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# Deterrent Action of Acamprosate: A Case Report

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**Case Report**

## Abstract

**Background:** Among the three pharmacological agents available for alcohol de-addiction, acamprosate and naltrexone are considered anti-craving agents. Among these two, acamprosate is better tolerated, has low abuse potential, and is safe in overdose. But the mechanism of action of acamprosate still remains unclear.

**Case Report:** This case report gives a description of a 46-year-old male patient diagnosed with alcohol dependence syndrome with prior admissions and failed treatments with naltrexone and baclofen. He developed skin reaction after relapsing with alcohol use while receiving acamprosate therapy. The severity of the adverse effects varied with the amount of alcohol consumed by the patient. This suggests the possibility of deterrent-like action of acamprosate in our patient. The symptoms reduced after abstinence from alcohol and the patient was continued on acamprosate and relapse prevention therapy (RPT).

**Conclusion:** Clinicians should consider the possible deterrent effect of acamprosate and manage such patients accordingly.

**Keywords:** Adverse effects; Acamprosate; Urticaria

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## Introduction

Alcohol use disorders (AUDs) are the most common substance use disorders (SUDs) as per the recent National Mental Health Survey conducted in India. The prevalence of AUD ranks only next to tobacco dependence syndrome.[1] These disorders have significantly high rates of mortality and morbidity. Only three pharmacological agents are approved for the management of AUDs. Among them, disulfiram is the deterrent which acts by inhibiting the enzyme acetaldehyde dehydrogenase. The disulfiram ethanol reaction which occurs after consuming alcohol is due to the effects of accumulated acetaldehyde. Symptoms usually appear after 5-15 minutes of alcohol consumption and the intensity of reaction depends upon the amount of alcohol consumed which sometimes can be life-threatening.[2-4]

Acamprosate is an anti-craving agent apart from naltrexone which is widely in use for AUDs. It can be a better option in patients with mild to moderate hepatic impairment and those with co-occurring medical conditions and protracted withdrawal. It is generally well tolerated and has less risk of drug interactions as it is not metabolized in the liver.[5] It is also a better option in patients with comorbid psychiatric conditions and drug misuse.[6]

Recent review has suggested that combination of acamprosate with psychosocial interventions can increase the complete abstinence rate, time to first drink, and percentage of alcohol-free days.[7] Despite this evidence of efficacy and safety, the mechanism of action of acamprosate is unclear. It is calcium salt of N-acetyl homotaurine, synthetic analog of endogenous amino acid taurine. It has chemical resemblance to amino acids like gamma-aminobutyric acid (GABA), glutamate, glycine, and aspartate. Recent evidence contradicts these propositions and suggests that the effects of acamprosate are due to the co-administered calcium moiety but not the compound itself.[8]

This leads us to hypothesize that there might be several other mechanisms by which acamprosate exerts its effects in patients with AUDs. We hereby report a case of 46-year-old man diagnosed with alcohol dependence syndrome who developed disulfiram-like reaction with acamprosate.

## Case Report

Informed consent was taken from the patient prior to reporting. Our patient was a 46-year-old man coming from rural background presenting with complaints of alcohol and tobacco use from the last 10 years. He would take both the substances in a pattern characterized by craving, tolerance, withdrawal, and neglect of alternative pleasures. The usual daily amount of alcohol used by the patient was about 600-800 ml of country made liquor (CML). Along with that, he would chew 3-4 pouches of tobacco per day in about 15 times. Patient has been in contact with our hospital since 2017; during that period, he was admitted for management of alcohol dependence and started on baclofen 60 mg along with provision of motivational enhancement therapy (MET). The patient remained off alcohol for 4 months post discharge followed by relapse under peer pressure. This time, he developed withdrawal seizure in June 2017. Naltrexone was started along with brief sessions of relapse prevention therapy (RPT) on out-patient basis. Despite this, patient would take alcohol once in 10-15 days, but was regular to follow up and compliant to treatment till December 2017. Thereafter, he stopped medications and started using alcohol. There were 2 admissions in between in January and May 2018, as he relapsed with alcohol use for 20 days in between, developing 3 episodes of withdrawal seizures in the latter admission. High-risk situations were identified and addressed and patient was educated about the harms of continuing use. He was restarted on naltrexone in view of past response with the same. From September 2018, patient restarted taking 360 ml of CML regularly for about a month and was admitted again in October 2018. He was given option of disulfiram, but patient was not willing to take it. So he was started on acamprosate 1998 mg/day and relapse prevention counseling was continued. He remained off alcohol for about 3 months. No adverse effects of the drugs were reported during this period. From February 2019, patient started to take alcohol (CML) at about 360 ml in the evening and had his medications as usual. The next day from afternoon, patient developed reddish lesions over his chest and upper limbs along with itching. He also developed swelling

of his lips. Patient visited hospital and dermatological consultation was taken. He was diagnosed with drug-induced urticaria and was managed appropriately. He was prescribed lorazepam 2 mg at night and was advised to follow up in 2 weeks. However, patient continued to take previous treatment of acamprosate and lorazepam. After a week, he took CML of about 180 ml in the evening and took morning/afternoon doses of acamprosate (March 2019). After 2 hours of taking alcohol, he developed itching and rashes over forearms and chest (Figures 1, A and B). On examination, the patient had red maculopapular rashes all over the chest and abdomen. The patient scored 9 on Naranjo Adverse Drug Reaction Probability Scale which suggests definite chance of adverse drug reaction. Patient denied that any others who took alcohol from the same place had developed such sort of reaction. He did not have any past history of physical illness like diabetes, hypertension (HTN), and allergy/allergic reaction to any drugs. There was no family history of any physical illness. Investigations showed deranged liver function test (LFT) [alkaline phosphatase (ALP)-126, aspartate aminotransferase (AST)-60, gamma-glutamyl transferase (GGT)-146], platelet count of 1.24 lakhs, normal total count, normal differential count, and normal renal functions and electrolytes. Patient was followed up twice in the next 3 months and remained abstinent to alcohol during this period. He did not develop any such skin rash subsequently in the follow up.

