

## Review

# Alternative management of seizures in patients of drug users

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### ABSTRACT

*Use of almost all the substances like opioid, alcohol, cocaine, benzodiazepines and stimulants like amphetamines has been related to either precipitate or causation of seizures in drug users. However there is no evidence that using the nicotine and caffeine in usual or 'normal' amounts affects seizure. Many report found that marijuana use may have a protective or provocative effect for new-onset seizures.*

### Alcohol and seizures

Despite being a considerable problem of seizure with alcohol that is responsible for one third of seizure-related admissions, there is little consensus as to the optimal investigation and management of alcohol-related seizures 1,2. ( Earnest MP et al 1976, Jallon P et al 1999, Leone MA et al 2007). When alcohol is related to seizures, it is often the state of alcohol withdrawal that causes the seizures, not the drinking itself. Binge drinking and alcohol withdrawal can even lead to status epilepticus, a life-threatening and potentially fatal problem. Research also suggests that repeated alcohol withdrawal seizures may make the brain more excitable for disturbances of sleep and have adverse drug interactions with antiepileptic drugs. Thus, people who have experienced seizures provoked by drinking may begin to experience unprovoked epilepsy seizures regardless of alcohol use<sup>3</sup>.

### How to manage seizures or epilepsy with alcohol use

Good history taking of alcohol consumption is important for its management and to support the history taking use of a structured questionnaires focus on Cutting down, Annoyance by criticism, Guilty feeling, and Eye-openers (CAGE), Alcohol Use Disorders Identification Test (AUDIT) are also recommended. When the drinking history is inconclusive, then other parameters like elevated values of carbohydrate-deficient transferrin and gamma-glutamyltransferase can support a clinical suspicion. A first epileptic seizure should prompt neuroimaging (CT or MRI) if needed. Before starting any carbohydrate containing fluids or food, patients presenting with suspected alcohol overuse should be given prophylactic thiamine parenterally. After an alcohol withdrawal seizure (AWS), the patient should be observed in hospital for at least 24 h and the severity of withdrawal symptoms needs to be followed. For patients with no history of

withdrawal seizures and mild to moderate withdrawal symptoms, routine seizure preventive treatment is not necessary. Generally, benzodiazepines are efficacious

and safe for primary and secondary seizure prevention; diazepam or lorazepam, is recommended. However antiepileptic medicines can lower tolerance for alcohol therefore alcoholic intoxication can occur. Many times rapid intoxication becomes a big problem because the side effects of antiepileptic medicines can be similar to the acute effects of alcohol itself<sup>4, 5, 6</sup>.

### All patients with symptoms of alcohol withdrawal not require seizure prophylactic treatment

Patients with mild- to- moderate alcohol withdrawal symptoms can successfully be

detoxified with supportive care only. Supportive treatment includes a calm, reassuring atmosphere, dim light, tea coffee restriction, and hydration<sup>7</sup>.

### Patient management

Subsequent to the acute treatment of alcohol related seizures, attention should be given to other potential complications of alcohol overuse such as thiamine deficiency, electrolyte disturbances, acute intracranial lesions, infections, and development of the alcohol withdrawal syndrome, potentially leading to delirium tremens, these factors are addressed below.

### Thiamine therapy

Diagnosis of thiamine deficiency is difficult, and the consequences of not treating may be severe. Prolonged heavy drinking causes reduced absorption and increased excretion of thiamine, its deficiency can cause Wernicke's encephalopathy. In a research found that only 5 – 14% of patients with Wernicke's encephalopathy are diagnosed. The majority (80%) patients those show CNS lesions caused by thiamine deficiency are chronic alcoholic<sup>8</sup>. Oral administration is insufficient as the intestinal thiamine absorption may be severely impaired. In a Cochrane review, only one sufficiently large randomized double-blind trial on the preventive effects of different doses of thiamine could be identified, from which it could be concluded that a daily dose of 200 mg thiamine was better than 5 mg. For the treatment of imminent or manifest Wernicke's

encephalopathy, uncontrolled trials and empirical clinical practice suggest daily dose of at least 200 mg thiamine parenterally for minimum 3 – 5 days and patients with Wernicke's encephalopathy may benefit from continued treatment for more than 2 weeks<sup>9</sup>.

#### **Treatment of electrolyte disturbances**

Due to large fluid intake (beer), hyponatremia may develop in alcohol overusers. Hyponatremia in alcohol over users generally shows a benign clinical course, and usually repairs with cessation of alcohol intake and re-institution of a normal diet. If infusion is considered necessary, according to a retrospective study the rate of serum sodium correction should not exceed 10 mmol/day. The evidence is insufficient for treatment recommendations<sup>10</sup>.

