Brief report

Interaction between disulfiram and betel chewing: A case series

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Abstract

Disulfiram is used for the treatment of alcohol dependence. Betel chewing is a practice seen in Sri Lanka. This article reports a case series describing an aversive reaction between disulfiram and betel,

in persons who were abstinent from alcohol. This association has not been reported previously in the literature.

SL J Psychiatry 2016; 7(1): 28-30

Introduction

Disulfiram is used for the treatment of alcohol dependence. Betel chewing is a practice seen in Sri Lanka from very early times. This article reports a case series describing an aversive reaction between disulfiram and betel, in persons who were abstinent from alcohol. To our knowledge this association has not been reported previously in the literature.

Case Report 1

A 43 year old farmer who had been consuming excessive amounts of alcohol presented with features of alcohol dependence complicated by alcohol withdrawal seizures. He had no features of other psychiatric disorders such as depression or anxiety. In addition to alcohol dependence, he was dependent on betel and chewed about 10 portions of betel per day. He was discharged on oral thiamine and topiramate after successful detoxification.

He was started on disulfiram 250mg daily as an outpatient after a careful discussion on advantages and disadvantages of this medication. The patient presented to the mental health clinic four days after starting on the medication. He complained of excessive sweating, headache, fine tremors and nausea after betel chewing. He denied using of any alcohol or alcohol containing foods and drinks or mouthwash which was corroborated by patient's family. Due to this reaction he had stopped both disulfiram and chewing of betel.

Case Report 2

A 40 year old teacher was brought to the outpatient psychiatry clinic by his concerned wife. His regular alcohol use affected his work as he attended school under the influence alcohol. He had been consuming

three-quarter to one bottle of spirits daily and had features of dependence including withdrawal symptoms. He was dependent on betel and used to chew betel with each drink of alcohol. There was no history of other substance use. He was determined to stop alcohol. Following successful community detoxification he was started on disulfiram after a discussion on various management options of alcohol abstinence.

The patient presented prior to the next scheduled appointment as he had experienced a throbbing headache, nausea and panic attacks after betel chewing while on disulfiram. He denied the use of alcohol or alcohol containing food or drinks since the commencement of disulfiram. He had continued disulfiram and had stopped chewing betel due to the unpleasant experience. There had been no such experience after he stopped chewing betel.

Case Report 3

A 40-year-old male security officer with a history of hypertension and dyslipidaemia was admitted to a medical ward with delirium tremens on a background of heavy alcohol use for more than 10 years duration and precipitous cessation of alcohol use. He was also dependent on betel and nicotine. Following successful treatment for delirium tremens he requested medication to remain abstinent. He opted to use disulfiram and was started on 250mg daily dose.

He was again admitted to a medical ward one day after discharge. The patient had experienced vomiting, body aches, tremors, excessive sweating and a headache. He had been adherent with medication after discharge, and had been abstinent from alcohol. However, he had resumed betel chewing on the very next day after hospital discharge. He had experienced the above symptoms and signs a few hours after chewing two portions of betel.

Case Report 4

A 41-year-old teacher sought medical treatment for his alcohol dependence following a disciplinary action against him owing to alcohol use at work. In addition to use of alcohol, he was a chronic betel chewer. He had been consuming half bottle of arrack and about 10 portions of betel a day. Following initial management a discussion ensued regarding treatment strategies for alcohol abstinence. Subsequently he was commenced on disulfiram 250mg mane, after a two week period of total abstinence from alcohol.

After the commencement of disulfiram, during the next review, he complained of palpitations, drowsiness, sweating, and difficulty in breathing and abdominal discomfort. The above reactions had commenced few minutes after he had started to chew betel. Due to this he subsequently stopped chewing betel entirely. He also reported that the above reaction was less severe if he did not take arecanut.

Case Report 5

A 45-year-old postman who had been consuming alcohol for nearly 20 years presented to the clinic requesting help to stop alcohol. He had features of alcohol dependence and started using alcohol in the morning, before going to work. In addition to drinking, he smoked 10 cigarettes and chewed 5-6 portions of betel a day.

After discussing with the patient and his wife, he was started on disulfiram 250mg mane. At the next review, one week after the commencement of disulfiram, he described episodes of sweating and abdominal discomfort along with tightness of the chest after starting to chew betel, while he was abstinent from alcohol. The discomfort was so unpleasant it led him to stop his long-term habit of betel chewing. As a result, at the time of presentation to the clinic he was abstinent from both alcohol and betel.

Discussion

Disulfiram is used for the management of alcohol dependence. It irreversibly inhibits the enzyme aldehyde dehydrogenase that is involved in the second stage metabolism of alcohol (1). If an individual taking disulfiram consumes alcohol, unpleasant adverse effects are caused by the accumulation of acetaldehyde (2, 3). This experience is expected to give rise to a negative conditioning, prompting the patient to stop taking alcohol in order to avoid distressing effects. Flushing, headache, nausea, tachycardia and vomiting are the commonest effects of toxic levels of acetaldehyde (4). Myocardial infarction, congestive cardiac failure and respiratory suppression are potentially lethal effects of alcohol consumption while on disulfiram (5).

Disulfiram should not be prescribed if the patient is allergic to same, under the influence of alcohol, diagnosed to have severe heart disease or psychosis, or if he / she is prescribed metronidazole, amprenavir, ritonavir or sertraline. It should be avoided for at least 12 hours after the last drink. A literature survey by the authors did not reveal published articles regarding interactions between disulfiram and chewing of betel.

Betel chewing is a practice seen in Sri Lanka from very early times. Betel is popular all over Sri Lanka and the leaf is mainly used for chewing, together with arecanut, slaked lime and tobacco. Betel chewing is also known to be associated with oral cancer which is the cancer with the third highest prevalence in Sri Lanka.

Betel nut is the seed of the fruit of the areca palm. The chewing of betel nut dates to antiquity. It is known to produce a sense of well-being, euphoria, heightened alertness, sweating, salivation, a hot sensation in the body and increased capacity to work (6). Dependence and withdrawal symptoms are not uncommon with long term chewing of betel, although the mechanisms of these effects are not well understood (6). Some of effects are reported to be related to arecoline, the major alkaloid of the areca nut (6). Betel chewing may affect central and autonomic nervous systems (6). However, these mechanisms do not explain the reason for an interaction between arecanut and disulfiram.

Slaked lime contains calcium hydroxide. The chemical formula is Ca(OH)_2 . It is obtained when calcium oxide is mixed with water. No reactions between slaked lime and disulfiram have been recorded in the literature. Tobacco used for betel chewing is prepared from dried tobacco leaves. There are no clear interactions recorded between tobacco and disulfiram.

Thus, the literature did not reveal reported interactions between disulfiram and ingredients used for betel chewing. However, this case series reports a reaction to betel chewing in patients who had been prescribed disulfiram as part of aversion induction therapy for alcohol. Since dependence on betel chewing is highly prevalent in Sri Lanka, and since it is known to contribute to oral malignancies, treatment with disulfiram could be a potential management strategy to reduce betel chewing. Clinicians prescribing disulfiram to help maintain abstinence from alcohol should also be aware of the potential interactions if the individual concerned chews betel. Future research should focus on further delineating the chemical reactions between disulfiram and ingredients used for betel chewing.

Conflicts of interest

None declared

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