



Review of Abstinence Syndrome: A Comprehensive Analysis of Current Practices and Recommendations

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Alcohol use disorder is frequently accompanied with the diverse and sometimes fatal consequence of alcohol withdrawal syndrome (AWS). Many patients with AUD may develop AWS during their Emergency Department stay, and AUD is one of the top causes of death worldwide. This study summarizes the etiology, epidemiology, and emergency management of Alcohol Withdrawal Syndrome and Alcohol Use Disorder. The influence of AWS on the therapy of ED is highlighted, along with its temporal course. Once AWS is diagnosed, the most common therapy is still symptom-triggered benzodiazepine injection; however, patients who have significant medical or psychiatric comorbidities or are about to be discharged may not be good candidates for this approach. In these circumstances, emergency department doctors can consider employing alternative regimens based on state-of-the-art anticonvulsants or shorter barbiturate durations. For clinical practice, specific treatment procedures are described. Lastly, in addition to managing acute patients' AWS, emergency physicians also need to provide the groundwork for effective AUD therapy. A strategy for the patient with AUD's disposition is offered.

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1. INTRODUCTION

One of the most prevalent mental health issues is alcoholism, however only when a more severe illness has occurred. 50% of those with alcohol addiction and up to 10% of those with alcohol dependence show symptoms. Within [1,2] Physical dependence and alcohol tolerance develop as a result of excessive and frequent alcohol consumption. The primary cause of withdrawal syndrome is the hyperexcitable response of the central nervous system to the absence of alcohol [3-6]. The potentially lethal medical condition known as alcohol withdrawal syndrome (AWS) is caused by an imbalance in two excitatory and inhibitory neurotransmitters: glutamate and gamma-aminobutyric acid (GABA) [7,8]. The diagnostic criteria for alcoholism are met by around 27% of people between the ages of 18 and 64 [9].

Alcohol Use Disorder (AUD) can lead to Alcohol Withdrawal Syndrome (AWS), a potentially fatal consequence that affects many patients in emergency departments (EDs) [10]. Inpatient hospitalization and the use of critical care services are more common when alcohol withdrawal occurs in the emergency room. Diagnosing alcohol withdrawal symptoms in middle-class, working adults is challenging because more than half of them have these symptoms [11].

Many physiological and psychological symptoms, including as insomnia, shaking, autonomic hyper-reactivity, anxiety, depression, restlessness, fidgetiness, seizures, hallucinations, and, in severe instances, delirium tremens (DT), are indicative of Alcohol Withdrawal Syndrome (AWS) [12]. Alcohol Use Disorders, or AUDs, are the third most common risk factor for illness and impairment worldwide. Surprisingly, AUDs are thought to be responsible for 2.3–3.3 million more fatalities per year than Human immunodeficiency virus and Tuberculosis combined [13–15].

The American Academy of Family Physicians states that six to twelve hours after stopping, withdrawal symptoms may manifest. These symptoms include headache, sweating, lack of appetite, mind and hand tremors, and sleep problems. b) 12–48 hours following the end of the seizures, which include hallucinations, tonic-clonic convulsions throughout the body, and withdrawal symptoms c) Delirium tremens,

elevated blood pressure, heart rate, and fever 48–72 hours after discontinuation [16]. An estimated 5% of the worldwide population has alcohol use disorder (AUD) each year, affecting around 18% of the total population [17]. Alcoholics with cirrhosis have a high mortality rate when they consume alcohol regularly [18]. Obesity, hypertension, obstructive sleep apnea, and left ventricular dysfunction are some of the risk factors for atrial fibrillation that are associated with alcohol use. [19] AWS is a spectrum of neurophysiological symptoms that vary in severity according to the amount of alcohol consumed [20,21].

2. STAGES OF ALCOHOL WITHDRAWAL SYNDROME

- 6 Hours Sober-Most withdrawal symptoms start: headache, anxiety, mood swings, nausea,nausea and so on.
- 12-24 Hours Sober- Symptoms continue and can escalate to hallucinations and seizures.
- 24-48 Hours Sober- Symptoms persists. On average symptoms peak after 24 hours for mildwithdrawal.
- 48-72 Hours Sober-Delerium Tremens (DT) can start which include increased heart rate, temperature, and seizure. DTs can be fatal.
- 72+Hours Sober-Symptoms and peak gradually subside after 5 days. Symptoms may persistsfor up to one month.