Hypomagnesaemia and respiratory alkalosis seem to be associated with alcohol withdrawal, and correction of hypomagnesaemia may raise the seizure threshold in the initial phase of alcohol withdrawal<sup>11</sup>. Unresponsiveness to parenteral thiamine therapy is a possible consequence of hypomagnesaemia. However, there is not sufficient evidence to recommend routine correction of hypomagnesaemia<sup>12</sup>.

#### **Management of epilepsy in patients with current alcohol overuse**

One should not abuse alcohol if he has history of seizures. If allowed to drink only few drinks could be taken slowly. Binge drinking (drinking too much at once or long periods of time) itself is a precipitating event for seizures, so better to be avoided. The comprehensive management of these patients includes careful counseling and information about the seizure - precipitating effect of alcohol along with acute management<sup>13</sup>.

#### **COCAINE**

All forms of cocaine use can cause seizures within seconds, minutes or hours after it is taken. Seizures caused by cocaine are uniquely dangerous and may be associated with heart attacks, disrupting the heart's normal rhythm (cardiac arrhythmia), and death. They can even occur in someone who has never had a seizure before. If one has epilepsy, he should definitely avoid cocaine<sup>14</sup>.

#### **Amphetamines and other stimulants**

Amphetamines are brain stimulants. When used under a doctor's supervision, amphetamines or other stimulants do not seem to increase the risk of seizures in people with epilepsy. However, there are a few exceptions.

- If one abuse amphetamines or related drugs like "Ecstasy" (MDMA), he can experience sleep deprivation, confusion, or major psychiatric disorders. When this happens, he is very likely to forget seizure medicine, which can also trigger

seizures.

- Some researchers have also found long-lasting damage to the brain from the use of some types of stimulants. Very high doses of amphetamines can cause severe tonic-clonic seizures, heart attacks, and death<sup>15</sup>.

#### **Marijuana**

Studies in animals have suggested that THC (tetrahydrocannabinoids), the active ingredient in marijuana, and cannabidiol, another substance in marijuana, can help seizures as well as provoke them. However, not enough is known about which ingredients and how much of them can help or harm people with seizures. Marijuana also has both some side effects, and stopping marijuana suddenly after using it recreationally could increase the risk for seizures. More study is needed about the use of marijuana and its risks or benefits<sup>16</sup>.

#### **Heroin**

Heroin and related narcotics are drugs derived from opium, such as oxycodone, or are manufactured drugs to be chemically similar to opium. High-dose opioid therapy can precipitate seizures; however, the mechanism of such a dangerous adverse effect remains poorly understood. The pro seizure effect of morphine is thought to be mediated through selective stimulation of mu and kappa opiate receptors. Taking large amounts of narcotics can cause serious lack of oxygen to the brain too, which can lead to seizures. People who use these drugs also often forget to take their prescribed seizure medicines<sup>16</sup>.

#### **Nicotine and caffeine**

There is no evidence that using these two popular licit drugs in usual or 'normal' amounts affects seizure in most people with epilepsy. Occasionally there are case reports of susceptible people who experience seizures, especially if they use large amounts.

- For caffeine, it may be difficult to tell how much amount you are getting, because in many different beverages, foods, and medications its contents are present.
- Caffeine may affect a person's seizures by interfering with sleep, rather than triggering seizures directly.
- Cigarette smoking is likely more dangerous than the effects of nicotine for people with seizures: the loss of consciousness or control of movement can cause you to drop a lighted cigarette and start a fire<sup>17</sup>.

#### **Alternative therapies of epilepsy in patients of substance use disorders**

Can be categorized as below

**Lifestyle changes**

- Exercise
- Avoidance of sleep deprivation
- Avoidance of excessive alcohol and other drugs consumption

**Psychological approaches**

- Techniques to abort seizures or reduce seizure frequency (forexample, avoidance, relaxation, biofeedback, aversive therapy)
- Promotion of emotional wellbeing (for example, yoga, meditation)
- Reduction of psychiatric co-morbidity that are very frequent to coexist in drug users(for example, anxiety or depression)
- Coping strategies for living with epilepsy along with drug use (for example cognitive behavior therapy, counselling, psychotherapy, educational interventions)

**Lifestyle changes****Exercise**

Participation in exercise should be recommended for persons with epilepsy. This is intended to have an impact on quality of life and social inclusion rather than seizure control. There is no RCT assessing the effect of exercise on patients with epilepsy. One prospective study of 21 adults (acting as their own controls) reported no difference in seizure control during a 4 week aerobic exercise programme<sup>18</sup>.

