

Reduction in self-harming behaviour after zuclopenthixol decanoate

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No psychotropic drug is specifically licensed for the management of emotionally unstable borderline personality disorder. Prescribing 'off-label' places additional responsibilities on the prescriber and may increase liability if there are adverse effects. This case report describes a patient with borderline personality disorder who was started on zuclopenthixol decanoate with successful outcome in terms of reducing self-harming behaviour and impulsivity.



Borderline personality disorder is one of the most contentious of all the personality disorder

subtypes.¹ The term 'borderline personality' was proposed in the United States by Adolph Stern in 1938 (most other personality disorders were first described in Europe). Stern described a group of patients who 'fit frankly neither into the psychotic nor into the psychoneurotic group' and introduced the term 'borderline' to describe what he observed because it 'bordered' on other conditions.

The term 'borderline personality organisation' was introduced by Otto Kernberg in 1975 to refer to a consistent pattern of functioning and behaviour characterised by instability and reflecting a disturbed psychological self-organisation. Whatever the purported underlying psychological structures, the cluster of symptoms and behaviour associated with borderline personality were becoming more widely recognised, and included striking fluctuations from periods of confidence to times of absolute despair, markedly unstable self-image, rapid changes in mood, with fears of abandonment

and rejection, and a strong tendency towards suicidal thinking and self-harm.

Transient psychotic symptoms, including brief delusions and hallucinations, may also be present. The characteristics that now define borderline personality disorder were described by Gunderson and Kolb in 1978 and have since been incorporated into contemporary psychiatric classifications.

According to the Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV), the key features of borderline personality disorder are instability of interpersonal relationships, self-image and affect, combined with marked impulsivity beginning in early adulthood.

The International Classification of Diseases 10th revision (ICD-10) equivalent is 'emotionally unstable personality disorder, borderline type' (F 60.31), which is characterised by instability in emotions, self-image and relationships. The ICD-10 category does not include brief quasi-psychotic features (criterion 9 of the DSM-IV category).²

Suicide is common in people with borderline personality disorder and may occur several years after the first presentation of symptoms.³ No psychotropic drug is specifically licensed for the man-

agement of borderline personality disorder, although some have broad product licences that cover individual symptoms or symptom clusters. Where there is a diagnosis of comorbid depression, psychosis or bipolar disorder, the use of antidepressants, antipsychotics and mood stabilisers respectively would be within their licensed indications. Where there are depressive or psychotic symptoms, or affective instability, that fall short of diagnostic criteria for mental illness, the use of psychotropic drugs is largely unlicensed or 'off-label'. Prescribing off-label places additional responsibilities on the prescriber and may increase liability if there are adverse effects.⁴ As a minimum, off-label prescribing should be consistent with a respected body of medical opinion and be able to withstand logical analysis.⁵

The Royal College of Psychiatrists recommends that the patient be informed that the drug prescribed is not licensed for the indication for which it is being used, be given the reason for use, and be provided with full explanation of the potential side effects.²

There has not been much research comparing the effects of different antipsychotics and so there is no evidence to say which

one, if any, is most effective in treating people given a diagnosis of personality disorder. However, we present a case report in which zuclopenthixol decanoate was used with successful outcome in terms of reducing self-harming behaviour and impulsivity.

Case report

The patient is a 32-year-old woman – currently unemployed and living independently – who had been self-harming by cutting superficially on a regular basis since the age of 15.

She had a history of mood instability with difficulty in controlling her emotions. Her upbringing contained elements of emotional abuse: she was bullied by her mother and other siblings. There were no childhood conduct disorder symptoms and no history of sexual or physical abuse. She always had intense relationships and feared abandonment. She only ever had one friend at a time with whom she had quite an intense relationship as she felt she was letting that friend down if she had to talk to someone else. There was no family history of any significant mental health problems. She had brief psychological intervention when she was 16 years old, with no improvement reported in her self-harming behaviour.

She gained a National Vocational Qualification in IT and Business Administration. She had no major physical health issues. She had never been in a stable relationship and had no children. She denied any use of alcohol or illicit substances; however, she used to binge drink when she was feeling low.

