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Review Article

ALCOHOL WITHDRAWAL SYNDROME, MANIFESTATION AND MANAGEMENT

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Abstract:

Introduction: Alcohol use disorder (AUD) is anticipated to affect about eighteen percent of the population and five percent yearly. Furthermore, it has been suggested that about twenty percent of adults in the emergency department have AUD and that the incidence of alcohol withdrawal syndrome (AWS) in patients admitted to surgical Intensive Care Unit (ICU) varies from eight to forty percent, and most likely to be linked to infectious complications and have a higher mortality rate. It is estimated that up to fifty percent of AUD patients will experience withdrawal symptoms, a minority of whom needs management. AWS represents a clinical condition recognized by symptoms of autonomic hyperactivity like agitation, tremors, irritability, anxiety, hyperreflexia, confusion, hypertension, tachycardia, fever and diaphoresis. AWS often presents in alcohol-dependent patients within six to twenty four hours after the sudden stop or reduction of alcohol intake. It is highly life-threatening condition. The severity can range from mild/moderate forms characterized by tremors, nausea, anxiety, and depression, to severe forms recognized by hallucinations, seizures, delirium tremens and coma. The mild-moderate form of AWS is usually self-managed by patients or symptoms improves within two to seven days from the last drink, whereas the more severe AWS needs medical treatment. The recognition and further management of AWS is of great clinical value, as AWS is one of the causes of morbidity and mortality.

Aim of work: In this review, we will discuss Alcohol withdrawal syndrome, manifestation and management

Methodology: We did a systematic search for alcohol withdrawal syndrome, manifestation and management using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). We only included full articles.

Conclusions: AWS exemplifies a possibly life-threatening medical illness usually affecting AUD patients suddenly reducing or stopping alcohol intake. AWS should be considered in the differential diagnosis of any patients presenting with symptoms of autonomic hyperactivity. The use of a clinician-administered scale (CIWA-Ar or Alcohol Withdrawal Scale) is of great value to diagnose AWS and start adequate treatment. BZDs represent the gold standard treatment as a result both for their high rate of efficacy and being the only medications with proven ability to prevent the complicated forms of AWS (seizures, DTs). The management of AWS may be difficult. The primary phase is recognized by patient agitation and non-collaboration. This phase should be managed aggressively, to decrease the risk of medical complications (seizures, DTs, death), decrease patient suffering and improve quality of life. The direct effect of these measures will be, in most of cases, a strong physician-patient relationship. The latter is essential to enhance patient's disposition toward medical management and to start a long-term, multidisciplinary treatment of alcohol dependence. While BZD's addictive characteristics limit their long-term use, the possibility of using other medications able to be effective both for the management of AWS and the further long-term program for alcohol relapse prevention represents an advantage, i.e. carbamazepine, SMO, baclofen, gabapentin and topiramate. The initial administration of a non-BZD agent together with gold-standard treatments represents a useful choice to reduce the need for extra-dose BZD prescription (BZD-sparing drugs) and to start a medication with anti-craving characteristics. But it is highly essential to keep in mind that at present, BZDs are the most effective and manageable medications for the management of AWS.

Key words: Alcohol withdrawal syndrome, manifestation, management

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INTRODUCTION:

Alcohol use disorder (AUD) is anticipated to affect about eighteen percent of the population and five percent yearly [1]. Furthermore, it has been suggested that about twenty percent of adults in the emergency department have AUD[2] and that the incidence of alcohol withdrawal syndrome (AWS) in patients admitted to surgical Intensive Care Unit (ICU) varies from eight to forty percent, and most likely to be linked to infectious complications and have a higher mortality rate [3].

It is estimated that up to fifty percent of AUD patients will experience withdrawal symptoms [4], a minority of whom needs management. AWS represents a clinical condition recognized by symptoms of autonomic hyperactivity like agitation, tremors, irritability, anxiety, hyperreflexia, confusion, hypertension, tachycardia, fever and diaphoresis. AWS often presents in alcohol-dependent patients within six to twenty four hours after the sudden stop or reduction of alcohol intake. It is highly life-threatening condition. The severity can range from mild/moderate forms characterized by tremors, nausea, anxiety, and depression, to severe forms recognized by hallucinations, seizures, delirium tremens and coma [5].

The mild-moderate form of AWS is usually self-managed by patients or symptoms improves within two to seven days from the last drink, whereas the more severe AWS needs medical treatment. The recognition and further management of AWS is of great clinical value, as AWS is one of the causes of morbidity and mortality [6].

In this review, we will discuss the most recent evidence regarding alcohol withdrawal syndrome, manifestation and management.

