Endoxifen in Treatment of Individuals with Borderline Personality Disorder with Predominant Impulsivity: A Case Series

Применение эндоксифена при пограничном расстройстве личности с выраженной импульсивностью: серия клинических случаев

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Case report

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ABSTRACT

Endoxifen, a protein kinase C inhibitor, has been approved for use in manic episodes in India. One of the symptom traits that it predominantly targets is impulsivity. Impulsivity can also be a symptom dimension of other mental health conditions, one of which is Borderline Personality Disorder (BPD). Management of BPD is challenging, with limited pharmacological options that are symptom-directed and psychotherapy sessions that are fraught with early dropouts and lack of compliance. Impulsive behaviors represent a major reason for seeking help in BPD, especially with regard to non-suicidal self-injury, substance abuse, high-risk sexual behavior, aggression, etc. Here, we present a case series comprising five individuals with a diagnosis of BPD whose treatment regimens were changed and endoxifen added at a dose of 8 mg once daily. Clinical improvement was monitored using the Borderline Evaluation of Severity Over Time (BEST). All the subjects improved in the impulsivity domains as well as with regard to attention deficits, mood fluctuations, and overall functioning. Endoxifen is thus potential promising in terms of the management of BPD, but needs more extensive study to fully substantiate its clinical benefits.

АННОТАЦИЯ

Эндоксифен, ингибитор протеинкиназы С, был одобрен в Индии для применения при маниакальных эпизодах. Импульсивность — один из симптомов, на который преимущественно направлено действие данного вещества. Импульсивность присуща различным психическим расстройствам, одним из которых является пограничное расстройство личности (ПРЛ). Лечение ПРЛ является сложной задачей, поскольку фармакологические средства, направленные на устранение симптомов, ограничены, а сеансы психотерапии могут спровоцировать прекращение лечения на ранней стадии и несоблюдение режима терапии. При ПРЛ импульсивное поведение зачастую является первопричиной обращения за помощью, особенно при несуицидальном самоповреждающем поведении, злоупотреблением психоактивных веществ, рискованным сексуальным поведением, агрессией и т.д. В данной статье представлена серия из пяти клинических случаев пациентов с диагностированным ПРЛ, которым в схему лечения был добавлен эндоксифен в дозе 8 мг один раз в день. Клиническая динамика отслеживалось с помощью опросника Динамической оценки тяжести проявлений пограничного расстройства личности (Borderline Evaluation of Severity Over Time, BEST). У всех испытуемых улучшились показатели в отношении импульсивности, дефицита внимания, колебаний настроения и общего функционирования. Таким образом,

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эндоксифен является потенциально перспективным препаратом для лечения ПРЛ, но для полного подтверждения его клинических преимуществ необходимы более обширные исследования.

Keywords: *borderline personality disorder; impulsivity; protein kinase C; endoxifen; case series*
Ключевые слова: *пограничное расстройство личности; импульсивность; протеинкиназа С; эндоксифен; серия клинических случаев*

INTRODUCTION

Borderline personality disorder (BPD) is a complex clinical disorder, with symptoms ranging from identity diffusion to impulsive behaviors, self-injury, inappropriate intense anger, suicidal/self-harm behaviors, instability of interpersonal relationships, and affective instability [1, 2]. This disabling mental health condition leads to impaired function, and usually appears during youth, though it impacts patients throughout their lifespans [1]. Among the general adolescent population, the prevalence of BPD is 3% [2], whilst the lifetime prevalence of BPD is 1.4% [1, 2]. Among adolescents attending an outpatient clinic, the prevalence of BPD is 11%, while among suicidal adolescents attending an emergency department, the prevalence is a staggering 78%. The treatment approach to BPD includes evidence-based pharmacotherapy along with supportive psychotherapy, dialectic behavioral therapy, etc. [3, 4]. A combination of pharmacotherapy and psychotherapy is more effective than a single therapeutic approach for the management of BPD [2–4], though retention in treatment and insight facilitation are practical challenges.

There is currently no approved molecule for the BPD pharmacotherapy. Endoxifen, a protein kinase C (PKC) inhibitor, has antimanic properties and has been approved for manic episodes with or without mixed features of bipolar I disorder [5]. There are also reports of its effectiveness in patients with impulsivity and substance abuse. A common thread among these is PKC overactivity, and therefore endoxifen could be evaluated for these indications [6].

