**Case Study**

**Tobias, a two-year-old child, developed foetal valproate syndrome (FVS) as a result of sodium valproate/valproic acid (VPA) exposure in utero.**

Tobias’s mother Emily had epilepsy, which had been managed during the pregnancy with assistance from a neurologist and an obstetrician. At 18 weeks of pregnancy, she was taking 1500mg of sodium valproate per day in divided doses.

At 37 weeks and five days’ pregnancy, Emily was admitted to hospital for an emergency caesarean section as her obstetrician had identified intrauterine growth retardation.

The baby was born with a weight of 1856 grams. Upon examination by a paediatrician the next day, it was noted that Tobias exhibited features of trigonocephaly, facial dysmorphism, truncation of multiple digits, overlapping third and fourth toes on the right foot, and restriction of extension at both knees.

On the basis of the medical history and physical findings, and with the help of genetic services, Tobias was diagnosed with FVS. This was supported by the treating paediatrician.

Tobias was examined at two years of age and was assessed as having global developmental delay, but he has made good progress in growth and development.

A treatment injury claim was lodged for FVS as a result of sodium valproate exposure in utero. ACC accepted this claim as an injury caused by treatment. ACC was able to provide assistance with treatment as well as learning and rehabilitation services.

**Expert Commentary**

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None of the antiepileptic drugs (AEDs) currently available is completely safe during pregnancy, but sodium valproate/valproic acid (VPA) appears to be the most teratogenic of them all. This case illustrates some of the classic dysmorphic features of FVS, issues with the use of AEDs in pregnancy and the importance of counselling.

VPA has been in use since 1964 and still remains a commonly used AED today. The first teratogenic effects were published in 1980, with the term ‘foetal valproate syndrome’ first used in 1984. This term encompasses multiple birth defects, dysmorphic facies, developmental delay, learning

**Key points**

- Women who are on antiepileptic drugs and are considering pregnancy should be counselled well in advance about the risks of congenital abnormalities
- Sodium valproate carries the highest risk
- The risk of congenital abnormalities is lower with sodium valproate doses less than 1000-1400mg/day; however, no safe sodium valproate dose has been established
- In the event of an unexpected pregnancy, sodium valproate should not be stopped suddenly; consider reducing the dose and/or starting an alternative antiepileptic drug.
difficulties and/or behavioural problems\(^1\). Trigonocephaly, as in this case, is one of the classic dysmorphic features seen with FVS\(^1\).

Observational data from various pregnancy registries and small studies have reported a substantial risk of major malformations, including spina bifida, with valproate alone or with other AEDs\(^2,3,4\). The Australian Pregnancy Register for Women on Antiepileptic Medication has reported the risk to be as high as 16% for first-trimester foetal exposure at doses above 1400mg/day\(^4\). VPA doses less than 1400mg have been reported to be associated with lower rates of malformations in the order of 6-7%\(^2\). Other studies have suggested a change in risk at 1000mg/day\(^2,6\). The effect of VPA on malformation risk is dose dependent, and although some have suggested a cut-off threshold of 1000mg/day\(^2,5\), a lowest safe dose has not been established. It may be prudent to regard any VPA dose in pregnancy as carrying more risk than other commonly used AEDs.

Many AEDs carry some degree of foetal risk. The United Kingdom Epilepsy & Pregnancy Register has reported 4.2% congenital malformation for all AED’s versus 3.5% untreated; 6.0% with polytherapy versus 3.7% monotherapy; and 2.2% with carbamazepine monotherapy\(^3\). Uncontrolled or untreated epilepsy itself is also a risk to the foetus and the mother, therefore it is critically important to consider pregnancy carefully in epileptic patients.

**Current professional guidelines**

Women who are on AEDs who may become pregnant or are considering pregnancy should be carefully counselled on the foetal risks of their specific AED’s and the risks of uncontrolled epilepsy prior to conception. With adequate lead time prior to pregnancy, consideration could be given to alternative options, which may include VPA at daily doses below 1400mg if this is considered a safer option. If a dose is proven to be clinically inadequate, other suitable drugs may be added to the VPA particularly if the VPA can be reduced or substituted\(^3\). Ultimately it may prove difficult to achieve seizure control when balancing a lower VPA dose and a less risky AED. The patient therefore should fully understand these risks when contemplating pregnancy. The occurrence of an unexpected pregnancy while on VPA should not trigger the sudden discontinuation of therapy. Instead, a dose reduction to below the heightened risk threshold should be made, with another AED’s added if necessary.

**References/Websites**


**Claims information**

Between July 2005 and May 2014 ACC made decisions on 8544 treatment injury claims related to injuries caused by medication adverse reactions. Of these, 5395 (69%) claims were accepted and 2629 (31%) were declined. Approximately 32 claims were related to prescribed sodium valproate usage causing treatment injuries; of these, 17 (53%) claims were accepted and 15 (47%) were declined.

**How ACC can help your patients following treatment injury**

Many patients may not require assistance following their treatment injury. However, for those who need help and have an accepted ACC claim, a range of assistance is available, depending on the specific nature of the injury and the person’s circumstances. Help may include things like:

- contributions towards treatment costs
- weekly compensation for lost income (if there’s an inability to work because of the injury)
- help at home, with things like housekeeping and childcare

No help can be given until a claim is accepted, so it’s important to lodge a claim for a treatment injury as soon as possible after the incident, with relevant clinical information attached. This will ensure ACC is able to investigate, make a decision and, if covered, help your patient with their recovery.

**About this case study**

This case study is based on information amalgamated from a number of claims. The name given to the patient is therefore not a real one.

The case studies are produced by ACC’s Treatment Injury Centre, to provide health professionals with:

- an overview of the factors leading to treatment injury
- expert commentary on how similar injuries might be avoided in the future.

The case studies are not intended as a guide to treatment injury cover. Send your feedback to: TI.info@acc.co.nz