Stage-1

Uncomplicated withdrawal- Tachycardia, hypertension, and hyperthermia are some of the symptoms of mild to severe autonomic hyperactivity that may also be included in it. [22,23,24]

Stage-2

Alcohol hallucinosis - It affects 2-8% of people who use alcohol excessively and chronically, particularly those who started drinking when they were 17 years old or younger [25].

Stage-3

Alcohol withdrawal seizures- It usually presents as widespread tonic-clonic seizures and affects 5 10% of those with active Alcohol Withdrawal Syndrome (AWS) [26].

Stage-4

Alcohol withdrawal delirium- An alternative name for this syndrome is extent delirium, and 3-

5% of instances of AWS are associated with DT patients [27].

3. BIOMARKERS

Numerous research works have investigated possible signs of an approaching severe AWS. Examining medical history and testing for biomarkers are the two main techniques for determining high risk. The most reliable indicator of the occurrence of a DT or seizure episode seems to be a history of a comparable incident [28,29,30,31].

The first patient examination may simply screen for clinical indications such as raised heart rate, temperature, and systolic blood pressure, even though these measures have a low predictive value for determining which AWS patients are more likely to develop DT. In cases where a patient's level of awareness is compromised, test indicators may bolster the clinical suspicion of a AUD [28,29,32].

4. COMORBIDITIES

- Alcohol withdrawal delirium is a condition that cannot be treated with benzodiazepines, thus it is important to differentiate it from hepatic encephalopathy.
- Because they are metabolized by the kidneys, intermediate-acting benzodiazepines like oxazepam and

lorazepam are thought to be more secure to use.

- When using benzodiazepines, care should be taken if there are symptoms of end-stage liver disease, such as ascites, variceal bleeding, or hepatic encephalopathy.
- Furthermore, in cases of hepatorenal syndrome, further caution is necessary. For the treatment of mild to moderate AWS, gabapentin and baclofen are suitable substitutes.
- Thiamine supplements at high doses are imperative for all patients experiencing severe AWS to prevent the onset of Wernicke's encephalopathy [34].

5. BRAINIMAGING

Since status epilepticus (SE) and first-onset seizures are often linked with concurrent risk factors more than 50%, neuroimaging is recommended to rule out other neurological ailments in these individuals.

- The most common MRI abnormalities associated with seizures are cerebral hyperintensities and hyperperfusion, along with a low apparent diffusion coefficient in CT regions with decreased attenuation, effacement of sulci, and absent grey-white differentiation [35].

Table 1. Severe alcohol withdrawal: A distinctive diagnosis [33]

Distinctdiagnoss Comments	Comments
Hyponatremia	The causes are poor oral intake, uremia, and dehydration; these conditions usually result in hypoactive delirium.
Hepatic encephalopathy	Common symptoms of severe liver illness, especially cirrhosis, include hematemesis, melena, ascites, icterus, jaundice, sleep wakereversal, and flapping tremor.
Pneumonia	Before quitting alcohol usage, some people may have symptoms including fever, coughing, low arterial blood oxygen saturation, andpre-cessation delirium, which might indicate a complicated interaction of elements impacting their health.
Psychosis	The presence of persistent hallucinations or delusions without any clouding of the sensorium is a noteworthy clinical characteristic thatcan be found in several mental illnesses.
Encephalitis/Meningitis	Meningeal symptoms, specific neurological impairments, fever, and abnormalities found in MRI and cerebrospinal fluid (CSF) studies can all be indicators of different neurological disorders.
Lithium intoxication	Past medical history including mental disorders, drug abuse, fever,diarrhoea, and use of diuretics or NSAIDs.
Subacute encephalopathywith seizures in AUD	People may have simple or complicated partial seizures with reversible motor impairments a few days after stopping drinking. While MRI may indicate reversible T2-weighted flare hyperintensities,focal slowness and periodic lateralized

Distinctdiagnoss Comments	Comments
	discharges are frequently seen in EEG data.
Head injury	Unconsciousness, bleeding from the nose or ears, pinpoint pupils,and localized neurological impairments.
Atropine/Tricyclicintoxication Thyrotoxicosis	Hyperthermia, desiccation, and dilated pupils Past thyroid conditions such as thyromegaly, exophthalmos, and lagophthalmos
Antidepressant intoxication	SSRI use; constipation, myoclonus, anxiety, convulsions, and altered sensory perception

