IS VALPROATE (VPA) AN OBLIGATORY TERATOGEN, OR IS IT JUST A MATTER OF DOSE?

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Valproate has been the main antiepileptic drug (AED) for the treatment of primary generalised epilepsy (PGE), uncharacterised and symptomatic generalised epilepsies since the mid 1970's. Pioneered in France and introduced in the US and Australia in 1975, VPA teratogenicity was first reported from the Rhone Alpine region. The matter was not pursued because of the excellent seizure control profile of VPA. An increasing body of evidence focussed on an association of VPA exposure during gestation with occurrence of neural tube defects and other major malformations. Many physicians have suggested that VPA should not be used in women with epilepsy in child-bearing age. Psychiatrists on rather tenuous grounds are concerned of risks of polycystic ovary syndromes.

On more informed analysis, VPA is the most effective AED for seizure control of PGE. Adverse effects are dose -related. At doses of 400-650 mg per day, there is no statistical evidence that malformations are more frequent with VPA than other AEDs. Concern has been raised about a potential risk of VPA exposure on neurocognitive development. At lower doses the risks of VPA exposure are statistically not greater than that for other AEDs. There are reports of significant loss of seizure control when VPA is discarded because of concerns of teratogenicity. Careful monitoring of the epilepsy before and during pregnancy and using minimum effective doses of VPA, are likely to provide the optimal risk-benefit ratio for many women of childbearing potential.