirtazapine was better tolerated than amitriptyline, as measured by the Udvalg for Kliniske Undersogelser Side Effect Rating Scale (UKU). The ameliorative effect of mirtazapine on depressive symptoms and craving was also confirmed by Yoon, S.J. et al. 22). Muhonen, L.H. et al. 13) reported that escitalopram (20 mg) for 26 weeks improved the Montgomery-Åsberg Depression Rating Scale (MADRS) and quality of life. Pettinati, H.M. et al. 15) evaluated the efficacy of sertraline (200 mg) and naltrexone

(100 mg) administered alone or in combination for 14 weeks in 170 patients with comorbid alcohol dependence and depression under the conditions of a double-blind, placebo-controlled study. The two-drug combination group showed higher abstinence rates, significantly fewer heavy drinkers, and a longer time to heavy drinking than the single-drug group. They also reported milder depressive symptoms and fewer adverse events in this group. However, these reports indicate that antidepressants are not effective against depression in patients with comorbid alcohol use disorder/dependence. Therefore, abstinence and reduction of alcohol consumption should be considered first, and not just the administration of antidepressants. Therefore, use of the anti-craving agents acamprosate and nalmefene should be considered.

Conclusion

We presented a hypothetical case and discussed the importance of early detection and early treatment of alcohol dependence hidden behind depression and other psychiatric disorders, because alcohol dependence can lead to prolonged and intractable depression and other disorders. The goal of treatment for comorbid depression and alcohol dependence is abstinence from alcohol, but for patients with depression and mild (and sometimes moderate) alcohol use disorder, reduction of alcohol consumption may be a treatment goal. Antidepressants have limited efficacy, and treatment focuses on psychotherapeutic attempts to abstain from alcohol use and reduce alcohol consumption. Use of the anti-craving agents acamprosate and nalmefene should be considered as adjuncts to treatment.

The authors' self-reported conflicts of interest to the Japanese Neuropsychiatric Society for the year 2020 are as follows. Payments (between 500,000 yen and 2,000,000 yen) related to the provision of labor, such as conference attendance and lectures: Otsuka Pharmaceutical Co.

References

1) Altintoprak, A. E., Zorlu, N., Coskunol, H., et al.: Effectiveness and tolerability of mirtazapine and amitriptyline in alcoholic patients with co-morbid depressive disorder: a randomized, double-blind study. Hum Psychopharmacol, 23 (4); 313-319, 2008

2) American Psychiatric Association: Diagnostic and Statistical Mannual of Mental Disorderes, 4th ed (DSM-IV). American Psychiatric Association, Washington, D. C., 1994 (髙橋三郎, 大野 裕, 染矢俊幸訳: DSM-IV 精神疾患の診断・統計マニュアル. 医学書院, 東京, 1995)
3) American Psychiatric Association: Alcohol-Related Disorders. Diagnostic and Statistical Manual of Mental Disorders, 5th ed (DSM-5). American Psychiatric Publishing, Arilington, p.490-503, 2013 (日本精神神経学会 日本語版用語監修, 髙橋三郎, 大野 裕監訳: アルコール関連障害群. DSM-5 精神疾患の診断・統計マニュアル. 医学書院, 東京, p.483-496, 2014)
4) Edwards, G., Gross, M. M., Keller, M., et al.: Alcohol-related disabilities. WHO Offset Publication, Geneva, 1977
5) Fortney, J. C., Booth, B. M., Curran, G. M.: Do patients with alcohol dependence use more services? A comparative analysis with other chronic disorders. Alcohol Clin Exp Res, 23 (1); 127-133, 1999
6) 橋本恵理, 齋藤利和: アルコール依存症と気分障害. 精神経誌, 112 (8); 780-786, 2010
7) Hashimoto, E., Tayama, M., Ishikawa, H., et al.: Influence of comorbid alcohol use disorder on treatment response of depressive patients. J Neural Transm, 122 (2); 301-306, 2015
8) 石川央弥, 橋本恵理, 田山真矢ほか: 問題飲酒を併発したうつ病性障害の治療反応性について. 日本アルコール・薬物医学会雑誌, 48 (5); 282-292, 2013
9) Knox, J., Wall, M., Witkiewitz, K., et al.: Reduction in non-abstinent World Health Organization (WHO) drinking risk levels and drug use disorders: 3-year follow-up results in the US general population. Drug Alcohol Depend, 201; 16-22, 2019
10) 厚生労働省: 平成 23 年患者調査(傷病分類編). (http://www.mhlw.go.jp/toukei/saikin/hw/kanja/10syoubyo/dl/h29syobyo.pdf) (参照 2020-01-12)
11) 松本俊彦, 小林桜児, 今村扶美ほか: うつ病性障害患者における問題飲酒の併存率—文献的対照群を用いた検討—. 精神医学, 54 (1); 29-37, 2012
12) 松下幸生, 樋口 進: 飲酒とうつ状態の早期発見. こころの科学, 125; 43-48, 2006
13) Muhonen, L. H., Lönnqvist, J., Juva, K., et al.: Double-blind, randomized comparison of memantine and escitalopram for the treatment of major depressive disorder comorbid with alcohol dependence. J Clin Psychiatry, 69 (3); 392-399, 2008
14) 尾崎米厚, 樋口 進, 神田秀幸ほか: WHO 世界戦略を踏まえたアルコールの有害使用対策に関する総合的研究—わ

が国の成人の飲酒行動に関する全国調査 2013 年, 2003 年, 2008 年全国調査との比較―. 平成 25 年度総括研究報告書 (厚生労働科学研究費補助金疾病・障害対策研究分野循環器疾患・糖尿病等生活習慣病対策総合研究事業). p.19-28, 2014

15) Pettinati, H. M., Oslin, D. W., Kampman, K. M., et al.: A double-blind, placebo-controlled trial combining sertraline and naltrexone for treating co-occurring depression and alcohol dependence. Am J Psychiatry, 167 (6); 668-675, 2010

16) 齋藤利和: アルコール依存症の治療. 医学のあゆみ, 254 (10); 955-958, 2015

17) 齋藤利和: アルコール依存・使用障害とうつ病. Depression Journal, 6 (1); 24-25, 201

18) 新アルコール・薬物使用障害の診断治療ガイドライン作成委員会監, 樋口 進, 齋藤利和ほか編: 新アルコール・薬物使用障害の診断治療ガイドライン 新興医学出版社, 東京, 201

19) Sullivan, L. E., Fiellin, D. A., O'Connor, P. G.: The prevalence and impact of alcohol problems in major depression: a systematic review. Am J Med, 118 (4); 330-341, 2005

20) 田山真矢, 齋藤利和: アルコール依存症とうつ病. Frontiers in Alcoholism, 4 (1); 20-24, 2016

21) World Health Organaization: The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. World Health Organaization, Geneva, 1992 (融 道男, 中根允文ほか監訳: ICD-10 精神および行動の障害-臨床記述と診断ガイドライン-, 新訂版. 医学書院, 東京, 2005)

22) Yoon, S. J., Pae, C. U., Kim, D. J., et al.: Mirtazapine for patients with alcohol dependence and comorbid depressive disorders: a multicentre, open label study. Prog Neuropsychopharmacol Biol Psychiatry, 30 (7); 1196-1201, 2006