Prescribing Guideline for Valproic Acid and Women of Reproductive Potential: Forget It Exists

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I am writing in response to two brief publications (Tastenhoye et al[1] and Andrade[2]) and a third older publication[3] in this journal that underscore the lack of rigorous safety protocols around prescribing valproate in women of reproductive potential. This pertains to the well documented lack of knowledge on the part of both health care providers and patients about risks of valproate use during pregnancy, and the frequent failure to ensure that valproic acid is used in conjunction with effective contraception. Even with effective contraceptive methods, contraception can fail. Reassessment of the use of this known serious teratogen is a timely topic.[4]

No matter how well thought out and well written these contributions,[1–3] I fear that the reader may be left with the message that if we just enhance the education around these topics, valproic acid can be safely prescribed in women of reproductive potential. Also, there is a belief—not rooted in study—that supplemental folic acid mitigates this risk. I would like to leave you instead with a less nuanced message: Do not prescribe valproic acid to women until they are without a doubt postmenopausal or post-hysterectomy. In response to the question, "How do I prescribe valproic acid to women of reproductive potential?" the best answer is, "Don't do it at all."

Most psychiatric prescribers will find themselves in the role of perinatal psychiatrist, intended or not. If you are a prescriber, the medication you select for a female patient of reproductive age, or younger than reproductive age, should be one that can be used long term, as many of the illnesses we diagnose and treat are chronic and recurrent. Women will often require medications during pregnancy to stay well, and ideally they will have regimens that are reasonable to continue during pregnancy. Many of us while training did not imagine we would be caring for pregnant women. The reality is that if you treat individuals of reproductive potential, you will find yourselves on the front lines of perinatal health care. The ideal time to select a psychotropic for pregnancy is well before conception, planned or not. Unplanned pregnancies are common,[5,6] and women with psychiatric disorders may be more likely than the general population to have unplanned pregnancies.[7] We can plan on unplanned pregnancies in our practices. We must treat *all* women of reproductive potential as if they will become pregnant while taking the prescribed medication, as unplanned pregnancies are commonplace. If they were not, the US would not be in such a tumultuous and divisive debate over access to reproductive health services.

Valproic acid is a known teratogen that can cause major fetal malformations, including neural tube defects, before most women would even know they were pregnant.[4] The news just gets worse across the developmental trajectory, with long-term neurodevelopmental detriments for children exposed to valproic acid in utero.[8] A valproic acid syndrome has been described.[9] There is even evidence suggesting damage that is transgenerational after exposure to valproic acid in utero.[10]

There is no nuance to this: Valproic acid should not be prescribed to women of childbearing potential for psychiatric disorders. While some countries have sought to regulate its use and disseminate the dangers of use during pregnancy more prominently, there is no sufficient threading of this needle. Not today, when we have so many other options as mood stabilizers than we did decades ago.

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