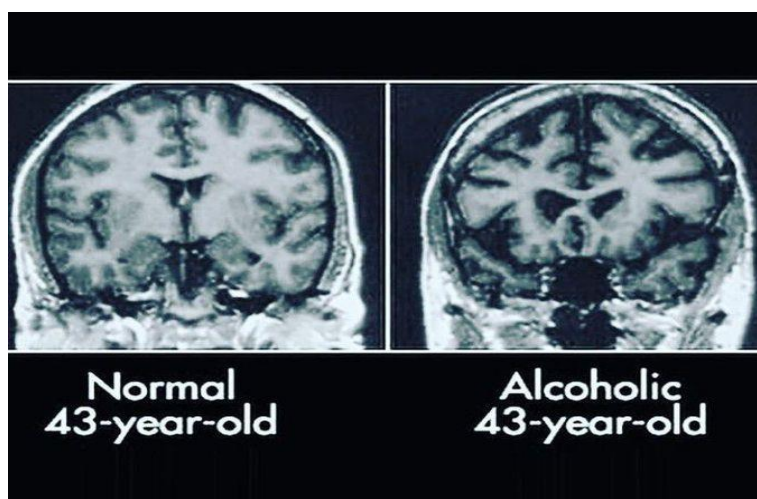


Fig. 1. Neuroimaging [35]

Table 2. Radiographic Markers in Patients' Brain Images Associated with Alcohol-Related Syndromes [36]

Disease Associated withAlcoholism	Abbreviation	Principal Area(s) Targeted	Subsequent Areas of Focus	Alcoholism Prevalence (Percent)
Marchiafava Bignami Disease	MBD	Corpus callosum	Cortex	<0.002
Alcohol-Related Dementia	ARD	Frontal cortex		3-24
Alcoholic Cerebellar Degeneration	ACD	Cerebellum		0.4-42
Wernicke's Encephalopathy	WE	Mammillary bodies, periaqueductal grey matter,dorsal medulla, tectal plates, olivary bodies, pons,tissue surrounding 3 rd ventricle		12–18
Korsakoff's Syndrome	KS	Mammillary bodies, hippocampus, thalamus, orbitofrontal cortices	Cerebellum,pons	12-15
Central Pontine Myelinolysis	CPM	Pons	Basal ganglia, thalamus, cerebral grey white matter	<0.5

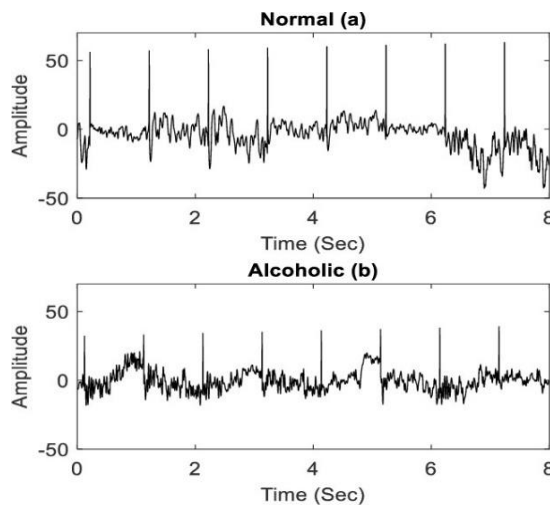


Fig. 2. Electroencephalogram signals

6. ELECTROENCEPHALOGRAM

- Brain activity may be recorded using an electroencephalogram, or EEG.
- In order to detect the electrical impulses generated by the brain, tiny sensors are affixed to the scalp during this painless examination
- The primary purpose of an EEG is to diagnose and study epilepsy, a condition that causes recurring seizures [37]

Types of EEG

- **Regular EEG:** An EEG recording normally lasts 20 to 40 minutes. Another option is to use a flashing light to see how your brain reacts to this.
- **Ambulatory EEG:** This type of EEG monitors brain activity during the day and at night for a period of one or more days. A small, wearable, clippable EEG recorder will be attached to the electrodes.
- **Sleep EEG:** An electroencephalogram is recorded while you are asleep. When a standard EEG is insufficient to diagnose sleep issues, it can be utilized as a test.
- **Video telemetry:** Also referred to as video EEG, video telemetry is a special kind of EEG in which you are being recorded while being videotaped. This may help to clarify further information on how your brain works.

