News

Clinical update on the pharmacotherapy of borderline personality disorder

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Abstract

Patients with borderline personality disorder (BPD) are currently managed with psychotherapy and symptom-targeted prescribing, usually leading to polypharmacy, which is against the current NICE guidelines. Research shows that most drug therapies currently used for BPD have no clinical benefit and that the side effects of these drugs may be harmful to patients. Some of the BPD treatments that require further investigation are mood stabilisers and antipsychotics. Other potential treatments, such as omega-3 fatty acids/food supplements and oxytocin should also be investigated. NICE guidelines should be updated following further study.

Abbreviations

APA - American Psychological Association
BPD - Borderline personality disorder
CSF - Cerebrospinal fluid
EUPD - Emotionally unstable personality disorder
RCT - Randomised controlled trial

Introduction

Emotionally unstable personality disorder (EUPD) is a disorder of mood experienced by 20% of psychiatric in-patients and 10-30% of outpatients.[1] It can be caused by a genetic predisposition and/or an environmental cause.[2] These patients form their identity around an extremely traumatic childhood and this causes them to have a very different way of perceiving and interacting with the world around them.[2] There are two types of EUPD: impulsive and borderline personality disorder (BPD). The latter will be the focus of this paper.

> *BPD is characterised by a disturbed self-image, self-harming, fear of abandonment, emotional instability and, hence, an inability to form stable relationships.*[3]

These symptoms vary for every patient, especially since EUPD patients have other psychiatric disorder comorbidities. This makes it difficult to isolate which disorder is responsible for the presenting symptoms, hence diagnosis and treatment vary too.[4] To complicate things even more, there is contrasting evidence and different guidelines concerning the way BPD should be managed.[5-8] As a result, there are no clear guidelines to be followed and BPD patients are often on polypharmacy.[4]

The aim of this clinical update is to evaluate the current research and guidelines and to explore the pharmacological management of BPD. It will address the lack of research on the topic and the disparity between guidelines and practice. Lastly, it will highlight some fields for future research.

Current guidelines vs clinical practice

According to the NICE guidelines and the NHS website,[2,7] the main treatment for BPD should be individual or group psychotherapy. It is likely that this choice was made on the evidence for psychotherapy's positive effects on BPD patients and in not causing side effects.[6] The NICE guidelines emphasise that pharmacotherapy, especially polypharmacy, should be avoided unless the patient is comorbid; in this case, they approve giving medication for the comorbidity. In

contrast, the guidelines of the American Psychological Association (APA) recommend personalised therapy using a symptom-targeted approach.[8] Surprisingly, these guidelines have not been reviewed since 2009 and 2001, respectively. Although novel research is limited, enough new papers exist to motivate a review of these guidelines.

A national audit published in 2015 on the use of psychotropic drugs in patients with EUPD illustrates the reality within clinical practice in contrast to the guidelines.[4] In this study, of 786 patients who had EUPD without comorbidity, only 13% had not been prescribed psychotropic medication. In addition, two-thirds of the same patient group had polypharmacy aiming to target different aspects of EUPD, such as depression, anxiety and disturbed sleep. This shows that

> *the current approach in British hospitals follows the APA guidelines rather than the NICE guidelines for the NHS,[4] which emphasises the need for the NICE guidelines to be reviewed.*

Moreover, this audit found that the most prescribed classes of drugs were antidepressants and antipsychotics. Interestingly, several recent systematic reviews show that there is not enough evidence to support the use of either in BPD and noted that certain antipsychotics, like olanzapine and asenapine, might even be counterproductive in BPD patients due to their well-known side effects.[5,9] As a result, the audit findings may suggest that some BPD patients are being overmedicated,[4] and the lack of evidence for the medication that they are receiving makes one wonder if this is doing them more harm than good. This highlights the need for further research to evaluate the use of pharmacotherapy for BPD.

Update on the treatment of BPD and controversies

In the early 2000s, some promising papers were published on the use of mood stabilisers or antipsychotics in BPD.[10,11] The NICE guidelines even followed up on this by encouraging further research to strengthen the proposed clinical relevance of these drugs.[7] As a result, more studies looked into this[5,9] and found conflicting results to the previous studies.[10-14] The general consensus was that

> *more thorough research was required to establish a link between mood stabilisers/ antipsychotics and improvements in BPD outcomes.*