Evidence on endoxifen is accumulating and would serve to increase our understanding of the value of this molecule. This case series describes the utility of endoxifen in the management of patients with BPD who displayed traits of impulsivity such as non-suicidal self-injury (NSSI), easy anger outbursts, and inappropriate sexual behavior (ISB). All cases involved individuals who had been diagnosed with BPD prior to the current presentation (for a period of over three years) and who had been treated with various drugs during that time. Treatment with endoxifen was effective and well-tolerated, signifying the importance of this drug in the management of BPD. Informed consent for endoxifen treatment and publication of data was obtained from all patients in their own languages.

CASE DETAILS

The individual case demographics, medications on which they presented, the treatment changes and improvement observed are presented in Table 1. The symptom dimensions of the patients are highlighted below. Clinical diagnosis was made as per DSM-5. We used the Borderline Evaluation of Severity Over Time (BEST) scale to objectively record the improvement with treatment. The BEST scale rates the behaviors, emotions, and thought patterns typical of BPD. The scale is sensitive to clinical change as early as four weeks into interventions and the score correlates positively with symptom severity [7]. This scale is a 15 items rated on a Likert scale. The BEST scale composed of 3 subscales: subscale A (thoughts and feelings), which includes eight items each with a maximum score of 5 (maximum score for subscale A is 40); subscale B (behaviors-negative), which includes three items each with a maximum score of 5 (maximum score for subscale B is 15); and subscale C (behaviors-positive), which includes 3 items each with a maximum score of 5 (maximum score for subscale C is 15).

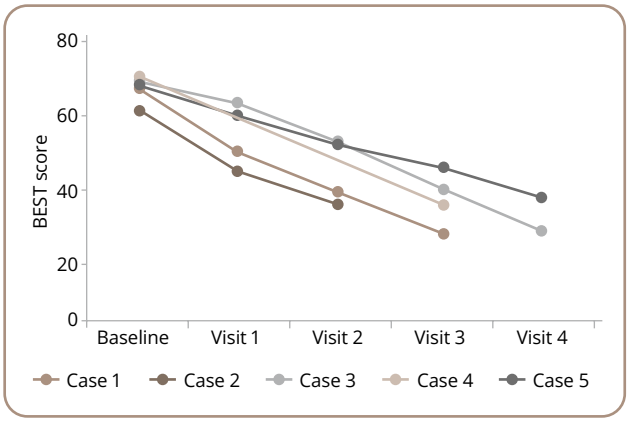

Figure 1. Improvement in BEST score for the individual patients after the introduction of endoxifen treatment.

Note: Each visit is at a monthly interval.

Table 1. Summary of the treatment details of the reported patients

Parameter	Case 1	Case 2	Case 3	Case 4	Case 5
Patient age	21	19	28	25	29
Patient gender	F	F	M	F	M
Comorbid diagnosis	No comorbidities	Adult ADHD	BPAD (?)	Adult ADHD	Nil
Initial treatment	Fluoxetine 40 mg, aripiprazole 10 mg, oxcarbazepine 900 mg	Lamotrigine 100 mg, lithium 450 mg, risperidone 1 mg, clonazepam 1 mg, atomoxetine 36 mg	Carbamazepine 600 mg, clonazepam 1.5 mg, escitalopram 10 mg, risperidone 4 mg + trihexyphenidyl 2 mg, multivitamins	Lithium 1200 mg, haloperidol 5 mg, amisulpride 100 mg	Amisulpride 100 mg, vortioxetine 20 mg, divalproex 1 g
Change in treatment	Endoxifen 8 mg, lamotrigine 300 mg, oxcarbazepine 900 mg (for three months) then 600 mg; aripiprazole was tapered and stopped	Endoxifen 8 mg, escitalopram 15 mg, lamotrigine 200 mg, atomoxetine 36 mg; risperidone 2 mg (for one month) then tapered and stopped; clonazepam and lithium were tapered and stopped	Endoxifen 8 mg, carbamazepine 600 mg, clonazepam 1 mg, risperidone 2 mg; escitalopram was tapered and stopped	Endoxifen 8 mg (for 1 month) then 16 mg, lithium 1200 mg, haloperidol 5 mg, methylphenidate; amisulpride was tapered and stopped	Endoxifen 8 mg, divalproex 750 mg, vortioxetine 20 mg
Duration of endoxifen treatment	Three months	Two months	Four months	Three months	Four months
No. of reviews after first visit	3	2	4	2	4
BEST score at baseline	67	61	69	70	68
BEST score at last visit	28	36	29	36	38
Improvement observed with endoxifen	Reduced consumption of alcohol and tobacco; markedly reduced impulsivity; more composed and functional in relationships; no instances of harming others and herself	Improvement in mood and focus; symptoms of ADHD were alleviated; able to actively engage with family members; no further instances of self-harm or violence	No classical mood episodes; reduction in mood fluctuations and irritability; improvement at the workplace (fewer altercations and better attendance)	Reduction in impulsivity, grandiosity, anger outbursts, and ADHD symptoms; improvement in overall biological functions	Reduced suicidal tendency; fewer episodes of violence and anger outbursts; improvement in depressive symptoms; improved work performance (more days of perceived productive work, more flexibility with shifts, more alert)
Laboratory investigations during treatment with endoxifen	Hemoglobin: 10.2 g/dL, total leukocytes: 6600/μL with normal differential count, fasting blood sugar: 108 mg/dL, thyroid stimulating hormone: 1.2 mIU/L, vitamin B12: 457 pg/mL	Hemogram, fasting blood sugar, thyroid profile, vitamin B12, and vitamin D levels — normal	Hemogram, vitamin B12 levels, liver function tests, and serum electrolytes — normal	Hemogram, thyroid profile, fasting lipid profile, and liver function test — normal	Hemogram, liver function test, gamma-glutamyl transferase, fasting blood sugar, and thyroid profile — normal
Present status	Sustains improvement (last seen — one month previously)	Sustains improvement (last seen — two months previously)	Sustains improvement (last seen — one week previously)	Relapsed (after drug default)	Lost to follow-up

