See article by Paton et al

Pharmacotherapy for Borderline Patients: Business as Usual or by Default?

Theo Ingenhoven, MD, PhD

In their analysis of a representative sample from the Prescribing Observatory for Mental Health in the UK health services, Paton et al[1] found that 92% of patients with borderline personality disorder (BPD) received prescriptions for psychotropic medications. Although international guidelines recommend pharmacotherapy for comorbid psychiatric disorders whenever necessary, 82% of the UK BPD patients without such comorbid conditions nevertheless received pharmacotherapy "by default," mostly off-label polypharmacy without adequate psychiatric controls for effectiveness and tolerability. Business as usual? Bad care? International practice guidelines for the treatment of BPD all recommend evidence-based psychological treatment whenever possible (especially manualized psychotherapy like dialectical behavior therapy, schema-focused therapy, mentalization-based treatment, transference-focused psychotherapy) as the first-choice treatment.[2–6] However, with respect to pharmacotherapy, these guidelines diverge in their recommendations.

Guidelines' Conflicting Views on Pharmacotherapy

The American Psychiatric Association (APA) introduced the Practice Guideline for BPD,[2,7] which was based on work by Soloff[8,9] and targets cognitive-perceptual symptoms, impulsivity, and affective dysregulation. In contrast, the UK NICE guideline[6] clearly states that drug treatment should *not* be used for BPD (unless treatment focuses on clear comorbid Axis I disorder). The more recent published Guideline from the Australian government[5] echoes the NICE guideline by stating that medications should not be used as a primary treatment because the effects are only modest at best, research findings are inconsistent, and pharmacotherapy is not helpful for modifying the course of the disorder, although short-term use of medications as adjunct to psychological treatment may be considered for temporary diminution of specific symptoms. According to the British and Australian guideline, pharmacotherapy can be used in acute crisis situations and should be discontinued after the crisis is resolved. In contrast, the Dutch guideline for personality disorders[3] and the German guideline for personality disorders[4] both revised Soloff's algorithms based on systematic reviews of all available placebo-controlled randomized controlled trials (RCTs) studying the efficacy of classical and atypical antipsychotics, first- and second-generation antidepressants, and antiepileptics used as mood stabilizers.[10,11] More recently, these algorithms were validated by a series of meta-analyses[12–16] confirming limited but acceptable effect sizes on specific symptom domains and overall functioning.

So, where the results of an increasing number of placebo-controlled RCTs slowly converge, international guidelines diverge in their interpretations, conclusions, and recommendations. In line with the APA practice guideline, the Dutch[3] and German[4] guidelines recommend classical and atypical antipsychotics for cognitive-perceptual symptoms. However, they seriously question the efficacy of modern antidepressants (selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors) on impulsivity and affective dysregulation, as recommended by the APA practice guideline. In contrast, mood stabilizers, especially topiramate and lamotrigine, seem a more promising alternative with respect to affect regulation and impulse control. All mentioned guidelines agree that sedatives, like benzodiazepines, should not be primarily recommended because of the risk of abuse, dependence, and behavioral dyscontrol.

The use of psychotropic medications in UK borderline patients without comorbid disorders in the Paton study (68% antidepressants, 59% antipsychotics, 59% sedatives, 23% mood stabilizers) mostly fit in with the APA practice guideline, which seems to be outdated by not including results of RCTs published since 2000.[17]

How Do Clinicians Proceed?

From one point of view, the quality of the subsequent placebo-controlled RCTs using psychotropic drugs in personality disorder is seriously questioned or considered insufficient. Thus, are no firm conclusions justified? Do we have to wait for more placebo-controlled RCTs before we can draw evident sound conclusions? A current statement for abstinence, as dictated by the NICE and Australian guidelines, seems to have pros and cons. The upside of the UK abstinence approach is that it stimulates clinicians to be reticent in prescribing psychotropic drugs to borderline patients, preventing counterproductive polypharmacy and serious invalidating side effects like movement disorders, overweight, metabolic syndrome, sexual inhibitions, and numbness. Ineffective pharmacologic treatment interferes with a productive psychotherapeutic process, we assume. In contrast, the efficacy of pharmacotherapy can be underestimated, so the downside is that maybe some individual, difficult-to-treat borderline patients, who could benefit from temporary pharmacologic support, will be refrained from such evidence-based therapeutic

Submitted: *September 17, 2014; accepted September 17, 2014.*

Corresponding author: *Theo Ingenhoven, MD, PhD, Symfora Group, Treatment Center for Personality Disorders, Wim Sonneveldlaan 53, Utrecht, 3584ZP, The Netherlands (t.ingenhoven@tip.nl).*

J Clin Psychiatry 2015;76(4):e522–e523 (doi:10.4088/JCP.14com09522).

interventions. The Dutch and German guidelines[3,4] advocate the use of symptom domain–specific pharmacologic algorithms based on serious systematic reviews and meta-analyses of available RCTs. Paton et al[1] made clear that, in the absence of unambiguous pharmacotherapeutic recommendations, borderline patients are at the mercy of arbitrariness and preferences of individual psychiatrists. So, in the end, is it perhaps better to have a perishable guideline based on the best evidence available and clinical expert opinion, providing pharmacotherapeutic algorithms for specific symptom domains, than to give no guidance at all?