METHODOLOGY:

We did a systematic search for alcohol withdrawal syndrome, manifestation and management using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). We only included full articles.

The terms used in the search were: Alcohol withdrawal syndrome, manifestation, management

3. AWS: identification of symptoms

AWS must be considered amongst the different probable differential diagnoses of patients with symptoms of AWS. Health care professionals must ask each patient about their drinking habits, the characteristic beginning of symptoms after just hours of alcohol stop, and previous history of AWS. The

Cut down-Annoyed-Guilty-Eye opener (CAGE) and Alcohol Use Disorders Identification Test (AUDIT) questionnaires [7] could assist recognizing AUD patients.

Moreover, patients with decreased level of awareness at risk for AWS have to be checked for the appearance of AWS symptoms, and safely and effectively treated. AWS characterizes a continuous spectrum of symptoms ranging from mild withdrawal symptoms to delirium tremens (DT). AWS could begin with mild symptoms and then develop to more severe methods, or could begin with DT, particularly in those patients with previous diagnosis of DT or with history of multiple AWS.

Often, the first-degree AWS symptoms start six to twelve hours after the last alcohol consumption. The second-degree AWS symptoms are considered by visual and tactile disturbances and begin twenty-four after the last drink. Almost twenty five percent of AWS patients have temporary variations of perception [8] like auditory (voices), or less frequently, visual (zooscopies) or tactile disturbances [9].

About ten percent of patients who have withdrawal symptoms also have alcohol withdrawal seizures (third degree AWS) , beginning after twenty four to forty eight from the last drink and categorized by diffuse, tonic-clonic seizures often with no postictal period [10].

Delirium tremens characterizes the most severe symptom (fourth degree) of AWS, as the result of no management of AWS, and about in five percent of patients with AWS. Often, it appears after the last drink, though it might start up to ten days later. Symptoms last about five to seven days [11]. DT is characterized by a fast variation of consciousness and alteration in thinking process occurring over very short time, occurs with severe autonomic symptoms and psychological symptoms.

The DT patient displays agitation, hallucinations and disorientation. The presence of disorientation differentiates delirium from alcoholic hallucinosis. Delirium, psychosis, hallucinations, hyperthermia, malignant hypertension, seizures and coma are common presentations of DT. DT can be accountable of injury to patient or to staff, or of medical complications, which may result in to death in one to five percent of patients [12]. After the management of acute AWS, some symptoms can persist from weeks to months following the five to seven days of acute detoxification period.

AWS: diagnosis

According to Diagnostic and Statistical Manual of mental disorders (DSM-5) criteria, the diagnosis of AWS is based on the observation of signs and symptoms of withdrawal in those patients who experienced a sudden reduction or stopping of alcohol consumption. DSM-5 needs the observation of at least two of the following symptoms: autonomic hyperactivity (sweating or tachycardia); increased hand tremor; insomnia; nausea or vomiting; transient visual, tactile or auditory hallucinations or illusions; psychomotor agitation; anxiety; and tonic-clonic seizures. Moreover, it is essential to differentiate symptoms related to the acute or chronic alcohol abuse or withdrawal, from those related to other psychiatric disorders [13]. But, from a practical point of view, the use of an interview can be difficult due to the facts that patients suffering from AWS usually show agitation and confusion. Furthermore, it should be highlighted that severe medical illnesses (i.e. pneumonia, coronary heart disease, alcohol liver disease and anaemia) have been concluded to induce AWS and to elevate the risk of severe AWS. In these patients a prophylactic management could be useful.

AWS: treatment**5.1 Goals of the treatment**

AWS symptoms are restricting and patients who experienced withdrawal. The main objective of the management is to minimize the severity of symptoms to prevent the more severe presentations like seizure, delirium and death and to improve the patient's quality of life. Furthermore, an effective treatment of AWS can be preceded by efforts in increasing patient inspiration to continue long-term alcohol abstinence and help them enter into a relapse prevention program [14].

Patients who suffer from mild to moderate AWS can be treated as outpatients whereas more severe forms should be checked and managed in an inpatient setting. The availability of an Alcohol Addiction Unit is of help in the clinical evaluation, management, and treatment of AWS patients, with a reduction in hospitalization costs. Patients can be treated mainly as outpatients and transferred to the inpatient unit only when the clinical situation requires [15].

5.2 General treatment and supportive care

Non-pharmacologic interferences are the 1st line approach and, the only approach required. They include frequent reassurance, reality orientation, and nursing care.

5.3 Drugs for the treatment of AWS

The treatment of AWS requires the use of a long-

acting drug as a substitutive agent to be gradually tapered off. The ideal drug for AWS should have a rapid onset and a long duration of action in reducing withdrawal symptoms and a relatively simple metabolism, not depending on liver function. It should not interact with alcohol, should suppress the "drinking behavior" without producing cognitive and/or motor impairment and it should not have a potential for abuse [16].

