

Endoxifen in the management of behavioral addiction – A case report exploring its use beyond mood stabilization

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ABSTRACT

Impulsivity is one of the core features of behavioral addiction. Recent evidence suggests a role of increased protein kinase C (PKC) activity in the pathophysiology of impulsivity. Consequently, it has been hypothesised that endoxifen, a direct PKC inhibitor, may be useful in the management of impulsivity. We report the case of a 29-year-old woman with a 5–6-year history of impulsive high-risk behaviors in the form of dating-app overuse, substance use, and mood symptoms such as impaired self-care, irritability, disturbed sleep, and appetite, for which she was diagnosed to have a mood disorder with behavioral addiction. Addition of endoxifen at a dose of 8 mg/day led to marked improvement in impulsivity, cravings for substances, and mood symptoms, with good tolerability and sustained benefit over 3 months.

Key words: Behavioral addiction, Dating app abuse, Endoxifen, Impulsivity, Protein kinase C, Substance abuse

Addiction is a complex and evolving concept, with behavioral addictions increasingly recognised alongside substance-related disorders [1]. The Diagnostic and Statistical Manual of Mental Disorders describes behavioral addiction under “Substance-Related and Addictive Disorders,” characterised by cravings, strong urges, functional impairment [2], although not yet included in the International Classification of Diseases [3]. Several behaviors, such as excessive internet use, sexual behavior, shopping, exercise, and compulsive eating, have been proposed as potentially addictive. Online dating apps, with their user-friendly design, widespread accessibility, and rapid interaction cycle [4], can promote addictive patterns of use that disrupt daily functioning [4,5]. Using Griffiths’ components model of addiction (2005) [6], problematic online dating apps may cause salience, mood modification, tolerance, withdrawal, conflict, and relapse [7]. Behavioral addiction related to dating-app use has been associated with psychiatric conditions, including depression, sleep disorders, attention-deficit/hyperactivity disorder, impulsivity, and substance use disorders [1,8,9].

There are no medications currently approved for the treatment of behavioral addictions. However, it is shown that engagement in addictive behaviors activates brain reward pathways in a manner comparable to substance use [10]. Consequently, therapeutic approaches used for substance use disorders have also been applied to

these behavioral addictions [4], with opioid receptor antagonists showing the most consistent early therapeutic promise [11,12]. Given the limited treatment options, there is a need for novel interventions. Endoxifen, a direct inhibitor of protein kinase C (PKC) [13], is a pathway implicated in the neurobiology of impulsivity, which is a core symptom of behavioral addiction [14]. Based on this rationale, we explored the use of Endoxifen in a young patient presenting with dating-app addiction co-occurring with bipolar affective disorder (BAD).

CASE DESCRIPTION

A 29-year-old unmarried female, who used to work in a small company earlier but is presently unemployed for 6–7 months, staying with her parents and a younger brother, presented with complaints of excessive use of dating apps, impaired self-care, irritability, disturbed sleep and appetite for the last 5–6 years, which substantially increased in the last 4–5 months. She was reported to be a difficult-to-handle child from the beginning. She secured above-average grades in academics with 86% marks in the 10th standard and completed a degree in Bachelor of Arts. Around 5 years back, she got introduced to cigarettes, alcohol, and gradually, with dating apps by her friends. Through these apps, she would meet strange people and would indulge in high-risk behavior. She was treated in the past but erratically and was diagnosed with Autistic Spectrum Disorder (ASD), attention deficit hyperactivity disorder (ADHD), and BAD. Family history revealed her father’s highly dominant nature. Her brother had also

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been reported to have anxiety, was treated, and recovered well.

At the time of presentation, she did not appear to have ASD or ADHD and was diagnosed with a mood disorder with behavioral addiction. She was admitted mainly because of an increase in her high-risk sexual behavior and staying out of the home often without informing.

At the time of admission, she was on lamotrigine 200, aripiprazole 20, and olanzapine 5/day. After admission, lamotrigine was tapered gradually and discontinued over 1 month. Her Barratt impulsiveness scale (BIS-11) score [15] and Mood Disorder Questionnaire (MDQ) score [16] were 71 and 13, respectively. Aripiprazole was tapered to 10 mg/day, olanzapine was increased to 10 mg/day, and fluoxetine 20 mg/day was added. After 1 week of admission, endoxifen 8 mg/day was added as there was no improvement in dating apps addiction and mood symptoms, while her BIS-11 score and MDQ scores were 71 and 13, respectively. After 3 weeks of endoxifen initiation, there was a significant improvement in her impulsivity, and repetitive talks about dating apps were decreased.