7. TARGETS OF THE TREATMENT

1. "To facilitate a gradual and safe taper off the drug or drugs of dependence,

supporting the patient in achieving a drug-free status."

2. "To offer a compassionate withdrawal process, preserving the patient's dignity during their journey to recovery."
3. "To prepare the patient for ongoing therapy and treatment for their alcohol or drug dependency" [38].

8. ASSISTIVE CARE

- **Comorbid medical conditions-**If they exist, they should be addressed. Oral or intravenous fluids should be used to treat metabolic disturbances. It must be a serene, tranquil, and unstimulating atmosphere [39].
- **Dietary Supplements-**It is recommended to experimentally supply thiamine (vitamin B1) in order to avoid Wernicke's encephalopathy (WE) and Korsakoff's psychosis. There are differences in protocols for thiamine dose and delivery routes. Institutions and rules of the medical profession, with dosages ranging from 100 mg of thiamine up to 200–500 mg per eight hours for a standard IV fluid infusion 72 hours at least if WE is detected [40,41].

9. AWS-SPECIFIC THERAPEUTICS

- **Anticonvulsants**

Long-term heavy drinkers may be affected by the prolonged abstinence syndrome, which implies that they depend on alcohol for stress relief, reward experiences, and a sense of normalcy [43]. It can take many months or even

years of sobriety to reverse the negative effects of alcohol on the brain. It is believed that National Bioethics Advisory Committee's efficiently treat the hallmarks of protracted abstinence syndrome, such as impaired hedonic function, stress reactivity, and craving. National Bioethics Advisory Committee may lessen the symptoms of prolonged abstinence syndrome by improving glutamatergic and GABAergic neurotransmission in the ventral striatum and related neurocircuitry. After a patient attains sobriety, anticonvulsants can support healing processes and equilibrium. It's possible that interactions between glutamate and dopamine are what keep addiction going [44]. Glutamatergic efferent originating from the hippocampus, amygdala, and prefrontal cortex innervate neurons located in the nucleus accumbens shell and ventral tegmental region. This process amplifies dopaminergic neurotransmission in these crucial circuits linked to the reward system [45].

With a fixed or tapering regimen spanning 5–9 days and daily dosages of 800 mg, Carbamazepines showed good tolerance and successfully reduced withdrawal symptoms. Nevertheless, obstacles including inadequate enrollment, postponed pharmacological administration, limited sample size, and incorrect dosage impede a definitive assessment of Carbamazepines function in averting seizures or delirium tremens (DT), and its relative effectiveness in comparison to benzodiazepines is still up for debate [46,47]. Levetiracetam's (LEV) exact mode of action in AWS is still unknown because it does not appear to have any affinity for either GABAergic or glutamatergic receptors. Nevertheless, the treatment of AWS with LEV appears promising; the available data indicate a steady and quick improvement in clinical outcomes. Studies are still being done to find out more about its applicability in treating AWS [48,49].

10. ALPHA ADRENOCEPTOR AGONISTS AND BETABLOCKERS

Blood pressure and heart rate are lowered by centrally acting α 2-adrenoceptor agonists like clonidine and lofexidine, as well as β -blockers like propranolol and atenolol, which help to regulate withdrawal-induced sympathetic activity. While some research studies [50,51] indicate the usefulness of these drugs in reducing certain withdrawal symptoms, other studies have not demonstrated any appreciable advantage over a placebo in managing

symptoms including nausea, anxiety, and agitation. Crucially, there is now no proof that these drugs are effective in treating DT or averting withdrawal symptoms [52].

11. BARBITURATES

Research conducted on small or uncontrolled populations has shown promise in the treatment of withdrawal with barbital, phenobarbital, and tetraborate [53,54]. In acute withdrawal scenarios, their smaller tolerance margin strongly suggests against their usage, and their efficacy does not considerably outperform that of benzodiazepines [55].

12. NITROUS OXIDE (NOx)

Gillman and Ojutkangas [56] found that 62% of 500 Finnish patients needed just one nitrous oxide treatment and recovered totally from withdrawal symptoms within 60 minutes [57], in contrast to the usual 4- to 5-day recovery period associated with benzodiazepine therapy. In South Africa, almost 7,000 people received nitrous oxide therapy for alcohol withdrawal during a ten-year period [58]. The study team located in South Africa suggests that nitrous oxide injection might be used as a screening method to identify withdrawal patients that need to be treated further with medicine to keep symptoms from dangerously getting worse [59]. To fully understand the potential of nitrous oxide as a monotherapy or polytherapy, however, extensive controlled research studies are required.