The patient first presented to secondary mental health services at the age of 25 when she was informally admitted following a significant planned overdose of

paracetamol and ibuprofen tablets with an intention to end her life. She rang her friend who called the ambulance. On admission to the ward, she requested to take her own discharge in order to end her life. As a result, she was detained under Section 2 of the Mental Health Act 1983. It was noted that she was very manipulative in her behaviour, splitting the health care staff and taking control in every situation. There were no psychotic features observed or reported. During her admission she was on mirtazapine initiated by her doctor. She remained on the ward for six weeks; she was diagnosed with emotionally unstable borderline personality disorder (EUPD) due to the evidence of personal distress, social disruption, difficulty in relating to her peers since childhood, dysregulation of mood, outbursts of emotions and anger, family conflict, and experiencing feelings of emptiness together with self-destructive behaviours via acts of self-harm.

Subsequently, the patient had numerous hospital admissions, both formal and informal, due to her history of overdoses or threatening self-harming behaviour. She had received cognitive analytic therapy and she was involved for seven months with the Therapeutic Community (Birmingham, UK) but subsequently did not engage further due to some difficulties with other patients. There was no documented evidence of any improvement in her mental health after any psychological interventions.

During her admissions, she had tried various antidepressants for sufficient duration and within *British National Formulary* limits, with no effect. After stopping mirtazapine she was treated with escitalopram,

sodium valproate and venlafaxine without any success.

She was eventually initiated on zuclopenthixol depot injection (Clopixol) 400mg fortnightly following her admission to the mental health unit due to another overdose of various medications. She tolerated the Clopixol injection well, with some improvement in her mental state within a few months of starting injection. She remained stable, with improved functioning for six months after discharge. Due to weight gain from Clopixol, her dose was reduced to 300mg fortnightly. On dose reduction, her mental health deteriorated within weeks and she was admitted again with some intrusive thoughts to harm herself. During her stay, her Clopixol dose was increased back to 400mg fortnightly. She continued to remain on 225mg of venlafaxine. She had a significant reduction in self-harming behaviour with improvement noted in her general functioning.

Again, reduction in Clopixol depot injection frequency was attempted; this resulted in increased self-harming behaviour which further confirmed the beneficial effects of Clopixol on her mental health. Eventually, Clopixol frequency increased to 400mg fortnightly which resulted in improvement within a few weeks.

Since that time, she never self-harmed. She still had intermittent self-harm thoughts, but she was able to control her impulsive acts effectively, was able to stop herself, and gave herself time to utilise alternative coping strategies. Her motivation had improved and she had engaged in various social and rehabilitative activities. She had resumed driving and did not report difficulties with her concentration. Recently, she had enjoyed a holiday in Spain without any difficulty.

Discussion

To the best of our knowledge this is the first reported case of significant reduction in self-harming behaviour after zuclopenthixol decanoate in EUPD.

The use of medication to 'treat' people given a diagnosis of personality disorder is, to say the very least, controversial. The term 'treat' suggests that it is possible, and desirable, to treat personality itself.² However, the clinical response to traditional drugs in heterogeneous disorders, such as borderline personality disorder, is often partial and limited to few symptoms; the identification of new agents is required to improve and extend treatment results in these patients. More recently, clinicians have been challenged to develop and provide evidence for effective treatments for personality disorders.⁶

National guidelines state that medication should not be used routinely for the treatment of people given a diagnosis of borderline personality disorder. There are relatively few randomised controlled trials (RCTs) examining the efficacy of drug treatments in people with borderline personality disorder, and the data for the efficacy of individual drugs are correspondingly weak.²

Some studies^{7,8} but not others⁹ have shown an advantage of traditional antipsychotic medications over placebo in terms of efficacy in the treatment of people with borderline personality disorder. However, there was no evidence for the effectiveness of antipsychotics or antidepressants for impulsivity in people with borderline personality disorder.²