After 3 months of endoxifen initiation, she was maintaining fair improvement on the same regimen of endoxifen 8 mg, olanzapine 10 mg, fluoxetine 20 mg, and aripiprazole 10 mg/day. In general, her repetitive thoughts of using dating apps were reduced, her mood was better and more reactive, and she became more receptive to therapeutic interventions. The BIS score was reduced to 54, and the MDQ score came down to 6. A decrease in substance use was also observed. No change in laboratory parameters (complete blood count, glucose levels, lipid profile and liver function) was observed

during the treatment with endoxifen. Furthermore, no adverse events were reported.

She was discharged at the end of a 4-month stay from the rehabilitation setup after confirming that she was maintaining the improvement with the treatment.

DISCUSSION

Impulsivity is defined as behavior that is risky in nature, insufficiently inhibited, resulting in premature actions, contextually inappropriate, and often associated with adverse consequences. It is a core feature of behavioral addiction [14]. Behavior science experts believe that any source that is capable of stimulating an individual could become addictive, known as behavioral addiction [1].

An experimental study in a mouse model has demonstrated that PKC-gamma (PKCγ) may be a key intracellular mechanism that mediates neurochemical pathways associated with increased behavioral impulsivity [17]. This evidence is further strengthened from a study conducted in an ethnically diverse cohort of youth in the United States, which showed a significant association between a highly heritable behavioral disinhibition phenotype and the PKCγ gene [18]. Collectively, these findings strongly suggest that PKC signaling in the brain represents a biologically plausible and promising therapeutic target for the pharmacological management of impulsivity. Various published care reports have highlighted the potential role of endoxifen in the management of impulsivity, which are summarized in Table 1 [19-25].

In the present case, adjuvant endoxifen prescription was associated with a significant improvement in behavioral addiction, manifested as problematic dating

Table 1: Evidence for endoxifen in management of impulsive behavior

Authors name and year	Study type	No. of patients	Diagnosis	Major observations
Joshi <i>et al.</i> (2024) [19]	Case series	10	Alcohol use disorder	Mean BIS-11 score: At baseline: 99.5; after 4 weeks of endoxifen treatment: 61.9 Mean PACS score: At baseline: 24.6; after 4 weeks of endoxifen treatment: 13.5 Reduced frequency and amount of alcohol consumption, and risk of hospital admissions related to alcohol use. 9 patients showed improvement.
Banerjee <i>et al.</i> (2023) [20]	Case series	5	Borderline personality disorder	Improvement in impulsivity domains, attention deficits, mood fluctuations, and overall functioning
Singh (2025) [21]	Case series	2	Borderline personality disorder	Clinical response in 10 days
Kannappan (2024) [22]	Case report	1	Pathological gambling	Impulsivity is a prominent symptom
Dave (2023) [23]	Case report	1	Bipolar disorder with excessive buying and substance abuse	Rapid improvement of impulsivity, Young Mania Rating scale (YMRS score, and reduction in alcohol intake
Kulkarni (2024) [24]	Case report	1	Borderline personality disorder, trichotillomania and alcohol abuse	Reduced alcohol craving and trichotillomania
Tharoor (2023) [25]	Case report	1	Substance abuse (alcohol and tobacco)	Reducing alcohol consumption and craving

BIS-11: Barratt impulsiveness scale-11, PACS: Penn alcohol craving scale, YMRS: Young mania rating scale

app use, along with concomitant improvements in mood symptoms and substance abuse. According to our knowledge, this is the first case evaluating the role of Endoxifen in the management of behavioral addiction. This observation further strengthens the emerging clinical evidence supporting the potential role of endoxifen in managing impulsivity related to behavioral addiction and substance abuse. Endoxifen was well tolerated with nil reported adverse events during the treatment phase. Nevertheless, large, well-designed randomised clinical trials are required to confirm the efficacy and safety of endoxifen in the treatment of impulsivity.

CONCLUSION

This case report demonstrates improvement in behavioral addiction manifested as dating apps addiction, substance use, and mood with endoxifen treatment without any reported adverse events. Future prospective, randomized controlled clinical trials are warranted to confirm these findings.

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