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Case Report

End of Craving with Endoxifen in Substance Use & Bipolar Disorder

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Abstract

This case report brings to light the role of Endoxifen, a tamoxifen metabolite and direct Protein Kinase inhibitor drug in Substance use and Bipolar disorder. The putative action of Endoxifen in reducing alcohol consumption and implications as a possible anti craving agent is highlighted.

Case Presentation

A 45 year old businessman from upper socioeconomic status with fifteen years of daily drinking (360 ml/day) of whiskey presented to the out-patient services of a General Hospital psychiatry unit. A detailed history of substance use revealed alcohol consumption and chewable tobacco use amounting to dependence. Patient was not keen on using anti-aversive medications such as disulfiram. In the past he had discontinued naltrexone and refused acamprosate because he did not like to take the prescribed dose of acamprosate thrice a day. His request in this consultation was to ask for a novel drug to reduce drinking.

Meanwhile patient had also had experienced 3 episodes of recurrent depression in the past and was on a maintenance dose of 150 mg sertraline. The episodes of depression were more bipolar in nature characterized by diurnal variation in mood, somatic obsessions, anhedonia, anergia and biological function disturbances. Patient was maintaining well on sertraline 150 mg and risperidone 1 mg. He was recently detected to have diabetes and hypertension and was receiving oral hypoglycemic agents and antihypertensives. Based on the above information a dual diagnosis of Alcohol Dependence, Tobacco Dependence and Recurrent Depressive Disorder based on ICD-10 [1] (International Classification of Diseases) was made. Patient was administered CAGE [2] and scores were 4 based on these questions (Have you felt the need to Cutdown on your drinking? Do you feel Annoyed by people complaining about your drinking? Do you ever feel Guilty about your drinking? Do you ever drink an Eye-opener in the morning to relive the shakes?). Patient answered yes to all of the four questions. The AUDIT (Alcohol Use disorder Identification test) [3] was administered to assess severity and he scored 36 indicating hazardous drinking. Psychoeducation and evidence based pharmacological strategies were discussed. However patient declined any old standard practices and wanted to initiate controlled drinking and expressed interest in adhering to new medications. A shared decision making was attempted and 8 mg of endoxifen was started in the morning. After 2 weeks patient reported improvement in anxiety and mood he specifically reported that he noticed that his craving or need to drink 360 ml had reduced. He increased the dosing to 16 mg in 3 weeks and by the end of 4 weeks reported that craving to drink in the evening had reduced significantly. AUDIT score at 4 weeks was 30. Patient continues to maintain taking 16 mg endoxifen and has cut down consumption to 120 ml/day-180 ml/day. Daily drinking has reduced and he is maintaining on 16 mg endoxifen for the last 8 months. No adverse effects were reported at the end of 8 months such as insomnia, headache, and gastrointestinal symptoms. To quote patient at the end of 8 months-all racing and negative thoughts have stopped and I feel calmer and craving for alcohol drastically reduced and drinking daily has stopped with endoxifen support.

Discussion

Endoxifen, an active metabolite of tamoxifen, is a potent direct PKC (Protein kinase-c) inhibitor [4,5]. There is preliminary evidence that both 3 μM-10 μM tamoxifen and 4-hydroxytamoxifen (endoxifen) inhibit dopamine efflux in male mouse and male rat striatal synaptosomes and human dopamine transporter [6,7]. These animal model studies show that protein kinase inhibitors may be modulating drug dependence and reward. These early findings in these above mentioned animal model studies could explain the improvement in craving with endoxifen therapy in our patient. An important observation is that alcohol consumption was reduced in the above patient. Selective inhibitors of Protein Kinase Enzyme (PKC) are known to target the catalytic activity and reduce ethanol consumption [6]. The patient has been maintaining well, controlled drinking and continued to receive 16 mg endoxifen in the last 8 months. The AUDIT scores monthly ranged from 20 to 25 and at the end of 8 months was 14. In the last 3 years multiple case reports and double blind trials have been published about efficacy of endoxifen in Bipolar disorder [8-10]. Our patient had a dual diagnosis of mood and substance dependence and the effect of endoxifen in mood disorder is established. This additional effect on substance is noteworthy and promising. Long term effects of cannabinoids and endoxifen are being studied. Lately PKCβ inhibitor as a pharmacological interevention for amphetamine use disorder is being studied too in proof of concept studies [10].

Conclusion

This case signifies the role of using drug Endoxifen (8-16 mg)

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doses in substance dependence and Bipolar disorder. In future, studying efficacy of endoxifen in substance disorders alone with or without mood disorders needed. Additionally dosing, tolerability, long term use in preventing lapse or relapses in addiction therapy should be studied. Written informed consent for publication of their clinical details was obtained from the patient.

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