Note: ADHD — Attention-deficit Hyperactivity Disorder, BEST — Borderline Evaluation of Severity over Time; BPAD — Bipolar affective disorder.

Box 1. Borderline Evaluation of Severity over Time (BEST) scale

Instructions: For the first 12 items, the highest rating (5) means that the item caused extreme distress, severe difficulties with relationships, and/or prevents getting things done; the lowest rating (1) means the item caused little or no problems. Rate items 13–15 (positive behaviors) according to frequency.

A. THOUGHTS AND FEELINGS

1. Worrying that someone important in your life is tired of you or is planning to leave you.
2. 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.
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.
4. Severe mood swings several times a day. Minor events cause major shifts in mood.
5. Feeling paranoid or like you are losing touch with reality.
6. Feeling angry.
7. Feelings of emptiness.
8. Feeling suicidal.

B. BEHAVIORS (NEGATIVE)

9. Going to extremes to try to keep someone from leaving you.
10. Purposefully doing something to injure yourself or attempting suicide.
11. Problems with impulsive behavior (not counting suicide attempts or injuring yourself on purpose). Examples include: overspending, risky sexual behavior, substance abuse, reckless driving, binge eating, other _____ (circle those that apply).
12. Temper outbursts or problems with anger leading to relationship problems, physical fights, or destruction of property.

C. BEHAVIORS (POSITIVE)

13. Choosing to use a positive activity in circumstances where you felt tempted to do something destructive or self-defeating.
14. Noticing ahead of time that something could cause you emotional difficulties and taking reasonable steps to avoid/prevent the problem.
15. Following through with therapy plans to which you agreed (e.g., talk therapy, homework assignments, coming to appointments, medications, etc.).

The composite score is calculated as 15 + A + B – C. A higher score indicates greater symptom severity in individuals with BPD and a greater degree of functional impairment [7]. The BEST scale is detailed in Box 1 [7].

Two individuals were followed up for four months, two patients for three months, and the remaining one for two months. Reviews were conducted at monthly intervals.

Case 1: A 21-year-old female student with a documented history of BPD spanning four years presented to the psychiatry clinic for a routine follow-up. The patient reported significant impulsive buying, poor distress tolerance, self-harm attempts, as well as problems at the workplace and with family (a severe anger outburst that resulted in harm to herself and her brother). The patient was unrepentant about the anger outbursts. The patient was experiencing reduced concentration and an erratic sleep-wake schedule, along with pronounced mood fluctuations. The patient had a dependence on tobacco and engaged in harmful alcohol use. The BEST score was 67. Previous treatment included lamotrigine 200 mg (for three months), lithium 600 mg (for one month), oxcarbazepine 1200 mg (for two months), risperidone 4 mg (for six months), fluoxetine 60 mg (for two years), and aripiprazole 15 mg (for nine months).