13. THERAPY

Relapse therapy: Relapses happen gradually, as you should be aware. Weeks or perhaps months pass before someone starts using drugs or alcohol. The major objectives of treatment are to help patients recognize the early warning indicators of relapse and to help them build coping abilities so they may stop relapses before they happen [60].

- **Stages of Relapse-**
- Emotional relapse
- Mental relapse
- Physical relapse

Alcohol Rehabilitation-The process of treating alcohol dependency using a combination of medical and psychological therapy is known as alcohol rehabilitation. In particular, alcohol rehab is a program or therapy utilized when someone who has misused or overindulged in alcohol

Table 3. Benzodiazepines [42]

Drugs used Available	Available Route of Dose	Comparative Equivalent Strength	Comparative Equivalent Strength Action Commencement (Following Oral Administration)	Peak Blood Levels (Hours)	Half-life (hrs)	Duration of Action	Metabolism
Midazolam	PO, IM IV	2	Rapid	Oral: 0.2-2.5 IM:0.5-12	2-7	Short	Short Hepatic,gut
Clorazepate	PO,IM	7.5	Rapid	0.5-2	48	Short	Hepatic
Lorazepam	PO,IM,IV	1	Intermediate	Oral:2IM: <3	12-18	Short to Medium	Hepatic
Diazepam	PO, IM,IV	5	Rapid	Oral:0.25 2.5 IM:1 IV:0.01	30-60	long	Hepatic
Chlordiazepoxide	PO		Intermediate	0.5-2	24-48	long	Hepatic

stops using it with the intention of staying sober for good. Detoxification, rehabilitation, and sobriety maintenance are typically included in the treatment process [61]. Recognizing the issue and getting treatment for alcoholism are the most crucial steps in the process.

Among the early warning indicators are: [62].

- Isolation from friends and family
- Signs of irritation and irritability
- Making excuses to consume more alcohol
- Choosing alcohol over other obligations in life
- Having a hangover without drinking

Various ways for de-addiction;

- Psychoeducation
- Detoxification
- Intensive psychotherapy

Cognitive Behavioural Therapy-Today, a lot of people utilize it to treat addiction. CBT helps people with substance use disorders (SUDs) discover links between their ideas, feelings, and behaviours raises understanding of how these factors affect recovery. Patients can overcome alcoholism and drug addiction with the use of CBT by:

- Offering self-help methods to improve their emotions;
- Assisting in the dismissal of incorrect ideas and anxieties that cause substance abuse
- imparting knowledge on effective communication [63]

Pulsed electrical stimulation-It is used in electroconvulsive therapy, an effective treatment for a range of acute mental and neuropsychiatric diseases [63,64,62]. Recognized adverse effects of ECT therapy include real delirium, agitation, and potential long-term consequences on cognition [65].

14. DISCUSSION

The main motivation for selecting this subject was to inform readers about the detrimental consequences suddenly stopping alcohol usage might have on one's health. The main advantage is that pharmacological and non-pharmacological therapies may be used to treat alcoholism at different stages. The disadvantage is that suddenly stopping alcohol use might result in death or insanity.

15. CONCLUSION

By this project we conclude that anything taking in excess dose may leads to organ damage and at last death. So before taking alcohol may sure that ready for all consequences relatedto it.

CONCENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Sachdeva A, Chowdary M, Chandra M. Alcohol Withdrawal Syndrome: Benzodiazepines and Beyond. J Clin Diagn Res. 2015 sept;9(9):VE01-VE 07. DOI:10.7860/JCDR/2015/13407.6538
2. Melson J, Kane M, Mooney R. Mc Williams J, Horton T5. Improving alcohol withdrawal outcomes in acute care. Prem J. 2014 Spring;18(2);e141-5. DOI:10.7812/TPP/13-099
3. Ito H. Intermediate to Long-term Results of Periacetabular Osteotomy in Patients Younger and older than 40years of Age. J Alcohol Drug Depend. 2016;4:235.
4. Zago P et al. Alcohol Use Disorder and Inflammatory Cytokines in a Population Sample of Young Adults. J Alcohol Drug Depend. 2016;4:236.
5. Montalto M. How Have Academic Theories of Domestic Violence Influenced Western 2016;4:237.
6. HiranitaT.(-)-Trans-9 Tetrahydrocannabinol-Like Discriminative-stimulus effects of Gabapentin in Cannabis Users . J Alcohol Drug Depend. 2016;4:e129.
7. Schmidt KJ, Doshi MR, Holzhausen JM et al. Treatment of Severe Alcohol Withdrawal. Ann Pharmacother 2016;50(5):389-401.
8. Awissi DK, Lebrun G, Coursin DB et al. Alcohol Withdrawal and Delirium tremens in the critically ill: A systematic review and commentary. Intensive Care Med. 2013;39(1):16-30.
9. Mckeon, Frye and Delanty; 2008.
10. White AM, Slater ME, Ng G, Hingson R, Breslow, R. Trends in alcohol related Emergency department visits in the United States:Results from Nationwide

