Management Approach to a Patient with Borderline Personality Disorder, Trichotillomania, and Alcohol Dependence Syndrome: Use of Endoxifen

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Received:- 6 March 2024/ Revised:- 17 March 2024/ Accepted: 24 March 2024/ Published: 31-03-2024

Abstract— *Borderline personality disorder (BPD) and alcohol abuse are both associated with impulsivity, while patients with trichotillomania demonstrate higher rates of co-morbid impulsive disorders. Impulsivity stems from overactive protein kinase C (PKC), and thus, targeting PKC can treat impulsivity. This case describes the effectiveness of endoxifen, a direct PKC inhibitor, in a patient with co-morbid BPD, alcohol dependence syndrome, and trichotillomania. There was reduced impulsivity and a motivation to cease alcohol consumption with endoxifen treatment. The patient transitioned from reluctance to disulfiram treatment to a willingness to take disulfiram. This case report adds valuable knowledge on the potential of endoxifen for patients with BPD and alcohol abuse.*

Keywords— borderline personality disorder, endoxifen, protein kinase C, substance abuse, trichotillomania.

I. INTRODUCTION

Impulsivity is a core feature of borderline personality disorder (BPD), and manifests as irresponsible behavior, problematic substance abuse, self-harm, and disordered eating, which thus impact quality-of-life. The high-trait impulsivity characteristic of BPD patients involves rapid and unplanned behaviors.[1] Trichotillomania was earlier classified as an impulse control disorder (involving an impaired ability to resist impulses to engage in ultimately self-destructive behavior), though it is now classified under obsessive-compulsive disorders. However, a higher prevalence rate of co-morbid impulsive disorders and alcohol use disorders has been reported in this population.[2] Impulsivity is reported to arise from overactivity of protein kinase C (PKC), suggesting that PKC can be a treatment target.[3,4]

The case study described in this report demonstrates the use of endoxifen in a patient with BPD, trichotillomania, and alcohol dependence syndrome, who was not responsive to multiple therapies. The use of endoxifen, a direct PKC inhibitor, along with other antipsychotics led to symptomatic improvement, and the resulting reduction in impulsivity prompted a motivation to reduce alcohol consumption.

II. CASE REPORT

A 22-year-old female presented with alcohol dependence syndrome, trichotillomania, and borderline personality disorder (BPD). Initial symptoms were noted approximately three years prior to the commencement of treatment. The patient had been under the care of another psychiatrist for 2 months, and the treatment did not lead to significant improvement. Previous interventions included lithium (400 mg twice-daily), aripiprazole (7.5 mg once-daily), and fluvoxamine (50 mg twice-daily) along with clonazepam (0.5 mg as required for sleep management) for two months. A total of six sessions of electroconvulsive therapy (ECTs) were also administered.

Upon presentation to the clinic, the patient's treatment plan was revised. Initial medications were discontinued, and lamotrigine was initiated at a dose of 25 mg twice-daily, titrated up to 100 mg twice-daily over 6-8 weeks. Ziprasidone (20 mg at night) and sertraline (100 mg, uptitrated to 150 mg once-daily) were prescribed for two months. Despite marginal improvement in symptoms of BPD, alcohol dependence and trichotillomania persisted. The Borderline Evaluation of Severity over Time (BEST) score was 68 (out of a maximum score of 70), and moderate-severe alcohol use disorder.

