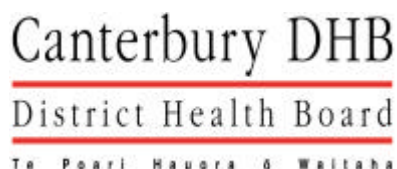


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SAFETY OF VALPROATE IN PREGNANCY

Question:

What is the safety of valproate in pregnancy?

Answer:

Valproic acid and its salt, sodium valproate, are considered to be human teratogens. Exposure between 17 and 30 days post-fertilization is reported to carry a 1-2% risk of neural tube defects^[1,2]. This risk is similar to that which occurs in women who have previously had a child with a neural tube defect^[2].

A foetal valproate syndrome has also been reported which includes facial abnormalities eg tall, narrow forehead, medial deficiency of the eyebrows, flat nasal bridge, broad nasal root, small downturned mouth, and thick lower lip, and digit and urogenital malformations^[2].

Other major malformations have been reported in association with valproic acid exposure including congenital heart disease, oral clefts and limb and genital abnormalities^[1,2]. However, causality is difficult to establish because epilepsy has been associated with an increased risk of congenital defects^[2]. It is generally accepted that epileptic women have 2-3 times greater risk of producing a child with abnormalities compared with the general population who have an incidence of 2-3%^[2,3].

Other effects that have been observed in neonates following *in utero* exposure to valproic acid include hyperbilirubinemia, hepatotoxicity, and neonatal distress^[1].

Conclusions:

Valproic acid is considered to be teratogenic and should be avoided (where feasible) in pregnancy especially during the first trimester during organogenesis.

References:

1. Briggs GG *et al.* Drugs in Pregnancy and Lactation (5th ed), 1998
2. Drugdex, Micromedex database
3. Rubin P (ed). Prescribing in Pregnancy (2nd ed), 1995

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The information contained within this document is provided on the understanding that although it may be used to assist in your final clinical decision, the Drug Information Service at Christchurch Hospital does not accept any responsibility for such decisions.