At the time of the visit, the patient was undergoing treatment with fluoxetine 40 mg, aripiprazole 10 mg, and oxcarbazepine 900 mg. The patient reported experiencing gastrointestinal disturbances (attributed to lithium), extrapyramidal side effects (EPS), and galactorrhea (attributed to risperidone), and syndrome of inappropriate antidiuretic hormone secretion (SIADH) due to oxcarbazepine. Endoxifen 8 mg once-daily and lamotrigine 300 mg once-daily were initiated, while aripiprazole was tapered and stopped due to akathisia; oxcarbazepine was continued for 3 months, after which the dose was reduced to 600 mg once-daily. Fluoxetine was stopped after a month due to gastric side effects. There was a gradual improvement in BEST score (Figure 1, Table 1), with reduced consumption of alcohol and tobacco usage. Due to sleeplessness experienced with endoxifen, the patient discontinued endoxifen for two weeks, leading to a relapse of mood dysregulation, anger dyscontrol, and

agitation within 21 days. Endoxifen was restarted at the same dose. After four months of treatment, the patient showed markedly reduced impulsivity.

Case 2: A 19-year-old female student diagnosed with BPD (for the last three years) and moderate depression with somatic syndrome (for the last year) presented for review. Over the course of her illness, the patient had been prescribed escitalopram 20 mg (for one year), olanzapine 10 mg (for six months), valproate 500 mg (for one year), and risperidone 2 mg (for eight months). At the time of presentation, the patient and her family expressed a desire to reduce the number of medications, which consisted of lamotrigine 100 mg, lithium 450 mg, risperidone 1 mg, clonazepam 1 mg, and atomoxetine 36 mg. The patient exhibited significant impulsivity, which involved NSSI, as well as mood fluctuations, irritability, and occasional episodes of unprovoked violence and high-risk ISB. The patient also displayed symptoms suggestive of attention-deficit hyperactivity disorder (ADHD). Childhood history was unclear. There was no history of substance abuse. The BEST score at presentation was 61.

The patient's treatment plan was altered to include once-daily endoxifen 8 mg and escitalopram 15 mg daily, while clonazepam and lithium were tapered and discontinued. The dose of risperidone was initially increased to 2 mg for a month, then tapered and stopped, while lamotrigine was increased to 200 mg. The patient experienced gastric irritation, nausea, and reduced sleep, possibly due to the timing of the late afternoon dosing. The patient reported an improvement in mood and focus. There were no further instances of self-harm or violence. Additionally, endoxifen demonstrated efficacy in alleviating symptoms of ADHD. BEST scores showed improvement (Table 1, Figure 1). The dose of lamotrigine was tapered down. She could engage in psychotherapy sessions after two months of treatment.

Case 3: A 28-year-old obese male working as an information technology (IT) professional was diagnosed with BPD 10 years ago. The patient presented with symptoms of severe impulsivity, including gambling, excessive spending, feeling deceived, mood episodes resembling mania, overspending, increased familiarity, grandiosity, and heightened libido. The duration of these episodes was typically several hours. The patient also experienced occupational dysfunction, frequent absenteeism, and fights and verbal altercations with co-workers. There was a history of changing jobs, incomplete assignments, and periods of heightened productivity. The episodes were too brief to consider a syndromal diagnosis of bipolar disorder. The patient had a cannabis dependence and a history of alcohol consumption. The baseline BEST score was 69.

The patient's prescribed treatment regimen included carbamazepine 600 mg, clonazepam 1.5 mg, escitalopram 10 mg, risperidone 4 mg, and trihexyphenidyl 2 mg, in addition to multivitamins. Since the patient experienced mood fluctuations resembling those seen in bipolar disorder, a diagnosis of bipolar spectrum was made. Endoxifen 8 mg once-daily was initiated, and escitalopram was tapered and stopped. Carbamazepine 600 mg was continued along with clonazepam 1 mg, and risperidone 2 mg. After two months, the dose of endoxifen was increased to 16 mg once-daily. There was progressive reduction in the BEST score (Figure 1). The patient demonstrated a significant decrease in alcohol consumption, and laboratory investigations were normal. The patient did not exhibit any classical mood episodes, and there was improvement at the workplace functioning (Table 1). No adverse effects were reported following the addition of endoxifen to the treatment regimen. Clonazepam was tapered and stopped.