5.4 Benzodiazepines

At present benzodiazepines (BZDs) represent the "gold-standard" in the treatment of AWS ¹⁶. Furthermore, BZDs represent the only class of medications with proven efficacy in preventing the development of complicated forms of AWS, with a reduction in the incidence of seizures, DT and the associated risk of mortality [17]. In particular, in the United States, BZDs are the first choice treatment, while in Europe, clomethiazole is also widely used. The efficacy of BZDs in the treatment of AWS seems to be mediated by their stimulation of GABAA receptors with alcohol mimicking effects.

Treatment of DT requires the use of BZDs as primary drugs, with the possible use of neuroleptics to control psychosis and dysperceptions. The use of BZDs is, however, associated with increased risk of excessive sedation, motor and memory deficits and respiratory depression, and these effects are more pronounced in patients with liver impairment. Moreover, the risk of abuse and dependence limits BZD use in AD patients.

5.5 Barbiturates and propofol

Using of barbiturates in the management of AWS has been restricted due to their narrow therapeutic window, the risk of extreme sedation and the interfering with the clearance of several medications ¹⁸. But, in ICU, in those who need high doses of BZDs to manage AWS symptoms or developing DT, barbiturates still have a specific indication. The combination of phenobarbital with benzodiazepines supports BZD binding to the GABAA receptor, and this will probably increase the efficacy of the benzodiazepine [19]. In patients have suffered by severe DT requiring mechanical ventilation, the combination of benzodiazepines and barbiturates produces both a reduction in the need of mechanical ventilation and a decrease length of stay in the ICU.

5.6.1 Alpha2-agonists, beta-blockers and neuroleptics—

These classes of drugs have been checked and can be administered as adjunctive management for AWS. But, the lack of efficacy in preventing severe AWS

and the risk of masking AWS symptoms make these medications not suggested as monotherapy. They should only be given as adjunctive treatment, in patients with co-existing comorbidities, and in order to control neuro-autonomic presentations of AWS when not it is not enough to control by BZDs administration.

5.6.2 Carbamazepine—

Carbamazepine is a tricyclic anticonvulsant that can produce a GABAergic effect and to block NMDA receptors [20]. It has been proved to be an effective medication in the treatment of AWS, at least in mild to moderate forms, producing an effect superior to placebo and non-inferior to BZDs. The proposed management algorithm is 600–eight hundred milligram per day on day 1, tapered down to two hundred mg over five days. A decrease of alcohol relapse has also been showed in the post-AWS phase²¹. But, adverse effects associated with long-term administration could limit its wide use.

5.6.3 Valproate—

Valproic acid can produce a dose-dependent recovery of AWS symptoms, with a decreased incidence of seizures and a protection toward the worsening of AWS severity (anti-kindling effect). These features make valproic acid a promising medication in the outpatient treatment of mild-to-moderate forms of AWS [22]. The most commonly observed adverse-effects are gastrointestinal distress, tremor and sedation.

6 CONCLUSIONS:

AWS exemplifies a possibly life-threatening medical illness usually affecting AUD patients suddenly reducing or stopping alcohol intake. AWS should be considered in the differential diagnosis of any patients presenting with symptoms of autonomic hyperactivity. The use of a clinician-administered scale (CIWA-Ar or Alcohol Withdrawal Scale) is of great value to diagnose AWS and start adequate treatment. BZDs represent the gold standard treatment as a result both for their high rate of efficacy and being the only medications with proven ability to prevent the complicated forms of AWS (seizures, DTs). The management of AWS may be difficult. The primary phase is recognized by patient agitation and non-collaboration. This phase should be managed aggressively, to decrease the risk of medical complications (seizures, DTs, death), decrease patient suffering and improve quality of life. The direct effect of these measures will be, in most of cases, a strong physician-patient relationship. The latter is essential to enhance patient's disposition toward medical management and to start a long-term,

multidisciplinary treatment of alcohol dependence. While BZD's addictive characteristics limit their long-term use, the possibility of using other medications able to be effective both for the management of AWS and the further long-term program for alcohol relapse prevention represents an advantage, i.e. carbamazepine, SMO, baclofen, gabapentin and topiramate. The initial administration of a non-BZD agent together with gold-standard treatments represents a useful choice to reduce the need for extra-dose BZD prescription (BZD-sparing drugs) and to start a medication with anti-craving characteristics. But it is highly essential to keep in mind that at present, BZDs are the most effective and manageable medications for the management of AWS.

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