Valproate Prescribing Practices in Individuals of Childbearing Age at a Tertiary Care Women's Hospital

To the Editor: We read with interest Andrade and colleagues' recent JCP article, "Use of Valproate in Women: An Audit of Prescriptions to 10,001 Psychiatry, Neurology, and Neurosurgery Outpatients"[1] and applaud their attention to this important topic. We would like to highlight opportunities in inpatient settings to address this issue and present data from a needs assessment done at our institution.

As Dr Andrade's group outlines,[1] valproate is prescribed for seizure prophylaxis and mood stabilization. Valproate exposure in pregnancy is associated with a several-fold increase in neural tube, cardiac, skeletal, and limb defects and higher risk of developmental delays in offspring.[2] Best practice guidelines caution prescribing valproate to women of childbearing age, with recommendations including negative urine pregnancy test (UPT) prior to initiation, discussion and prescription of contraception, discussion of reproductive intentions and risk, and folate supplementation.[3] Psychiatrists working in perinatal settings are well-versed in risk-benefit conversations for teratogenic medication use and can ensure that these critical conversations occur.

Methods. Our institution's Quality Research Committee approved this study. Our sample is from a pharmacy database of a tertiary care women's hospital and consists of all women aged 12–52 years who received valproate during medical admission from January 1, 2019, to December 31, 2019. The electronic medical record was manually reviewed, and extracted data included primary service, valproate indication, UPT result, current contraception, folate coprescription, presence of a psychiatric consultation, and documented discussion with the patient of valproate teratogenicity.

Results. Seventeen encounters were identified for 15 unique patients. Documented indications for valproate use included bipolar disorder (7/15), seizure disorders (7/15), and termination of migraines (2/15). The home dosage of valproate was continued in 14 encounters. Six encounters had a documented negative UPT. Three patients were pregnant. One patient was prescribed high-dose folate prior to admission; the other 14 patients had no documented folate supplementation. There were no documented risk-benefit discussions. Primary care teams included a range of medical and surgical teams. One patient had a psychiatric consultation.

Discussion. This study shows opportunities for improvement in valproate prescribing practices at a tertiary care women's hospital in the United States, a finding consistent with prior studies.[4] Andrade and colleagues' work was done in India, illustrating that concerns with valproate prescribing are a salient global issue. This care gap was present across different specialties. Psychiatry was consulted for only 1 patient, though 7 patients had psychiatric indications for use. Involving psychiatry teams in inpatient hospital settings could optimize care through primary team education.

Physicians would benefit from additional education about the risks of valproate use in women of childbearing age and best practice standards on reproductive counseling, testing, and contraceptive and folate coprescribing. Access to contraception, UPTs, and folate may be limited in developing nations, so we recommend thoughtful consideration of safer alternatives for women of childbearing age.

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Addressing the Problem of Prescription of Valproate to Women of Childbearing Age: Reply to Tastenhoye et al

To the Editor: I thank Dr Tastenhoye and colleagues[1] for their interest in our study.[2] Tastenhoye et al[1] found that, in a tertiary care women's hospital in the US at which the highest standard of care could be expected, as many as 17 women of potentially reproductive age received valproate during a period of inpatient management; negative pregnancy tests were obtained in only 6 of these women, and 3 women were actually pregnant while receiving valproate.

In our own audit[2] of 10,000 consecutive prescriptions issued to psychiatry, neurology, and neurosurgery outpatients, we found that valproate was included in nearly 17% (n = 647) of prescriptions issued to women (n = 3,837); of these, 71% (n = 460) were in the 15–45 year age band. Because no denominator is stated by Tastenhoye et al,[1] the magnitude of the deviation from the ideal cannot be estimated as it was in our study. The ideal, of course, is no prescription of valproate to women of reproductive potential because the drug is associated with an unacceptably high risk of morphological and neurodevelopmental teratogenicity.[3]

Whereas deviations from the ideal may be inevitable in contexts in which other treatment options are unavailable or are available but do not work, the presence or absence of such contexts could not be determined in either our study[2] or that by Tastenhoye et al.[1] Finally, we could not ascertain in our study[2] about checks, balances, guidance, and documentation associated with the prescription of valproate, but Tastenhoye et al[1] did provide information and offered recommendations in this regard.

I agree with Tastenhoye et al[1] that physician education is necessary but continue to believe that, especially in countries in which the continuing medical education structure after graduation is weak, strong regulatory guidance is also necessary to reduce reproductive risks related to valproate use.[3] At the very least, individual units, such as departments or hospitals, should develop their own standard operating procedures for risk minimization.

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