With regard to antipsychotics, a study found that BPD patients may have higher concentrations of dopamine metabolites in their plasma and cerebrospinal fluid (CSF), suggesting that some antipsychotics might have a positive effect on BPD since they target the dopamine pathway.[12] In particular, aripiprazole, olanzapine, haloperidol and quetiapine occasionally resulted in a positive response in previous studies.[12-14] However, many also reported side effects, especially with olanzapine, and questioned the reliability of the research on the topic, usually for methodological reasons or simply for the lack of further evidence.[5,9] Indeed, as seen in a recent systematic review,[5] most of the positive findings with antipsychotics has come from research conducted before 2010, none of which provides overwhelming evidence that would support the use of these drugs in BPD, hence its exclusion from current guidelines. To illustrate the issue, the case of aripiprazole can be used as an example: there is one placebo-controlled randomised controlled trial (RCT) on aripiprazole in BPD patients,[11] which reports an improvement in several symptoms of BPD (depression, anxiety, hostility, paranoia and psychoticism) and considers this treatment a safe and effective option. However, this paper was published in Austria in 2006 and included 57 BPD patients only, five of whom dropped out. Furthermore, patients with suicidal ideation, schizophrenia, and users of psychotropic drugs or psychotherapy were excluded, even though one might argue that, in the clinical reality of BPD, all of these presentations are fairly common.[1,4] The findings from this RCT have not been supported by any other research.[9] In conclusion, due to methodological limitations, there is a risk that these results may be inaccurate and, hence, they would need to be confirmed by further research.

With respect to mood stabilisers, a 2015 Cochrane collaboration reported that there has been past evidence of lamotrigine and topiramate occasionally reducing anger and impulsivity in BPD patients,[9] although the sources of this evidence were of questionable reliability. In particular, the Cochrane collaboration commented on two small placebo-controlled RCTs that found lamotrigine to improve anger and impulsivity in BPD patients.[15,16] In contrast, a double-blind placebo-controlled RCT published later, in 2018, showed that lamotrigine had no statistically relevant effects in a large group of BPD patients recruited from six different places in the UK.[17] This last study was carried out over 52 weeks and comprised of three follow-up periods, as opposed to the previous studies, which lasted less than 12 weeks.[15,16] Furthermore, the 2018 study[17] was more inclusive of patients with more severe BPD symptoms, whereas the two earlier studies excluded people who self-harmed, were unemployed, etc.[15,16] Hence, it becomes evident that the 2018 study has better methodology, which makes it more reliable and representative of the patients that would actually present in the clinical setting. Lastly, to explain the different results between these studies, it has been suggested that lamotrigine might be more likely to be effective for patients who have milder BPD symptoms.[17] Surprisingly, despite these mixed findings, the NICE guidelines still show interest in the use of mood stabilisers in BPD patients (although they would like further research on the topic), and a portion of BPD patients are receiving this treatment despite the absence of evidence to support its use.[4] This shows once again that further research and up-to-date guidelines are needed.

On a more positive note, some new unconventional therapies have been identified for BPD. The first of these are omega-3 fatty acids;[18,19] a recent study was carried out on 43 BPD outpatients, 18 of whom initially received omega-3 fatty acids and a mood stabiliser (valproic acid), and the remaining received valproic acid alone.[19] Both groups showed improvements after 12 weeks, especially in terms of anxiety, depression and social functioning. Moreover, the group that received omega-3 fatty acids and valproic acid showed less impulsivity, anger outbursts and self-injury. Subsequently, both groups took valproic acid alone for 24 weeks. At the end of the experiment, the group who had initially received combined therapy still showed reduced anger outbursts. Although this was a small study and did not include a placebo-controlled group, it did not find any serious side effects to the use of omega-3 fatty acids for BPD and cited appropriate research to support its findings. In conclusion, these results suggest that omega-3 fatty acid supplements show promise as a future treatment option in BPD, although further research will be needed to confirm this. Moreover, since psychiatric patients are known to have quite imbalanced diets, it might be interesting for future research to look into other food supplements and whether they improve BPD symptoms. Finally, despite the promising results, further research may be needed regarding valproic acid as a therapy, since its use in BPD is not backed up by any other evidence.

Another potential pharmacotherapy for BPD is oxytocin. A recent systematic review confirmed that oxytocin inhibits threat hypersensitivity and avoidance in BPD patients.[20] However, patients who received oxytocin were less trusting of others in a social dilemma.[20] Moreover, a correlation between childhood trauma and increased response to oxytocin was found,[21] which will have clinical implications if oxytocin is implemented in the care of BPD patients. In conclusion, the findings relating to oxytocin therapy for BPD are promising but further research is needed to understand the

contraindications of this therapy and the circumstances in which oxytocin could be beneficial for BPD patients.

Conclusion

EUPD/BPD patients are currently being managed with psychotherapy and symptom-targeted prescribing, usually leading to polypharmacy, which is against the current NICE guidelines. Research shows that most of the current drug therapies have no clinical benefit to patients and the side effects can actually be harmful. However, it also suggests that some treatments can be used in very specific circumstances.

These findings need to be reflected in the NICE guidelines. Some treatments that require further investigation are mood stabilisers and antipsychotics. Other potential treatments that require further research are omega-3 fatty acids/food supplements and oxytocin.

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