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Reaksi

DRUG SAFETY NEWS

DRUG SAFETY MONITORING CENTRE, NPCB

Mission: This publication provides information and recommendations to healthcare professionals to enhance communication of drug safety updates, raise awareness of adverse drug reactions reported, and stimulate additional adverse drug reaction reporting. It is a newsletter published bimonthly by the Drug Safety Monitoring Centre, National Pharmaceutical Control Bureau (NPCB), Malaysia.

In This Issue:

TO REPORT AN ADVERSE DRUG REACTION

Online

1. Visit www.bpfk.gov.my.
2. Click on ADR Reporting and Product Complaints.
3. Click to report as a healthcare professional via online or hardcopy.
4. Submit the form once completed.

Mail

1. Print out ADR form available on website and complete it.
2. Mail or fax to:
   The Drug Safety Monitoring Centre,
   National Pharmaceutical Control Bureau,
   Ministry of Health
   PO Box 319, Jalan Sultan,
   46730 Petaling Jaya,
   Selangor.

Telephone

03-78835400
(ext. 5542/ 8461 / 8463)

Fax

03-79567151

Sodium Valproate: Risk of Decreased IQ Scores in Children after Foetal Exposure

A recent prospective observational study Neurodevelopmental Effects of Antiepileptic Drugs (NEAD Study) by Meador *et al* published in the Lancet Neurology Journal (March 2013), revealed that children born to mothers who took valproate during pregnancy had IQ scores which were between 8 to 11 points lower at 6 years of age compared to children exposed to carbamazepine, lamotrigine and phenytoin. These effects were dose dependent.

According to the Consensus Guidelines on the Management of Epilepsy 2010 by the Epilepsy Council, Malaysian Society of Neurosciences, valproate is an important first-line antiepileptic drug (AED) in adolescents and young adults. Currently there is insufficient evidence of a higher risk of teratogenicity with any one AED. However, as with most other AEDs, valproate must not be used in women of child-bearing potential unless the benefits outweigh the risks.

Valproate is approved in Malaysia for the treatment of epilepsy and mania associated with bipolar disorder. There have been reports of off-label use for the prevention of migraine headaches, however prescribers are reminded not to practice this use. The United States Food and Drug Administration (US FDA) recently contraindicated valproate for migraine use in pregnant women.

Ideally, women should be advised not to become pregnant until they are seizure-free and stop taking AEDs. If antiepileptic drug withdrawal is impossible, the treatment plan should aim to avoid polytherapy and use the lowest effective dose of AED. The risk of adverse effects of AEDs should also be taken into consideration when choosing an AED. Women on AEDs should be monitored throughout pregnancy to detect foetal malformations. Children who had foetal exposure to antiepileptic drugs are recommended to have regular assessment of cognitive function.

In Malaysia:
Since the year 2000, NPCB has received 175 reports related to sodium valproate, of which only one (1) report involved maternal drug exposure. Meningomyelocele was reported in a three year old child exposed to sodium valproate which his mother took for generalised epilepsy secondary to arrested hydrocephalus, before and during pregnancy. She was also taking folic acid and multivitamins. The case was given the causality 'possibly-related (C3)'.

Advice to healthcare providers:
- The teratogenic effects of AEDs as well as possible adverse effects of uncontrolled seizures during pregnancy must be discussed with patients well before conception.
- Women of child-bearing potential must use effective contraception during treatment and until AED adjustment is achieved if they wish to conceive.
- Pregnant women currently taking sodium valproate should be advised NOT to stop their medications immediately but should seek medical advice, because sudden discontinuation can lead to serious health problems such as breakthrough seizures.
- Folic acid supplementation of at least 0.4mg daily should be recommended for all women of child-bearing age taking AEDs, starting before conception.
- Any adverse event suspected to be associated with the use of sodium valproate should be reported to the Drug Safety Monitoring Centre, NPCB.

Codeine Use in Children: Rare but Life-Threatening Adverse Events or Death After Tonsillectomy and/or Adenoidectomy

The safety of codeine use in children was reviewed following reports of death or serious adverse reactions when used as a painkiller after tonsillectomy and/or adenoidectomy for obstructive sleep apnoea syndrome. The children involved had evidence of a genetic ability to rapidly convert codeine into life-threatening or fatal amounts of morphine in the body due to a polymorphism of enzyme cytochrome P450 2D6 (CYP2D6).

The United States Food and Drug Administration (US FDA) Adverse Event Reporting System (AERS) data from 1969 to 2012 revealed 10 fatalities and 3 cases of overdose associated with the use of codeine in children. The children were aged between 21 months to 9 years old. Most of the cases involved codeine used after adenotonsillectomy (n=8) or for respiratory tract infection (n=3). Enzyme CYP2D6 metaboliser status for seven (7) of the children mentioned above were three (3) ultra-rapid metabolisers, three (3) extensive metabolisers and one (1) likely ultra-rapid metaboliser.

NPCB has issued a letter to the Malaysian Paediatric Association and the Malaysian Society of Otorhinolaryngologists Head & Neck Surgeons (MSO-HNS) to highlight this incidence of fatalities among children. NPCB has been informed that in Malaysia, codeine is not generally used as a painkiller after tonsillectomy and/or adenoidectomy.

In Malaysia:
There are a total of nine (9) registered products containing codeine. Eight (8) of the products are indicated for children above 6 years, and one (1) is indicated only for adults. Eleven (11) ADR reports on combination products containing paracetamol and codeine have been received but none involved children. The reactions reported for these combination products included rash, breathing difficulty, face oedema, nausea and vomiting.

Advice to healthcare providers:
- Avoid using codeine products for pain control post-tonsillectomy and/or adenoidectomy especially among paediatric patients.
- Kindly report any adverse events suspected to be associated with the use of codeine to the Drug Safety Monitoring Centre, NPCB.