Case 4: A 25-year-old female had received a diagnosis of BPD at the age of 18. She had previously tried multiple medications without significant benefits. Her drug history included lithium 1500 mg, valproate 1 g, risperidone 8 mg, haloperidol 10 mg, and amisulpride 600 mg. She was currently taking lithium 1200 mg, haloperidol 5 mg, and amisulpride 100 mg. The patient appeared to be in a manic/euphoric state at the time of assessment and reported increased sleep. Recent symptoms included impulsivity, frequent mood fluctuations, fluctuant energy levels, pervasive patterns of problems in interpersonal issues (not amounting to bipolar affective disorder), and thoughts of self-harm and suicidality. The patient experienced non-specific paranoia, reduced self-esteem, easy anger outbursts, and low distress tolerance. The patient was not employed, and was living apart from her husband. The BEST score was 70, and the Young Mania Rating Scale (YMRS) score was 18. A high BEST score shows the greater intensity and frequency of symptoms associated with borderline personality, whereas the YMRS score indicates the presence of clinical mania. A diagnosis of bipolar affective disorder (BPAD) was considered, with possible adult ADHD.

Endoxifen 8 mg once-daily was added to the treatment regimen, while amisulpride was tapered and discontinued after 1 month. Endoxifen was increased to a twice-daily dose. Even after the YMRS reduced to 4, which indicated clinical remission of the manic episode, impulsivity and NSSI persisted. Significant attention deficits were noted, and atomoxetine was added up to 36 mg daily.

The patient reported rashes during the first few days of treatment, followed by headaches and insomnia. Benzodiazepines were prescribed to manage insomnia. There was no intermittent review for this individual and they consulted only after three months. At this review, the patient's family reported a reduction in impulsivity, grandiosity, anger outbursts, and ADHD symptoms. There was an improvement in overall biological functions. Retrospectively, they reported the improvement in agitation, mood, sleep and impulsive behavior to have started within three weeks of starting endoxifen. The BEST score at follow-up had reduced to 36 and the YMRS score was 2. Due to financial constraints, the family could not continue with endoxifen and stopped it after a total four months of treatment. Three weeks after stopping medications, the patient experienced outbursts of anger, agitation, and NSSI wishes, although these were not as severe as before starting treatment.

Case 5: A 29-year-old male, employed as a police constable, had received a diagnosis of BPD at the age of 19. He had a history of stuttering and recurrent depressive disorder, was dependent on tobacco, and consumed alcohol. His illness exhibited a fluctuating course, and he was inconsistent with his medication regimen. The patient had a history of unprovoked severe aggression followed by a subsequent calm period. He lacked remorse following these outbursts but experienced feelings of depression. Mood instability negatively affected his relationships, and the patient was unable to report to work. A complaint had been lodged against him for undue altercations with members of the public, and being authoritative and argumentative. The patient mentioned that anxiety made him irritable, and that he had reduced appetite. The patient had subjective memory deficits. The BEST score was 68, which increased to 70 after one week. Childhood history indicated oppositional behavior and difficult temperament.

The patient was undergoing treatment with amisulpride 100 mg, vortioxetine 20 mg, and divalproex 1 g daily. Endoxifen 8 mg once-daily was added to the regimen, whilst amisulpride and vortioxetine were discontinued, and the dose of divalproex was reduced to 750 mg daily. Laboratory investigations undertaken during treatment showed normal results. There was a progressive decrease in the BEST score (Figure 1). Symptom assessments revealed fewer episodes of violence and anger outbursts, improvement in depressive symptoms, and improved work performance (Table 1).

However, upon discontinuation of the medication (due to sleeplessness with endoxifen), the patient experienced a relapse of easy irritability, impulsivity, and alcohol abuse. A revisit has been planned.

The authors would also like to present narratives from two individuals in this case series who were treated with endoxifen. Informed consent has been obtained from same. These narratives are from the final visit (Case 1: after 3 months and Case 2: after 2 months).

They were asked: *"How different do you feel after you received the treatment? Can you please detail it?"*

"I was always under fire. Every single time I was irritated it felt like I could break the world. It was very difficult to interact and work. After treatment, I feel better. I can talk to my friends and colleagues without the fear of turning aggressive. My sudden decision making has reduced and I am able to give it a thought before I decide on turning rash towards myself or others. I wish it stays the same".

Case 1

"My mood was almost never steady. I myself didn't know when I would get sad, frustrated or furious! Besides, if I didn't break things or hurt myself — I didn't feel that I could get through things. I cannot explain — there is this intense desire to just burst out on everyone and everything. I was doubtful about the treatment, but it helped me. The medicines calm me down and I can engage with my counselling sessions. I am not that much at unrest anymore but I wish to improve further".

Case 2

Such narratives have a subjective bias but nevertheless give us a living experiential account of how the individuals must have felt with the treatment change.