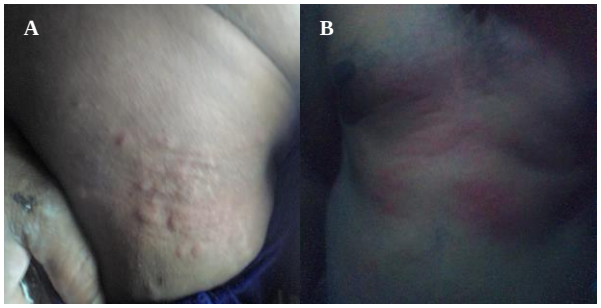


**Figure 1.** Urticaria over the abdomen (A) and chest (B)

## Discussion

We described a patient with alcohol dependence syndrome who developed skin reaction in the form of urticaria after consuming alcohol while receiving acamprosate therapy. This suggests the possibility of acamprosate ethanol reaction. It is not acamprosate-induced cutaneous adverse effect because the patient did not develop the symptom while he was receiving only the drug throughout the treatment. Rechallenged by the drug alone while remaining abstinent to alcohol, he did not produce any such symptoms. The intensity of these effects was dose-related as he developed swelling of lips and itching at the lesions with higher doses of alcohol. Possibility of CML consumed by the patient leading to the skin reaction was ruled out by enquiry from the patient that others who had alcohol from the same place did not develop any such effects. One reason for such development might be deranged liver function which served as a risk factor in this patient. However, individual predisposition to adverse effects cannot be negated.

The common adverse effects due to acamprosate are diarrhea and intestinal cramps, itchiness, dizziness, muscle weakness, headache, flatulence, nausea, anxiety, and insomnia. Among these, the gastrointestinal (GI) side effects are self-limiting and some of them require discontinuation of the drug if troublesome to patient.[9] Dermatological side effects which are common are pruritus and rash, others like eczema, vesicular lesions, urticaria, and ecchymosis are uncommon. To our knowledge, we could not find a single report on possibility of acamprosate ethanol reaction except for a report which suggested the possibility of extrapyramidal symptoms with acamprosate.[10] Apart from the effects on GABA, glutamate, and glycine, a recent study also found effects of acamprosate on hypothalamic-pituitary-adrenal (HPA) axis which is yet to be replicated.[11] As hypothesized by Kalk and Lingford Hughes regarding anti-craving properties, these unusual effects of the drug might be explained by novel mechanisms which are yet to be discovered.[11]

## Conclusion

The possible deterrent action as one of the modes of action of acamprosate should be kept in mind while one encounters such patients as in the index case. Clinicians should be aware of these rare adverse effects, so as to manage and educate the patients appropriately. More molecular level and imaging studies need to be conducted to understand the multitude of mechanisms of acamprosate.

## Conflict of Interests

The Authors have no conflict of interest.

## Acknowledgements

None.

## Authors' Contribution

All the three authors were involved in the management of the patient. MSS and SG were involved in preparing the manuscript. All three authors finalized the manuscript.

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# اثر بازدارنده آکامپروسات: یک گزارش موردی

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**گزارش مورد**


## چکیده

**مقدمه:** از بین سه عامل دارویی موجود برای ترک اعتیاد الکل، آکامپروسات و نالتروکسون جزء عوامل ضد ولع مصرف محسوب می‌شوند که از بین این دو دارو، آکامپروسات بهتر تحمل می‌شود، پتانسیل سوء مصرف کمتری دارد و در صورت مصرف بیش از حد، ایمن می‌باشد، اما مکانیسم اثر آن هنوز نامشخص است.

**گزارش مورد:** گزارش موردی حاضر، توصیفی از یک بیمار مرد ۴۶ ساله با تشخیص سندرم وابستگی به الکل و پذیرش‌های قبلی و درمان ناموفق با نالتروکسون و باکلوفن بود. او پس از برگشت به مصرف الکل، دچار واکنش پوستی شد؛ در حالی که تحت درمان با آکامپروسات قرار داشت. شدت تأثیرات نامطلوب بر حسب مقدار الکل مصرف شده توسط بیمار متغیر بود. این امر احتمال اثر بازدارنده آکامپروسات در بیمار را نشان می‌دهد. پس از پرهیز از مصرف الکل، علایم کاهش یافت و بیمار به مصرف آکامپروسات و درمان پیشگیرانه از عود ادامه داد.

**نتیجه‌گیری:** پزشکان باید اثر بازدارنده آکامپروسات را در نظر گیرند و چنین بیمارانی را مطابق با آن مدیریت کنند.


**واژگان کلیدی:** تأثیرات نامطلوب، آکامپروسات، کهیر

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