- Emergence Department Sample, 2006-2014. *Alcohol Clin Exp Res*. 2018;42(2):352-359.
DOI:10.1111/acer.2018.42.issue-2
11. Klein LR, Cole JB, Driver BE, Battista c, Jelinek R, Martel ML. Unsuspected critical illness among emergency Dept patients presenting for acute alcohol intoxication. *Ann. Emerg Med*. 2018;71(3):279-288.
 12. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington VA; American Psychiatric Association. 2013;501.
 13. Clinical Manifestations of Complicated Alcohol withdrawal and uncomplicated alcohol withdrawal: A comparative study- Alcohol Withdrawal Syndrome- *American Family Physician* 69,1443-1450.
 14. WHO. Management of Substance Abuse Team. Global status report on alcohol and health; 2014.
Available:<http://apps.who.int/iris/bitstream/10665/112736/1/9798240692763-eng.pdf?ua=1> Accessed 20 Aug 2014
 15. WHO Management of Substance Abuse Team. Global status report on alcohol and health. Geneva: WHO;2011.
 16. Yanta JH, Swartzentruber GS, Pizon AF. Alcohol Withdrawal Syndrome: Improving outcomes through early identification and aggression treatment strategies. *Emerged Practical*. 2015 June;17(6):1-18;quiz 19
 17. Organization WHO Global status report on alcohol and health 2018, WHO :2019
 18. Pession F, Ramond MJ, Peters et al. Five year survival predictive factors in patients with excessive alcohol intake and cirrhosis: Effect of alcoholic hepatitis smoking and abstinence. *Liver Int* 2003;23:4.5-53.
 19. Voskoboinik A, Prabhu S, Ling LH, Kalman JM, Kistler J *AM Coll Cardiol*. 2016;2567-76.
 20. Turner RC, Lichstein PR, Peden JG Jr, Busher JT, Waivwers LE, Alcohol Withdrawal Syndrome; A review of the pathophysiology, clinical presentation and treatment *J. Gen Intern Med*. 1989;4:432-444.
 21. Clapp P, Bhave SV, Hoffman PL. How adaptation of the brain to alcohol leads to dependence; A pharmacological perspective. *Alcohol Res Health*. 2008;31:310-339.
 22. Long D, Long B, Koyfman A. The emergence medicine management of server alcohol withdrawal. *Am J Emergence Med*; 2017.
 23. Long D, Long B, Kolffman A. The emergency medicine management of severe alcohol withdrawal. *Am J Emerg Med*. 2014;35:1005-1011.
DOI: 10.1016/j.ajem.2017.02.002
 24. Cohen B. *Theory & Practice of psychraby*. NewYork NY: Oxford University Prett 1; 2003.
 25. Mingello A, D'Angelo (Ferrulle A et al. Identification & management of alcohol withdrawal *Sy. Drugs* 2015 75 (u) 13153-365
DOI. 10.1007/s40265-015-0358-1
 26. Stephane M, Amarut B, Yoon & Alcohol withdrawal hallucination? In general population an epidemiological study *Psychialty Res*. 2018;262:129-134.
DOI: 10.1016// psycheres. 2018.02.031 2
 27. Maldonado J, Sher Y, Das S et al. Prospective Validation of Prediction of Alcohol withdrawal Severity Scale (PAWSs) in medically ill so patients a new scale for Prediction of complicated AWS alcohol alcoholism. 2015;50(5):509-5/8.
DOI:10 1093/ alcohol / agv 043
 28. Perry EC. Inpatient management of acute alcohol withdrawal syndrome. *CNS Drugs*. 2014;28:401–410.
EPUB 2014/05/02
 29. Kattimani S, Bharadwaj B. Clinical management of alcohol withdrawal: A systematic review. *Ind Psychiatry J*. 2013;22:100–108.
EPUB 2014/07/12
 30. Berggren U, Fahlke C, Berglund KJ, Blennow K, Zetterberg H, Balldin J. Thrombocytopenia in early alcohol withdrawal is associated with development of delirium tremens or seizures. *Alcohol Alcohol*. 2009;44:382–386.
EPUB 2009/03/1
 31. Goodson CM, Clark BJ, Douglas IS. Predictors of severe alcohol withdrawal syndrome: A systematic review and meta-analysis. *Alcohol Clin Exp Res*. 2014;38:2664–2677.
EPUB 2014/10/28.
 32. Monte R, Rabunal R, Casariego E, Bal M, Pertega S. Risk factors for delirium tremens in patients with alcohol withdrawal syndrome in a hospital setting. *Eur J Intern Med*. 2009;20:690–694.
EPUB 2009/10/13.
 33. Chelsea Wolf, Ashley Curry, Jacob Nacht, Scott A Simpson Management of Alcohol

