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Poor man's vortioxetine

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Letter to the Editor

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Dear Editor,

While it is well-known that drug–drug interactions may produce problematic and dangerous reactions there are also instances where one may repurpose these interactions to one's clinical advantage.

One of these potentially useful interactions occurs where one medicine by blocking the metabolism of another increases the blood levels of this second medicine, thereby enhancing its efficacy or tolerability as a result. For example, one such drug–drug interaction used in past psychiatric treatment involved the Cytochrome p450 1A2 inhibitory properties of fluvoxamine inhibiting the metabolism of clozapine.

In particular, this fluvoxamine-clozapine drug–drug interaction was colloquially referred to as the *poor man's clozapine*, dating back to the days before clozapine was available generically. Utilizing this combination carefully allowed for generating a higher clozapine level at a lesser prescribed dose to minimize the cost of the expensive trade name medicine.[1] Clinical data testified to the usefulness of this interaction from an efficacy perspective as well from a tolerability standpoint by diminishing clozapine's sedative potential.[1]

We suggest a somewhat parallel situation may be utilized with the interaction between the antidepressant agents vortioxetine and bupropion.

Reviews of the pharmacotherapeutic treatment of refractory obsessive–compulsive disorder (OCD), note the potential use of vortioxetine, a newer serotonergic system modulator, for this disorder.[2] Antidepressant doses higher than doses typically used to treat depression are sometimes required to treat OCD.[2] Similarly, one would expect the potential need for higher dosing of vortioxetine as well for OCD treatment (ie, greater than 10–20 mg/day) and anecdotally that has been our experience.

However, as there is not presently a generic version available for vortioxetine, the brand name medicine's high cost per pill potentially limits raising the dose above its maximum 20 mg size pill. To counter this obstacle, we suggest a means of working around this issue with a described drug–drug interaction; bupropion's cytochrome p450 2D6 significant inhibitory properties that may potentially double the blood levels of vortioxetine.[3]

Thus we report here, a case of a patient with longstanding OCD who had limited response to 20 mg/day of vortioxetine who reported increased benefit with both an increased daily dose of vortioxetine and subsequently the addition of bupropion to this 20 mg/day dose.

CASE: Ms. A was a 27-year-old woman who presented with an exacerbation of a long history of OCD dating back to adolescence. Her most recent disruptive obsessional symptoms included worries involving her religious practices and fear of either her children or herself harming others. She had found multiple earlier Selective serotonin reuptake inhibitors(SSRIs) trials of varying clinical success all accompanied by a range of problematic intolerable side effects.

A trial of fluvoxamine of 200 mg/day was successful over 4 months in significantly diminishing her symptoms but produced unacceptable side effects: most problematic being weight gain, as well as sweating and sedation.

Due to vortioxetine's possible lower potential for weight gain,[4] Ms. A was cross tapered from fluvoxamine onto vortioxetine 20 mg/day. However, over the 3 months of this treatment she noted a partial loss of prior therapeutic benefit.

As her insurance did not provide coverage for additional vortioxetine tablets, Ms. A. paid out of pocket for additional pills allowing for a dosage increase to 40 mg/day. Over a few months, a clear additional decrease in OCD symptoms was reported along with weight neutrality, but also mild sedation. However, due to her inability to continue to pay out of pocket for medication she returned to 20 mg/day with diminished sedation, but loss of recent improvement.

After a discussion of treatment options Ms. A was started on bupropion XL 150 mg/day, increased to 300 mg/day within a few days. On this regimen she reported a return of satisfactory control of her OCD symptoms without issues of sedation. Persistent mild tremulousness on this bupropion dose led to her decreasing the dose to 150 mg/day with maintenance of symptomatic benefit, and continued weight stability.

The lack of satisfactory control of her OCD in two trials at the lower 20 mg/day dose of vortioxetine suggests, but does not prove, that symptom improvement was correlated with both dose increase and then again by bupropion addition. As bupropion has limited direct efficacy in the

treatment of OCD,[5] the assumption was that benefit was vortioxetine related. One cannot say whether the reported weight neutrality of this combination was enhanced by the mild weight loss properties attributed to bupropion, though practically speaking, the desired result, weight neutrality, was achieved regardless of mechanism. Additionally, due to bupropion's reported usefulness in minimizing serotonergic agents related sexual side effects, further exploration is also indicated to assess whether this specific combination may have a unique role in addressing this issue.

It would also seem clinically prudent when attempting this regimen to monitor for the potential theoretically to over medicate with vortioxetine because of bupropion's ability to rapidly elevate its blood level. In closing, we suggest that until vortioxetine becomes affordable as a generic agent, when necessary, one may maximize its benefits to treat OCD by prescribing only a single pill per day along with the judicious addition of bupropion utilizing this drug–drug interaction. Perhaps one might characterize this combination as a "poor man's vortioxetine."

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