**Sleep hygiene**

Sleep deprivation is well recognized as a precipitant for seizures (and most epilepsies), particularly in the idiopathic generalized epilepsy syndromes and temporal lobe epilepsy. Interictal EEG discharges are promoted by sleep deprivation, possibly by increasing neuronal excitability. Patients with epilepsy should therefore be advised to have good sleep hygiene. They should try to ensure regular and consistent sleep<sup>19</sup>.

**PSYCHOLOGICAL APPROACHES**

Techniques to abort seizures or reduce seizure frequency

**Avoidance**

In reflex epilepsies, patients describe specific triggers that can precipitate seizures. The most common reflex epilepsy is that triggered by visual stimuli (flickering lights or specific visual patterns or both). Other triggers include thinking, listening to specific types or pieces of music, eating, reading, immersion in hot water, chess playing, or brushing hair. Measures to try to avoid seizures should be advised including sitting more than 2.5 m away from the television in a well lit room, using the remote control, and approaching the television with

one eye covered. Covering one eye can also be used when a patient is exposed to other visual stimuli, such as flashing lights. These techniques are called avoidance techniques.

**Relaxation techniques**

The role of relaxation techniques in intractable epilepsy has been discussed in a Cochrane review. Four RCTs were examined and outcome measures included seizure frequency and improvement in quality of life scores. It has been found that successfully taught relaxation techniques might indirectly improve seizure control in a number of Patients with epilepsy (for example, through improved sleep)<sup>20</sup>.

**Aversive therapy**

According to the principles of operant conditioning, a seizure may be a behaviour that is learned to avoid something unpleasant or to gain a reward. Therefore, the chain of events which occurs during a seizure could be altered by presenting a noxious stimulus like administering skin shocks, shaking, and painful stimulus at the time of or following a seizure. The technique became popular in the 1960s and 1970s. Case reports and small series in the literature document studies where noxious smells or skin shocks were administered; shaking patient's shoulders and shouting "no" at seizure onset and painful dorsiflexion of the palm have also been described. These techniques have no obvious scientific basis and are clearly inappropriate and unethical in current practice<sup>21</sup>.

**Promotion of emotional well being****Yoga**

Stress is considered to be a precipitant for seizures and yoga is believed to induce relaxation.

Yoga involves breathing exercises, postures, and meditation techniques. Study with 50 epilepsy patients shows that yoga and Acceptance and Commitment Therapy had beneficial effect in control of seizures. Yoga treatment found to be better compared with no intervention<sup>22</sup>.

**Managing psychiatric co-morbidity**

Anxiety, depression, and psychosis may complicate epilepsy, both before certain seizures and also between seizures in individuals with epilepsy. The frequent co-occurrence of psychiatric disorders, particularly affective and anxiety disorders with substance use disorders are well documented in a variety of populations and settings. These symptoms may also be part of the epilepsy syndrome or iatrogenic arising as a consequence of the use (or withdrawal) of substance and AEDs<sup>23</sup>.

Thus, effective pharmacological treatment of the underlying psychiatric disorder may improve not only

the psychiatric disorder but also improve the perceived need of illicit drugs<sup>24</sup>. Examples of this type of approach includes the use of antidepressant treatment for depressed alcoholics opioid and cocaine-dependent individuals.

### Coping strategies for living with epilepsy

Epilepsy can have a profound effect on patient's lives. Psychological treatments that focus on the emotional impact of seizures are now considered as standard management practice in adult patients<sup>25</sup>. Techniques include both individual and group/family counselling and psychotherapy. Cognitive behaviour therapy (CBT) is another useful approach. Patients are taught coping skills to try to recognize and control their symptoms. There is some evidence that this technique may have a beneficial role in depression but not in seizure control in adults with epilepsy. Patient support groups and occasionally group meetings organized by nurse specialists may be helpful, and may even obviate (but never substitute) the need for formal psychological support, including CBT.

### Educational interventions

There have been several RCTs that have evaluated whether residential educational programmes for adults with epilepsy and drug use can improve their quality of life. Results suggest a significant improvement in the knowledge and understanding of epilepsy, coping with epilepsy, and concordance (adherence) with medication<sup>26</sup>.

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