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EDITORIAL

Should psychiatrists be more cautious about the use of antipsychotics for patients with borderline personality disorder?

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Five years ago, Murray et al.[1] published an article asking whether "psychiatrists should be more cautious about the long-term prophylactic use of antipsychotics." They brought up five important issues about the long-term use of antipsychotics in schizophrenia patients: a) the effects of antipsychotics on physical health; b) the effects of antipsychotics on brain structure; c) the efficacy of long-term antipsychotic use; d) antipsychotic-induced dopamine receptor supersensitivity, and e) treatment-resistant schizophrenia. However, they did not discuss the potential harm in other psychiatric diseases, such as in borderline personality disorder (BPD). In fact, no study has ever discussed the potential harm and iatrogenic potential of long-term antipsychotic use in BPD patients.

So far, the gold-standard treatment for BPD consists of non-pharmacological therapies, particularly psychological approaches such as dialectical behavioral therapy, mentalization-based treatment, transference-focused psychotherapy, and general ("good") psychiatric management.[2] Even though no pharmacological treatment has demonstrated greater efficacy than placebo in psychopathology, BPD patients are consistently prescribed pharmacotherapy, such as antidepressants, mood stabilizers, and antipsychotics.[3,4] A 6-year prospective cohort study of 290 BPD inpatients from one university hospital in the United States found that approximately 40% received three or more psychotropic medications, 20% received four or more, and 10% received five or more medications concurrently during the follow-up period.[5] Following up the same cohort 16 years later, the authors found increased rates of atypical antipsychotic prescription over time, in contrast to most other psychotropic medications, which remained stable.[6] Furthermore, the most recent American Psychiatric Association Practical Guideline for the Treatment of Patients with Borderline Personality Disorders (2001), in addition to the guidelines of other regulatory agencies around the world,[7] recommend several different antipsychotics for treating symptoms related to BPD.[8]

To our knowledge, no study has ever investigated the long-term impact of antipsychotics on BPD patients, their effect on brain structure, or their capacity to induce dopamine receptor supersensitivity and "treatment-resistant borderline personality disorder." Two more recent narrative reviews[9,10] highlighted the potential efficacy of atypical antipsychotics, such as quetiapine, for BPD. However, most randomized controlled trials are short term[11] and do not contradict our rationale. In our opinion, some important long-term findings from schizophrenia studies could and should be considered for BPD patients.

The first issue to consider is the effects of antipsychotics on physical health. The life expectancy of patients with BPD is 40 years lower than general population (only considering non-suicidal deaths), and these patients have high rates of obesity and metabolic syndrome.[2] It is well known that antipsychotics can induce an insulin-resistant state, as well as weight gain and metabolic syndrome. The second issue is the potential harmful effects of antipsychotics on brain structure.[1] Although this has not been directly investigated, it is possible that BPD patients who take antipsychotics, especially those with high D2-receptor affinity, could experience similar brain alterations to patients with schizophrenia who take antipsychotics. Third, the long-term efficacy of antipsychotics for BPD patients is little known, which should be considered in a time when medical practitioners are applying more "evidence-based psychiatry." Fourth, it has been demonstrated in both human and animal models that antipsychotics can induce a state of D2 supersensitivity in limbic areas,[12] which are highly related to affect regulation,[13] and it is possible that they can induce a state of "treatment-resistant borderline personality disorder." Naturalistic studies suggest that symptom remission occurs in more than 85% of BPD patients within 10 years

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(approximately 12% relapse rate).[14,15] However, there are many highly symptomatic individuals, as evidenced by the high suicide rates in this population.[16] This raises the question of which factors predict worse long-term outcomes.

We acknowledge that more symptomatic individuals might require pharmacological strategies, especially antipsychotic medications. We also acknowledge that short-term antipsychotic use can be useful in stressful situations and for acute psychotic symptoms that may emerge in chronic BPD patients.[11] However, we would like to point out the potential harmful effects of chronic high doses of antipsychotics in BPD patients and we suggest, when indicated, the use of low doses of partial D2 agonists or low-affinity D2 antagonists for short periods of time only. Undoubtedly, this statement should be considered with caution due to the lack of clinical support and the fact that most evidence comes from studies on typical antipsychotics. However, this is the first opinion piece to stress the potential harmful consequence of long-term antipsychotic use in this population, and original studies are needed to assess this assumption. In addition, further longitudinal studies investigating the impact (positive or negative) of long-term psychiatric medication use on BPD patients should be conducted in an effort to personalize treatment for these vulnerable individuals. Paraphrasing Murray et al., who point out the need for more evidence-based practice, as well as quaternary prevention strategies, ''it is unfortunate that so little attention has been paid to this cautionary statement.''

Disclosure

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