the children's hospital at Westmead

INTRAVENOUS ASPIRIN - CHW

DRUG PROTOCOL©

DOCUMENT SUMMARY/KEY POINTS

- Clinical indications for IV aspirin, including for neuro-interventional procedures and rapid anti-platelet blockade in ICU settings
- Dosing guidelines for children >6 months: 12.5 mg/kg to a maximum of 500 mg/dose
- Dilute to a convenient volume to ≥2 mg/mL in glucose 5 % or sodium chloride 0.9% and infuse over at least 20 minutes.
- Stop infusion immediately if severe anaphylactoid reaction or haemodynamic instability occurs and start treatment.

CHANGE SUMMARY

- This is a new document

READ ACKNOWLEDGEMENT

- Medical, pharmacy, and nursing staff who care for patients being treated with intravenous aspirin are required to read and acknowledge the document.

Note: Separate Practice Guidelines may be required to cover all aspects of management.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
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Team Leader:	VMO	**Area/Dept:** Radiology

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NSW GOVERNMENT

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Introduction / Background

Aspirin (acetylsalicylic acid) is a non-steroidal anti-inflammatory drug used as an anti-pyretic, anti-inflammatory, analgesic, and anti-platelet. The mechanism of aspirin's antiplatelet property is through irreversibly inhibiting cyclooxygenase-1 and 2 (COX) enzymes, decreasing prostaglandin and thromboxane formation, thereby preventing platelet aggregation.

Registered Use

Oral aspirin is registered for use in Australia as an antiplatelet agent for prophylaxis against myocardial infarction, cerebrovascular disease, unstable angina, transient ischaemic attack and stroke. Intravenous aspirin is not registered in Australia.

Approved Indications

Indications for intravenous aspirin include:

- Intra-procedural treatment of platelet aggregation or intravascular thrombus.
- Patients requiring ultra-rapid platelet blockade (e.g. acute requirement for intracranial flow diverter stent or bare metal stent).
- Urgent requirement for anti-platelet therapy in patients without nasogastric access and where oral administration is unsuitable or not possible, including patients with acute ischaemic stroke, arterial dissection, and endovascular placement of bare metal or flow-diverter stents.

Specific patient groups most likely to benefit

Patients undergoing neuro-interventional procedures requiring urgent antiplatelet therapy, without nasogastric access and where oral therapy is unsuitable or not possible.

Contraindications

- Allergy to aspirin (acetylsalicyclic acid) or excipients (aminoacetic acid) or NSAIDs
- Aspirin-sensitive asthma
- Severe active bleeding
- Severe hepatic failure
- Disease states with an increased risk of severe bleeding (e.g. bleeding disorders, gastric ulcers, portal hypertension with oesophageal varices)
- 3rd trimester of pregnancy

Precautions

- Risk of bleeding.
- Other medications that can affect the clotting process may increase the risk of bleeding – monitor closely.
- Spinal injection or puncture.
- Seek specialist advice before considering intrathecal or epidural analgesia, or lumbar puncture (risk of epidural haematoma which may cause paralysis).
- Severe renal impairment because of increased risk of bleeding or further deterioration in renal function, particularly if GFR <30 mL/min

- In children or adolescents with febrile illness, if persistent vomiting occurs after aspirin administration, Reye's syndrome should be considered and urgent Haematologist advice should be sought,
- Severe G6PD deficiency – aspirin can induce haemolysis.

Presentation

- Powdered vial containing 500 mg of acetylsalicylic acid (aspirin) as lysine acetylsalicylate and water for injection as diluent.
    - Aspegic: 900 mg lysine acetylsalicylate
    - Aspirin IV (Bayer): 1,000 mg lysine acetylsalicylate glycine

Dose

Children >6 months:

- Loading dose (intra-procedurally): 10 mg/kg/dose
    - Maximum dose: 12.5 mg/kg or 500 mg/dose (whichever is lower)
- Maintenance dose: 3 mg/kg/dose IV daily
    - Maximum dose: 150 mg/dose
    - Maintenance dose is initiated 24 hours post loading dose.
- Infuse intravenously over at least 20 minutes

Duration of treatment

- Continue IV aspirin until oral or nasogastric aspirin can be safely initiated.

Authorised Prescribers

- Neuro-interventionalists.
- Intensivists.
- Haematologists.
- Other prescribers under the supervision of an intensivist or neuro-interventionist.

Place in therapy in relation to alternatives

- As antiplatelet agent where oral anti-platelets are not suitable. To be transitioned to oral aspirin when clinically indicated.
- As part of combination therapy, IV aspirin may be used with other anti-platelet agents, such as clopidogrel.
    - Intra-procedurally, other agents such as heparin or tirofiban may be used in combination.

