Drug Guideline  Sodium Valproate

Summary: Sodium valproate blocks voltage-dependent sodium channels, thus limiting the propagation of seizure discharges.

Approved by: ICU Medical Director
Publication (Issue) Date: May 2013
Next Review Date: May 2016

Replaces Existing Drug Guideline: June 2007

Previous Review Dates: November 2003

1. Introduction:

Patient safety

The Aims / Expected Outcome of this drug guideline:

Sodium Valproate will be administered safely and appropriately without any adverse side effects

Related Policies
• C3.00 Drug prescribing
• C3.01 Drug administration
• C3.01 Administration of IV Medications

2. Drug Guideline: Policy Statement
• All care provided within Liverpool Hospital will be in accordance with infection control, manual handling and minimization and management of aggression guidelines.
• Medications are to be prescribed and signed by a medical officer/authorized nurse practitioner (NP) unless required during an emergency.
• All drugs administered during an emergency (under the direction of a medical officer/authorised nurse practitioner) are to be documented during the event, then prescribed and signed following the event.
• Medications are to be given at the time prescribed (as close to the time as is possible when multiple drugs require ‘same time’ administration and, when the nurse is caring for more than one patient, recognition is given to a possible short delay to administration – antibiotics and other lifesaving drugs are to be prioritized) and are to be signed by the administering nurse.
• Parenteral medication prescriptions and the drug are to be checked with a second registered or endorsed enrolled nurse prior to administration. The "rights of drug administration" must be followed: right: patient, drug, dose, route, administration, time, reason for the drug, documentation, education and evaluation/outcome.
• Adverse drug reactions are to be documented and reported to a medical officer.
3. Guideline

Actions
Sodium valproate is an anticonvulsant and antipsychotic.
• Its anticonvulsant effect is attributed to the blockage of voltage dependent sodium channels and increased brain levels of gamma-aminobutyric acid (GABA).
• The GABA-ergic effect is believed to contribute to the antimanic properties of sodium valproate.
• Its action against absence seizures depends on blocking T-type calcium channels in the thalamus.
• It does not have major hypnotic effects nor does it act on the autonomic nervous system, respiration, blood pressure, renal function or body temperature.

Indications
• Treatment and prophylaxis of epilepsy.
• Sodium valproate can be used in the treatment of absence seizures (petit mal), tonic-clonic seizures (grand mal), myoclonic seizures and partial (focal) seizures.
• In the treatment of acute mania.

Contraindications
• Pre-existing acute or chronic hepatic dysfunction or family history of severe hepatitis.
• Pregnancy – women treated with intravenous sodium valproate have potentially increased risk of giving birth to a baby with an abnormality.
• Hypersensitivity

Precautions
• Abrupt withdrawal – there is a possible risk of seizures after sudden cessation of sodium valproate.
• Severe liver damage or hepatic failure may occur in patients treated with sodium valproate. Patients most at risk are those on multiple anticonvulsant therapy and signs of failure occur within first 6 months of therapy. Monitor for clinical symptoms and liver function tests.
• Impaired renal function – lower doses may be required as free drug levels may be high due to poor urinary excretion of free drug metabolites.
• Urea cycle disorders – patients who develop symptoms of unexplained hyperammonaemic encephalopathy while receiving valproate therapy should receive prompt treatment (including discontinuation of valproate therapy) and be evaluated for underlying urea cycle disorders.
• Thrombocytopenia – evidence of haemorrhage, bruising or a disorder of haemostasis / coagulation is an indication for reduction of dosage or withdrawal of therapy.
• Pancreatitis – it may be associated with development of life threatening pancreatitis:
  => Abdominal pain, nausea, vomiting, and/or anorexia can be symptoms of pancreatitis requiring prompt medical attention.
  => If diagnosed, sodium valproate should be discontinued.

Significant interactions
• Anticonvulsants – these drugs when used together with valproate have the ability to increase the intrinsic clearance of valproate.
• Anticoagulants – drugs like aspirin may result in displacement of valproate from protein binding sites, resulting in a rise in free levels.
• Tricyclic antidepressants – sodium valproate may inhibit the metabolism of tricyclic antidepressants.
• Psychotropics, including MAOIs, benzodiazepines, chlorpromazine, felbamate and fluoxetine – may all inhibit the metabolism of valproate.
• Drugs with extensive protein binding may result in varying serum drug levels: eg. aspirin, carbamazepine, phenytoin, warfarin.

Adverse effects
• Liver dysfunction, hepatic failure.
• Thrombocytopenia, platelet aggregation defects.
• Prolonged bleeding time, haemorrhage, thrombocytopenia, platelet aggregation defects.
• Hyperammonaemia, hypothyroidism
• Pancreatitis.
• Tremor, hair loss, sedation and weight gain.
• Hyperactivity, aggressiveness.
• Anorexia, nausea and vomiting.

Presentation
Sodium valproate 400mg vial with 4mL ampoule water for injection (for reconstitution).

Administration Guidelines

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<tr>
<th>Reconstitute vial with accompanying 4mL water for injection = 400mg /4ml to give a solution of 100mg/mL</th>
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<tbody>
<tr>
<td>Dose(^{1,3,4}): Adults – Initial dose of 400-800mg (up to 10mg/kg) by slow IV infusion over 30-60 minutes.</td>
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<tr>
<td>Continuous IV infusion(^{1,2,3}): 1-2mg/kg/hr to a maximum of 2500mg/day. Dilute 2000mg (5 ampoules) in 500ml 0.9% sodium chloride = final concentration of 4mg/ml. Calculate dose of 1-2mg/kg/hr and infuse over 24 hours.</td>
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Clinical Considerations
- Monitor liver function tests and coagulation status during therapy.
- Monitor Sodium valproate levels – maintain between 350 - 700µmol /L. Toxic levels are > 830 µmol /L.

4. Performance Measures
All incidents are documented using the hospital electronic reporting system: IIMS and managed appropriately by the NUM and staff as directed.

5. References / Links
1. MIMS Online, CIAP: NSW Health Department, Copyright MIMS Australia Pty Ltd. February 2012. http://www.use.hcn.com.au

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