- Withdrawal in the Emergency Department: Current Perspectives, Open Access Emergency Medicine. 2020;53-65. DOI: 10.2147/OAEM.S235288
34. Rathlev NK, Ulrich AS, Delanty N, D'Onofrio G. Alcohol-related seizures. *J Emerg Med.* 2006;31:157–163. EPUB 2006/10/19.
 35. Alcohol's Effects on the Brain: Neuroimaging Results in Humans and Animal Models Natalie M. Zahr, Ph.D. and Adolf Pfefferbaum, M.D. PMID: PMC5513685
 36. NHS Website. Malcolm R, Ballenger JC, Sturgis ET, Anton R. Double-blind controlled trial comparing carbamazepine to oxazepam treatment of alcohol withdrawal. *Am J Psychiatry.* 1989;146(5):617–621.
 37. Sachdeva A, Chandra M, Deshpande SN. A comparative study of fixed tapering dose regimen versus symptom-triggered regimen of lorazepam for alcohol detoxification. *Alcohol.* 2014;49 (3):287–291. DOI:10.1093/alcal/agt181 of Addiction
 38. Kasser C, Geller A, Howell E, Wartenberg A. Detoxification: Principles and protocols. American Society and Medicine. Available: <http://www.asam.org/pub1/detoxification.htm>. [cited 2010 Sept 7].
 39. Whitfield CL, Thompson G, Lamb A et al. Detoxification of 1,024 alcoholic patients without psychoactive drugs. *JAMA* 1978;239:1409-10
 40. Flannery A, Adkins D, Cook A. Unpeeling the evidence for the banana bag: Evidence-based recommendations for the management of alcohol-associated vitamin and electrolyte deficiencies in the ICU. *Crit Care Med.* 2016;44(8):1545–1552. DOI:10.1097/CCM.0000000000001659
 41. Sharp C, Wilson M, Nordstrom K. Psychiatric emergencies for clinicians: Emergency department management of Wernicke-Korsakoff syndrome. *J Emerg Med.* 2016;51(4):401–404. DOI:10.1016/j.jemermed.2016.05.044
 42. Day E, Bentham P, Callaghan R, Kuruvilla T, George S. Thiamine for prevention and treatment of Wernicke-Korsakoff Syndrome in people who abuse alcohol. *Cochrane Database System Rev.* 2013;7. 45. Botswick J. Medication Table 6: Benzodiazepines. In: Chavez B, editor. CPNP Psychiatric Pharmacotherapy Review Course. 2018–2019 ed. Lincoln, NE: College of Psychiatric and Neurologic Pharmacists; 2018.
 43. Koob GF. Alcoholism: Allostasis and beyond. *Alcohol Clin Exp Res.* 2003;27(2):232–43.
 44. Tzschentke TM, Schmidt WJ. Glutamatergic mechanisms in addiction. *Mol Psychiatry.* 2003;8(4):373–82.
 45. Barrons R, Roberts N. The role of carbamazepine and oxcarbazepine in alcohol withdrawal syndrome. *J Clin Pharm Ther.* 2010;35:153–167. EPUB 2010/05/12.
 46. Bonnet U, Hamzavi-Abedi R, Specka M, Wiltfang J, Lieb B, Scherbaum N. An open trial of gabapentin in acute alcohol withdrawal using an oral loading protocol. *Alcohol Alcohol.* 2010;45:143–145. EPUB 2009/12/19.
 47. Krebs M, Leopold K, Richter C et al. Levetiracetam for the treatment of alcohol withdrawal syndrome: An open-label pilot trial. *J Clin Psychopharmacol.* 2006;26:347–349. EPUB 2006/05/17.
 48. Muller CA, Schafer M, Schneider S et al. Efficacy and safety of levetiracetam for outpatient alcohol detoxification. *Pharmacopsychiatry.* 2010;43:184–189. EPUB 2010/05/27
 49. Hoiseth G, Bernard JP, Stephanson N et al. Comparison between the urinary alcohol markers EtG, EtS, and GTOL/5-HIAA in a controlled drinking experiment. *Alcohol Alcohol.* 2008;43:187–191. EPUB 2008/01/31
 50. Bleich S, Bayerlein K, Hillemacher T, Degner D, Kornhuber J, Frieling H. An assessment of the potential value of elevated homocysteine in predicting alcohol-withdrawal seizures. *Epilepsia.* 2006;47:934–938. EPUB 2006/05/12.
 51. Burns E, Gray R, Smith LA. Brief screening questionnaires to identify problem drinking during pregnancy: A systematic review. *Addiction.* 2010;105:601–614. EPUB 2010/04/21
 52. Maldonado JR, Sher Y, Das S et al. Prospective Validation Study of the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) in Medically Ill Inpatients: A New Scale for the Prediction of Complicated Alcohol Withdrawal Syndrome. *Alcohol Alcohol.* 2015;50:509–518.