Administration

- Reconstitute the 500 mg powdered aspirin vial with the supplied water for injection diluent immediately before use.
- If supplied diluent is unavailable, may use water for injection for reconstitution.

- **Note the brand being reconstituted** (Aspirin IV (Bayer) contains 0.8 mL powder displacement in 500 mg vial):
    - *Aspegic*: Add 5 mL water for injection to 500 mg acetylsalicyclic acid (= 100 mg/mL).
    - *Bayer Aspirin IV*: Add 4.2 mL water for injection to 500 mg acetylsalicyclic acid (= 100 mg/mL). Use a 5 micrometre filter (5 micron filter needle) to withdraw the reconstituted solution from the vial.Dilute the prescribed dose to a convenient volume in a compatible fluid (glucose 5%, Hartmann's, sodium chloride 0.9%). Dilute 500 mg dose to a maximum volume of 250 mL of compatible fluid.
- Infuse over at least 20 minutes.
- The reconstituted solution is for single use only and unused solution must be discarded. Supplied diluent contains water for injection.
- Consult The Paediatric Injectable Medicines Handbook for further information.

Safety and Patient Monitoring

- Usual PICU/procedural observations as appropriate
- Hypersensitivity reactions
- Signs of bleeding
- Serum creatinine in severe renal impairment.

Adverse effects

- Common adverse effects: hypersensitivity (skin rashes, itching, wheezing, coughing, difficulty breathing); nausea and vomiting; ringing in ears; abdominal discomfort, bleeding.
- Reye Syndrome is a rare side effect in children, particularly with high dose aspirin. *This is a rare condition affecting the brain and liver in children with recent viral infections and is associated with aspirin use. Symptoms and signs to watch for include persistent vomiting, confusion, seizures, and rash on the hands and feet.*

Significant drug interactions

- Other NSAIDs: increased risk of bleeding and gastric ulceration
- Anticoagulants: increased risk of bleeding
- Methotrexate: increased serum concentration of methotrexate (high dose aspirin contraindicated with methotrexate doses >15 mg/week). Low, antiplatelet dose aspirin unlikely to be of concern. Monitor for methotrexate toxicity if combination cannot be avoided.
- Valproate (sodium valproate/valproic acid): increased serum concentration of valproate.
- SSRIs: increased risk of gastrointestinal bleeding through enhanced anti-platelet effect of aspirin.

Management of complications

- Management of anaphylaxis: resuscitation equipment and medication should be readily available as anaphylactoid reactions have occurred. Stop infusion immediately if severe anaphylactoid reaction or haemodynamic instability occurs and start treatment. Notify the medical officer urgently.
- Management of severe bleeding: as per local protocol.

References

1. Prince of Wales Hospital, Prescribing Protocol Intravenous Aspirin: https://www.seslhd.health.nsw.gov.au/sites/default/files/documents/SESLHDPR%20700.pdf
2. Aspegic. Product information. Mulgrave, Vic: Medsurge.
3. Aspirin IV. Summary of product characteristics. Leverkusen, Germany: Bayer Vital GmbH. Approved 06/07/2005. Updated April 2021.
4. Bayer Health Care. A prospective, randomized, verum controlled, open label, parallel group, multi-center phase III clinical trial to determine the superiority of 500 or 250 mg Aspirin i.v. (BAY81-8781) treatment versus 300mg Aspirin N tablets PO in patients with acute coronary syndrome, measured by time dependant thromboxane inhibition. NIH, NLM. https://clinicaltrials.gov/ct2/show/NCT00910065. Accessed 8/09/2021.
5. Schoergenhofer C, Hobl EL et. al. Acetylsalicylic acid in critically ill patients: a cross-sectional and a randomized trial, Eur J Clin Invest 2017; 47 (7): 504–512
6. Meves, Saskia H et al. "Is There an Ideal Way to Initiate Antiplatelet Therapy with Aspirin? A Crossover Study on Healthy Volunteers Evaluating Different Dosing Schemes with Whole Blood Aggregometry." BMC research notes 4.1 (2011): 106–106. Web.
7. Vivas, David et al. "Impact of Intravenous Lysine Acetylsalicylate Versus Oral Aspirin on Prasugrel-Inhibited Platelets: Results of a Prospective, Randomized, Crossover Study (the ECCLIPSE Trial)." Circulation. Cardiovascular interventions 8.5 (2015): n. pag. Web.
8. Ries T, Buhk JH, Kucinski T, Goebell E, Grzyska U, Zeumer H, et al. Intravenous administration of acetylsalicylic acid during endovascular treatment of cerebral aneurysms reduces the rate of thromboembolic events. Stroke. 2006;37:1816–1821.
9. Society of Hospital Pharmacists Australia (SHPA). Australian Injectable Drugs Handbook. 8th ed. Collingwood, Australia.2020.