Lieb *et al.* conducted a Cochrane Collaboration systematic review and meta-analysis of randomised comparisons of drug versus placebo, drug versus drug, or

single drug versus combined drug treatment in adult patients with borderline personality disorder. Twenty-seven trials were included in which first- and second-generation antipsychotics, mood stabilisers, antidepressants and omega-3 fatty acids were tested. Evidence from RCTs suggested that drug treatment, especially with mood stabilisers and second-generation antipsychotics, may be effective for treating a number of core symptoms and associated psychopathology, but the evidence does not currently support effectiveness for overall severity of borderline personality disorder.¹⁰

In an open trial study, olanzapine given to patients suffering from borderline personality disorder and dysthymia was able to substantially reduce symptoms of anger and interpersonal sensitivity, which is related to the impulsive reactions presented by these patients.¹¹ In another double-blind, placebo-controlled study with borderline personality disorder patients, where all patients were treated with dialectical behavioural therapy and were randomly assigned to receive olanzapine or placebo, the group treated with olanzapine (mean dose of 8.83mg/day) showed a significant improvement over placebo in impulsive and aggressive behaviour.¹²

Polyunsaturated fatty acids (PUFAs) have long been investigated for their cardioprotective and anti-inflammatory action, leading to an increased use of PUFAs as dietary supplements.¹³ In 2003, Zanarini and Frankenburg conducted an eight-week, placebo-controlled, double-blind study to compare the efficacy of omega-3 fatty acids such as ethyl-EPA (at a dose of 1g/day) and placebo in 30 female patients with a diagnosis of borderline personality disorder, showing a significant

beneficial effect of ethyl-EPA in reducing aggressive behaviours and depressive symptoms. However, the main limitations were that only women were studied and all subjects were moderately ill.¹⁴ Similarly, Silvio *et al.* conducted an RCT which showed that a combined therapy with omega-3 fatty acids and valproic acid was significantly superior to single therapy with valproic acid in reducing the severity of self-rated and clinician-rated symptoms of impulsivity and outbursts of anger. The study suffered from some limitations that should be considered: (1) the small sample size; (2) the lack of a placebo-controlled group; (3) the exclusion of patients with an Axis I co-diagnosis.¹³

A study on clozapine used in women with borderline personality disorder and comorbid learning disability demonstrated a reduction in the rates of self-injury and use of restraint in women.¹⁵ Zarzar *et al.* also reported a series of four patients with severe borderline personality disorder and persistent self-injurious behaviour treated with clozapine at a state psychiatric hospital. After treatment with clozapine, these patients ceased self-injurious behaviours and aggression, and no longer required intensive levels of observation or restrictive procedures.¹⁶ Frogley *et al.* reported in case series the beneficial effects of clozapine in 22 female inpatients with a primary diagnosis of borderline personality disorder. The results revealed clozapine's clinically relevant effect across multiple domains. Symptom severity, number of days on enhanced observations, the use of additional emergency antipsychotic and anxiolytic medication, and the number and severity of aggressive and self-harm incidents all improved. The temporal relationship with

clozapine initiation–improvement was greatest early on and was sustained. The mechanism by which clozapine could be mediating any beneficial effect in borderline personality disorder is unknown. Clozapine’s advantage in treatment-resistant schizophrenia is well established but not the pharmacological mechanism.¹⁷ Contenders range across its D₁, D₂, D₄, 5-HT₂, and 5-HT₆ and gamma-aminobutyric acid receptor binding properties.¹⁸ From a more clinical perspective, it may be that clozapine is a better anxiolytic than other antipsychotics which is of critical importance in borderline personality disorder.¹⁹

Carbamazepine demonstrated efficacy in decreasing impulsive aggression, defined as ‘behavioural dyscontrol’ (including overdoses, self-burning, cutting, violence and rage episodes) in a double-blind, crossover trial performed by Gardner and Cowdry.²⁰

Divalproex was superior to placebo for the treatment of patients with cluster B personality disorders and impulsive aggression in a multicentre, randomised, double-blind study.²¹

There is a lack of evidence about the use of zuclopenthixol decanoate in this condition. Zuclopenthixol is a typical antipsychotic neuroleptic drug of the thioxanthene group. It was introduced in 1962 by Lundbeck. Zuclopenthixol decanoate is a long-acting intramuscular injection. Its main use is as a long-acting injection given every two or three weeks to people with schizophrenia who have poor compliance with medication and suffer frequent relapses of illness. There is some evidence that it may be more helpful in managing aggressive behaviour.²²