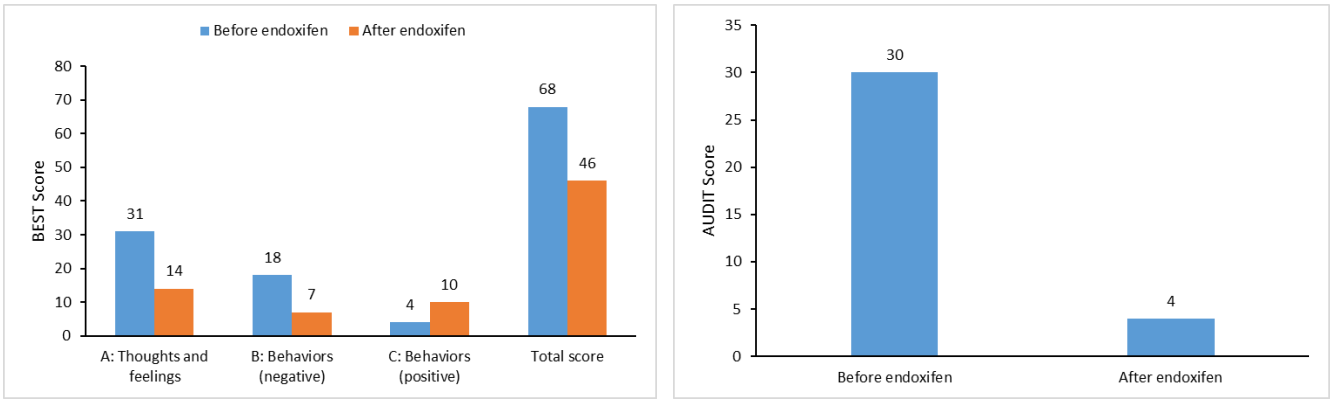
TABLE 1
COMPARISON OF BEST SCORE AND AUDIT SCORE BEFORE AND AFTER TREATMENT WITH ENDOXIFEN

BORDERLINE EVALUATION OF SEVERITY OVER TIME (BEST)	Before endoxifen	After endoxifen
A: Thoughts and feelings	**(31)**	**(14)**
Worrying that someone important in your life is tired of you or is planning to leave you	4	1
Major shifts in your opinions about others such as switching from believing someone is a loyal friend or partner to believing the person is untrustworthy and hurtful	4	3
Extreme changes in how you see yourself. Shifting from feeling confident about who you are to feeling like you are evil or that you don't even exist	3	2
Severe mood swings several times a day. Minor events cause major shifts in moods	5	2
Feeling paranoid or like you are losing touch with reality	3	2
Feeling angry	4	1
Feelings of emptiness	4	1
Feeling suicidal	4	2
B: Behaviors (negative)	**(18)**	**(7)**
Going to extremes to try to keep someone from leaving you	5	3
Purposefully doing something to injure yourself or making a suicide attempt	4	1
Problems with impulsive behavior (not counting suicide attempts or injuring yourself on purpose). Examples include: over-spending, risky sexual behavior, substance abuse, reckless driving, binge eating, other	5	1
Temper outbursts or problems with anger leading to relationship problems, physical fights, or destruction of property	4	2
C: Behaviors (positive)	**(4)**	**(10)**
Choosing to use a positive activity in circumstances where you felt tempted to do something destructive or self-defeating	1	3
Noticing ahead of time that something could cause you emotional difficulties and taking reasonable steps to avoid/prevent the problem	2	3
Following through with therapy plans to which you agreed (e.g., talk therapy, (homework assignments, coming to appointments, medications, etc.)	1	4
ALCOHOL USE DISORDERS IDENTIFICATION TEST (AUDIT)	**Before endoxifen**	**After endoxifen**
1. How often do you have a drink containing alcohol?	4 (4 or more times a week)	1 (Monthly or less)
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	0 (1 or 2)	0 (1 or 2)
3. How often do you have six or more drinks on one occasion?	0 (Never)	0 (Never)
4. How often during the last year have you found that you were not able to stop drinking once you had started?	4 (Daily or almost daily)	1 (Less than monthly)
5. How often during the last year have you failed to do what was normally expected from you because of drinking?	4 (Daily or almost daily)	4 (Never)
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	4 (Daily or almost daily)	1 (Less than monthly)
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	4 (Daily or almost daily)	1 (Less than monthly)
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?	4 (Daily or almost daily)	0 (Never)
9. Have you or someone else been injured as a result of your drinking?	0 (No)	NA
10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?	0 (Yes, during the last year)	NA

AUDIT: Alcohol Use Disorders Identification Test; BEST: Borderline Evaluation of Severity over Time.
NA: Not applicable; questions 9 and 10 of the AUDIT were Not Applicable as the total score for questions 2 and 3 was 0.
For the BEST scale, total composite score is calculated as 15 + A + B + C.