Unfortunately, within the last decade, only very few new RCTs on pharmacotherapy in BPD have been initiated. Within the next years to come, there will be only a limited number of new peer-reviewed published studies. So for the revision of our international guidelines, we have to rely on the current, limited, and controversial database with respect to efficacy and tolerability. As a consequence, clinical wisdom will have to guide us to the most appropriate treatment algorithms for the near future.

In the meantime, clinicians should not concentrate exclusively on efficacy alone. Since the context and therapeutic relation of prescribing drugs is important in medicine, and in psychiatry in particular, one can prevent iatrogenic harm by paying attention to some basic points of interest:

- Good psychiatric management as prerequisite
- Psychotherapy whenever possible!
- Medication only when necessary
- Invest in psychoeducation
- Invest in relationship management: "shared decision making"
- Start low, go slow!
- Avoid polypharmacy (No crisis management by desperate cocktails!)
- Treat Axis I disorders appropriately
- Discuss and register off-label medication
- Consider tapering off effective as well as ineffective medication
- Monitor compliance, side effects, and suicidal ideation
- Invest in adequate multidisciplinary cooperation (split treatment)

Author affiliations: Center for Psychotherapy Pro Persona, Lunteren, The Netherlands.
Potential conflicts of interest: None reported.
Funding/support: None reported.

REFERENCES

1. Paton C, Crawford MJ, Bhatti SF, et al. The use of psychotropic medication in patients with emotionally unstable personality disorder under the care of UK health services. *J Clin Psychiatry*. 2015;76(4):e512–e518.
2. American Psychiatric Association Practice Guidelines. Practice guideline for the treatment of patients with borderline personality disorder. *Am J Psychiatry*. 2001;158(suppl):1–52.
3. CBO. *Landelijke Stuurgroep Multidisciplinaire Richtlijnontwikkeling in de GGZ. Multidisciplinaire Richtlijn voor de diagnostiek en behandeling van volwassen patiënten met een persoonlijkheidsstoornis*. [Dutch Multidisciplairy Guideline for the Diagnosis and Treatment of Personality Disorders]. Utrecht, The Netherlands: Trimbos-instituut; 2008.
4. DGPPN. *Deutsche Geselschaft für Psychiatry, Psychotherapie und Nervenheilkunde. Behandlungsleitlinie Persönlichkeitstörungen*. [German guideline for personality disorders]. Dresden, Germany: Steinkopff Verlag; 2009.
5. NHMRC. Australian Government. *Clinical Practice Guideline for the Management of Borderline Personality Disorder.* 2012. http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/mh25_borderline_personality_guideline.pdf. Accessed January 27, 2015.
6. National Collaborating Centre for Mental Health. Borderline Personality Disorder: Treatment and Management. NICE Clinical Guidelines, No. 78. Leicester, United Kingdom:British Psychological Society; 2009.
7. Oldham JM. *Guideline watch: Practice Guideline for the Treatment of Patients with Borderline Personality Disorder*. Arlington, VA: American Psychiatric association; 2005. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/bpd-watch.pdf. Accessed January 27, 2015.
8. Soloff PH. Algorithms for pharmacological treatment of personality dimensions: symptom-specific treatments for cognitive-perceptual, affective, and impulsive-behavioral dysregulation. *Bull Menninger Clin*. 1998;62(2):195–214.
9. Soloff PH. Psychopharmacology of borderline personality disorder. *Psychiatr Clin North Am*. 2000;23(1):169–192, ix.
10. Rinne T, Ingenhoven T. Pharmacotherapy of severe personality disorders: a critical review. In: van Luyn B, Akhtar S, Livesley J, eds. *Severe Personality Disorders: Everyday Issues in Clinical Practice*. Cambridge, UK: Cambridge University Press; 2007.
11. Herpertz SC, Zanarini M, Schulz CS, et al; World Federation of Societies of Biological Psychiatry (WFSBP). World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of personality disorders. *World J Biol Psychiatry*. 2007;8(4):212–244.
12. Lieb K, Völlm B, Rücker G, et al. Pharmacotherapy for borderline personality disorder: Cochrane systematic review of randomised trials. *Br J Psychiatry*. 2010;196(1):4–12.
13. Ingenhoven T, Lafay P, Rinne T, et al. Effectiveness of pharmacotherapy for severe personality disorders: meta-analyses of randomized controlled trials. *J Clin Psychiatry*. 2010;71(1):14–25.
14. Ingenhoven TJ, Duivenvoorden HJ. Differential effectiveness of antipsychotics in borderline personality disorder: meta-analyses of placebo-controlled, randomized clinical trials on symptomatic outcome domains. *J Clin Psychopharmacol*. 2011;31(4):489–496.
15. Mercer D, Douglass AB, Links PS. Meta-analyses of mood stabilizers, antidepressants and antipsychotics in the treatment of borderline personality disorder: effectiveness for depression and anger symptoms. *J Pers Disord*. 2009;23(2):156–174.
16. Vita A. L. De Peri L, Sacchetti E. Antipsychotics, antidepressants, anticonvulsives, and placebo on symptom dimensions of borderline personality disorder. A meta-analysis of randomized controlled and open trials. *J Clin Psychopharmacol.* 2011;31:613–624.
17. Schulz SC, Nelson KJ. Somatic treatments. In: Oldham JM, Skodol AE, Bender DS, eds. *Textbook of Personality Disorders, DSM-5 Edition*. Arlington, VA: The American Psychiatric Publishing; 2014.