It is also worthwhile noting that in four individuals (all with the exception of Case 4), the frequency of positive behaviors (items 13–15 BEST scale, Box 1) also increased, starting from the first monthly review, after endoxifen was started. Increases in these positive coping behaviors

has been shown to reduce distress, improve mood dysregulation, and reduce dysfunction in individuals with BPD [2, 7].

DISCUSSION

To the best of our knowledge, this is the first case series or report to be published on the use of endoxifen in management of BPD. In this case series, all patients displayed traits of impulsivity and were not satisfactorily treated with various medications at the time of presentation. These patients had received diagnoses of BPD over three years prior and were treated with various medications over that time. Endoxifen was prescribed due to the lack of effectiveness or poor tolerability of various other drugs. Treatment with endoxifen was well-tolerated and resulted in improvements in BEST scores and clinical improvement in symptom domains [8]. Endoxifen was beneficial in managing BPD with a soft bipolar phenotype characterized by significant impulsivity, irritability, and mood fluctuations.

Impulsivity is a core feature of BPD that is precipitated by emotional stress, and can lead to suicidal and risky behavior [9]. Impulsivity is also a core feature of bipolar disorder, and both BPD and bipolar disorder lead to emotional dysregulation involving an inability to refrain from reacting to provocative stimuli. Debates on the overlap of these two conditions suggest that they either lie on a spectrum or that they are separate entities that can be comorbid [10]. In fact, the presence of borderline personality traits has been shown to adversely influence the clinical outcome of BPAD with increases in cycling, severity of episodes, and risk of substance abuse [11]. Targeting impulsivity, a core BPD trait, may hence have a favorable outcome in BPAD patients with comorbid Cluster B personality, and also those with the "soft bipolar" phenotype.

The current treatment approach for impulsive-behavioral dyscontrol symptoms involves selective serotonin reuptake inhibitors (SSRIs), and can be supplemented with an anti-psychitic, antidepressant, lithium, carbamazepine, or valproate. However, antidepressants have not displayed efficacy for impulsivity while evidence on antipsychotics for impulsivity is inconclusive. First-generation antipsychotics and antidepressants have limited benefit, and the long-term use of drugs has not been studied [12]. Pharmacotherapy for BPD is primarily adjunctive, with the aim of targeting impulsive behavioral dyscontrol [13–15], and it can be expected that symptomatic relief would positively impact treatment outcomes through better response to psychotherapy. Two individuals (Case 1 and 2) proved to be more amenable to psychotherapy after treatment with endoxifen, which is an interesting benefit.

The effect of endoxifen on impulsivity can be explained by the fact that impulses are regulated by the prefrontal cortex [16], and deficits in this region are associated with altered PKC intracellular signaling. PKC impairs cognitive functioning of the prefrontal cortex. Endoxifen is a PKC inhibitor utilized for the management of bipolar disorder that also exhibits impulsive behavior as a core symptom. Endoxifen has a four-fold stronger inhibitory effect on PKC compared to its parent molecule (tamoxifen), achieves steady-state concentration within two weeks of administration, and has a favorable safety profile [5, 17].

Specific data on use of endoxifen in young women is lacking. The risk of adverse effects of endoxifen are dependent on the dose and duration of treatment [18]. Studies on endoxifen for the treatment of breast cancer prescribe doses up to 160 mg for anti-estrogen activity [19]. Taking into account the dose and duration of treatment in this study (low-dose endoxifen [8 mg daily] for a short duration of four months or less), the risk of side effects was considered to be low. Furthermore, studies on the use of case reports demonstrate the safety and efficacy of endoxifen in women treated for four months and one year [20, 21].

In this case series, treatment with endoxifen led to a reduction in symptoms in people with BPD (predominant impulsivity traits), and in a few patients who discontinued endoxifen treatment a relapse of symptoms was noted. The patients in this case series included those who had had a BPD diagnosis for over three years and were either non-responsive to, or did not tolerate, other medications. Endoxifen was thus prescribed due to its action on PKC, which has been implicated in impulsivity, substance abuse, and mania. In this specific subset of patients, there was an improvement in BEST scores, along with reduced substance abuse, impulsivity, and NSSI, as well as improved interpersonal relationships and work productivity. There were also fewer episodes of violence/self-harm and anger. Side-effects were few but included nausea, sleeplessness, and anxiety. However, the high cost of the medication can be a potential constraint. Further large-scale studies are necessary to establish the efficacy and long-term safety of endoxifen as a potential therapeutic tool in the challenging management of BPD.

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