The patient was unwilling to take disulfiram due to the desire to engage in social drinking. Ziprasidone was discontinued, sertraline (150 mg once-daily) and lamotrigine (100 mg twice-daily) were continued, and endoxifen (8 mg once-daily) was prescribed. After six weeks, the patient demonstrated significant improvement in trichotillomania and alcohol abuse. Subsequently, she was motivated to start disulfiram therapy (250 mg once-daily), as Endoxifen helped reduce her impulsivity to engage in drinking. Endoxifen was continued at 8 mg once-daily, sertraline was downtitrated to 100 mg once-daily from 150 mg and lamotrigine was downtitrated to 100 mg once-daily from 100 mg twice-daily. The patient responded positively to the prescribed treatment. Trichotillomania symptoms decreased significantly, and the patient was motivated to cease alcohol consumption. Endoxifen was continued at 8 mg once-daily, along with sertraline (100 mg once-daily) and lamotrigine (100 mg once-daily).

After 12 weeks of Endoxifen treatment, the BEST score was 46 (out of a maximum score of 70), and the AUDIT score was 4 (low-risk consumption). Table 1 describes the change in scores for the individual components of the BEST and AUDIT tools. The patient is currently alcohol-free, with no trichotillomania symptoms, and has experienced a significant reduction in BPD symptoms (mood swings, anger, suicidal thoughts, self-harm, and impulsive behaviors reduced). Alcohol consumption reduced from 4 times a week to no alcohol, and the patient no longer needed to drink alcohol in the morning, compared to daily/almost daily consumption of alcohol in the morning). Body weight decreased from 94 kg to 80 kg during treatment. The patient continued regular follow-up visits, and Endoxifen was administered for a total duration of six months, with no adverse effects reported.



(A) **(B)**

FIGURE 1: Comparison of (A) BEST score and (B) AUDIT score before and after endoxifen treatment

AUDIT: Alcohol Use Disorders Identification Test; BEST: Borderline Evaluation of Severity over Time. For the BEST scale, total composite score is calculated as 15 + A + B + C.

III. DISCUSSION

The case described in this report highlights the use of endoxifen for the management of BPD, alcohol abuse, and trichotillomania, all of which are known to be associated with impulsivity. Targeting PKC overactivity as a cause of impulsivity led to a reduction in symptoms of BPD as well as trichotillomania. Furthermore, the patient transitioned from wanting to consume alcohol to being motivated to cease alcohol consumption.

Impulsivity has been linked to future alcohol use disorders, and conversely, heavy alcohol use can lead to impulsive behaviors through weakened self-regulation.[5] In addition, alcohol is reported to increase PKC isozyme levels or reduce the degradation of membrane-bound PKC isozymes.[4] Addictive behavior can stem from redistribution of PKC in different brain regions following ethanol exposure.[6] Therefore, drugs targeting PKC can reduce alcohol abuse.[4] PKC overactivity can be reduced through a PKC inhibitor such as endoxifen. Endoxifen can inhibit PKC by up to 78%[7] and has a good safety profile with a low rate of treatment discontinuation due to adverse effects.[8,9]

The anti-manic effect has been demonstrated in clinical trials,[8,9] and the expanded scope of use for the management of BPD, impulsivity disorders, and substance abuse has been described through recent case reports.[10-12] In consonance with a previous report by Banerjee and Ray,[11] endoxifen treatment of BPD led to improvement in BEST scores and curbed substance abuse.

In this case, the patient did not respond to treatment with lithium, aripiprazole, and fluvoxamine. Lamotrigine, ziprasidone, and sertraline led to partial improvement of BPD, but alcohol abuse and trichotillomania persisted until endoxifen was initiated. The resulting reduction in impulsivity translated into a reduced alcohol craving. The patient was then amenable to disulfiram

treatment for alcohol abuse. Therefore, endoxifen not only reduced impulsivity and BPD symptoms, but also permitted improved management of co-morbid alcohol abuse. This impact can be of particular benefit to patients with comorbid BPD and alcohol abuse, which are known to co-exist.

IV. CONCLUSION

This case report describes the impact of endoxifen treatment in a patient with co-morbid BPD, alcohol dependence syndrome, and trichotillomania, all of which are known to be linked to impulsivity. Impulsivity is mediated by PKC overactivity, and endoxifen is a direct PKC inhibitor with known anti-manic action. The patient responded well to endoxifen as part of combination therapy. The addition of endoxifen led to reduced symptoms of BPD, trichotillomania, and alcohol abuse, and the patient was subsequently motivated to stop consuming alcohol and take up treatment with disulfiram. The key action of reducing impulsivity thus had an extended impact on the range of comorbid conditions in this patient. This case report adds to the pool of literature and enhances our knowledge of this molecule for the management of psychiatric conditions.

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