In terms of its mechanism of action, it has a weaker histamine

H₁ receptor blocking activity and lower affinity for muscarinic cholinergic and alpha2-adrenergic receptors. It mainly acts by antagonism of D₁ and D₂ dopamine receptors. The effect of dopamine is less clear and seems controversial; for example, methylphenidate, which increases dopamine activity, can diminish impulsive behaviour in patients with attention deficit and hyperactive disorder,²³ while antipsychotic drugs, which are dopamine blockers, can also diminish such behaviour.²⁴ In addition, zuclopenthixol also has high affinity for alpha1-adrenergic and 5-HT₂ receptors. The serotonergic effect of zuclopenthixol may possibly explain its effect in reducing impulsivity and aggression. An impressive number of studies, using different techniques in clinical or pre-clinical research, have linked serotonin hypo-function with impulsive or aggressive behaviour.²⁴ Serotonin regulates pre-frontal cortical regions like the orbital frontal cortex and anterior cingulate cortex by acting on 5-HT₂ receptors. In a number of different research paradigms, it was found that there is a different and complementary role of the two 5-HT₂ receptors, 5-HT_{2A} receptors being involved in increased impulsivity and aggression and 5-HT_{2C} receptors in decreased impulsivity and aggression.²⁵

The anti-aggressive effects of zuclopenthixol may be explained by its dopaminergic mechanism, especially its high affinity to dopamine D₁ receptors. Its high selectivity, together with the low dosages, may also explain the low rate of adverse effects.²⁶

The above case report clearly shows that using zuclopenthixol decanoate can be significantly beneficial in improving patient symptoms as well as quality of life. We therefore suggest that

zuclopenthixol decanoate can prove very beneficial in EUPD. The generalisability of this finding must be determined through RCTs with larger numbers of patients.

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Declaration of interests

There are no conflicts of interest declared.

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POEMs



Intensive therapy versus standard weekly cognitive therapy for PTSD

Clinical Question

What is the comparative efficacy of 7-day intensive cognitive therapy, standard weekly cognitive therapy, and emotion-focused supportive therapy for the treatment of post traumatic stress disorder?

Reference

Ehlers A, Hackmann A, Grey N, et al. A randomised controlled trial of 7-day intensive and standard weekly cognitive therapy for PTSD and emotion-focused supportive therapy. *Am J Psychiatry* 2014;171 (3):294–304.

Study Design Randomised controlled trial (non-blinded) **Funding** Foundation **Setting** Outpatient (specialty) **Allocation** Concealed

Synopsis

Standard weekly cognitive therapy for PTSD is well-established as effective treatment. Sessions once weekly or twice weekly over three months is a typical course of therapy. This randomised controlled trial with 121 participants compared a standard regimen of up to 20 contact hours with (1) an equivalent number of therapy hours delivered in a 7-day intensive format, (2) emotion-

focused supportive therapy in a standard weekly format, and (3) a waiting list control group. The emotion-focused approach was nondirective and encouraged patients to clarify and resolve their emotions without attempting to elaborate on memories or triggers or change behaviours. Participants were aged between 18 and 65 years and met DSM-IV criteria for PTSD in a structured interview. Additional inclusion requirements were the identification of 1 or 2 discreet traumatic events in adulthood, PTSD as the main problem, and – if taking psychotropic medications – stable dosing for at least two months before randomisation. All active therapies were more likely to lead to recovery, defined as no longer meeting the criteria for diagnosis of PTSD, at the 14-week assessment as compared with waiting to treat (numbers needed to treat = 1.4 [95% CI, 1.14–1.87] for standard therapy; 1.5 [1.18–1.87] for intensive therapy; and 2.73 [1.77–5.95] for emotion-focused therapy. Total remission as rated by an independent assessor and patient self-ratings was also better with active treatments. Quality of life was improved with both cognitive therapies versus the waiting list, but was not significantly improved with emotion-focused therapy.