- EPUB 2015/05/23.
53. Hillemacher T, Frieling H, Wilhelm J et al. Indicators for elevated risk factors for alcohol withdrawal seizures: An analysis using a random forest algorithm. *J Neural Transm.* 2012;119:1449–1453. EPUB 2012/05/25
54. Maldonado JR, Sher Y, Ashouri JF et al. The “Prediction of Alcohol Withdrawal Severity Scale” (PAWSS): Systematic literature review and pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome. *Alcohol.* 2014;48:375–390. EPUB 2014/03/25
55. Pieninkeroinen IP, Telakivi TM, Hillbom ME. Outcome in subjects with alcohol-provoked seizures. *Alcohol Clin Exp Res.* 1992;16:955–959. EPUB 1992/10/01
56. Nair PP, Kalita J, Misra UK. Status epilepticus: Why, what, and how. *J Postgrad Med.* 2011;57:242–252. EPUB 2011/09/24.
57. G, Liang Y, Zhou J. A wide spectrum of variably periaxial MRI abnormalities induced by a single or a cluster of seizures. *J Neurol Sci.* 2014;343:167–172. EPUB 2014/06/22.
58. Ojutkangas R, Gillman MA. Psychotropic analgesic nitrous oxide for treating alcohol withdrawal in an outpatient setting. *Int J Neurosci* 1994;76: 35-9.
59. Gillman MA, Lichtigfeld FJ. Analgesic nitrous oxide for alcohol withdrawal: A critical appraisal after 10 years’ use. *Postgrad Med J.* 1990;66:5.
60. Gillman MA, Lichtigfeld FJ. The drug management of severe alcohol withdrawal syndrome. *Postgrad Med J.* 1990;66:1005-9.
61. Gorski TT, Miller M. *Counselling for Relapse Prevention.* Inneocence, MO:Herald House/Independence Press;1982.
62. A systemic review of modified electroconvulsive therapy to treat delirium Katie Lupke, Nicola Warren, Andrew Tedorczuk, Saraah Steele, Uday Kalour, Annie Wand, Gali Robinson, Stephen Parker. Available: <https://doi.org.10.1111.acps.13492>
63. A systemic review of modified electroconvulsive therapy to treat delirium Katie Lupke, Nicola Warren, Andrew Tedorczuk, Saraah Steele, Uday Kalour, Annie Wand, Gali Robinson, Stephen Parker. Available: <https://doi.org.10.1111.acps.13493>
64. Alcohol Reha biltation.
65. Available: <https://priorygroup/addictiontreatment/alcoholrehabhttps://www.addictioncentre.com/treatment/cognitive-behavioural-therap>

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