Argipressin (Vasopressin)

Newborn Use Only

2017

Alert	When using for diabetes insipidus (DI), Paediatric Endocrine consultation should be obtained. Management should be in intensive care where monitoring and expertise are readily available.
Indication	1. Treatment of refractory hypotension. 2. Adjunctive treatment of pulmonary hypertension. 3. Acute antidiuretic hormone (ADH) replacement when diagnosis of diabetes insipidus established. [The drug of choice for the treatment of diabetes insipidus is desmopressin (dDAVP). An argipressin infusion should be considered in the initial management of post-surgical or post-traumatic DI.] 4. Adjunct in acute massive haemorrhage of gastrointestinal tract or oesophageal varices (specialist use only) [Terlipressin or octreotide preferred].
Action	Antidiuretic hormone, also known as arginine vasopressin or argipressin, is a nine amino acid peptide secreted by the posterior pituitary. Its release is mediated either by high serum osmolality or by a hypotension/low right atrial pressure baroreflex. Argipressin acts via V_{1A} receptors in blood vessels, causing vasoconstriction, and via V_2 receptors in the renal tubules, causing anti-diuresis. Argipressin provokes vasodilatation in some vascular beds via its action on oxytocin receptors.
Drug Type	Vasopressor.
Trade Name	Pitressin.
Presentation	Ampoule contains 20 units/1 mL
Dosage / Interval	**For hypotension:** 0.01 to 0.05 units/kg/hour infusion **For pulmonary hypertension:** 0.01 to 0.02 units/kg/hour (can be commenced at 0.006 units/kg/hour to a maximum 0.07 units/kg/hour) **For diabetes insipidus:** Starting dose: 0.5 milliunits/kg/hour Dose range: 0.5 to 1.0 milliunits/kg/hour. May increase to 2.0 milliunits/kg/hour. The final wean may be from 0.5 to 0.25 milliunits/kg/hour **For acute massive gastrointestinal bleeding:** May not be best agent for this indication. Commence argipressin 0.12 units/kg/hour. Increase (titrate) over 2 hours to maximal dose of 0.6 units/kg/hour. Monitor carefully for side effects including fluid retention, electrolyte abnormalities, hypertension and cardiac arrhythmias. If bleeding not controlled at dose < 0.6 units/kg/hour (0.01 units/kg/minute) then unlikely to be controlled at higher doses and other measures should be used.
Maximum daily dose	For hypotension: 0.12 units/kg/hour (0.002 units/kg/minute). [Note up to 0.48 units/kg/hour (0.008 units/kg/minute) has been reported.] For acute massive gastrointestinal bleeding: 0.6 units/kg/hour (0.01 units/kg/min).
Route	Continuous IV infusion.
Preparation/Dilution	**FOR HYPOTENSION/PULMONARY HYPERTENSION:** **Single strength continuous IV infusion**

Infusion strength	Prescribed amount
1 mL/hour = 0.05 units/kg/hour	2.5 units/kg argipressin and make up to 50 mL

Draw up 0.125 mL/kg argipressin (2.5 units/kg) and dilute in 50 mL sodium chloride 0.9% or glucose 5% = 0.05 units/kg/mL solution.
Infusing at a rate of **1 mL/hour = 0.05 units/kg/hour.**

DOUBLE STRENGTH continuous IV infusion

Infusion strength	Prescribed amount
1 mL/hour = 0.1 units/kg/hour	5 units/kg argipressin and make up to 50 mL

<table>
<tr><td></td><td>
Dilution: draw up 0.25 mL/kg argipressin (5 units/kg) and dilute in 50 mL sodium chloride 0.9% or glucose 5% = 0.1 units/kg/mL solution.
Infusing at a rate of 1 mL/hour = 0.1 units/kg/hour.

QUADRUPLE STRENGTH continuous IV infusion
<table>
<tr><th>Infusion strength</th><th>Prescribed amount</th></tr>
<tr><td>1 mL/hour = 0.2 units/kg/hour</td><td>10 units/kg argipressin and make up to 50 mL</td></tr>
</table>

Dilution: draw up 0. 5 mL/kg argipressin (10 units/kg) and dilute in 50 mL sodium chloride 0.9% or glucose 5% = 0.2 units/kg/mL solution.
Infusing at a rate of 1 mL/hour = 0.2 units/kg/hour.

FOR DIABETES INSIPIDUS
Continuous IV infusion
<table>
<tr><th>Infusion strength</th><th>Prescribed amount</th></tr>
<tr><td>1 mL/hour = 0.8 milliunits/kg/hour</td><td>40 milliunits/kg argipressin and make up to 50 mL.</td></tr>
</table>

Step 1: Add 0.1 mL (2 units) of argipressin (20 unit/mL ampoule) to 500 mL bag of 0.9% sodium chloride to make a 4 milliunit/mL solution (SOLUTION A). Mix it well.

Step 2: Draw up 10 mL/kg of SOLUTION A (40 milliunits/kg) and make up to 50 mL with 0.9% sodium chloride to make a 0.8 milliunits/kg/mL solution.

Infusing at a rate of 1 mL/hour = 0.8 milliunits/kg/hour.

Note: 1 unit = 1000 milliunits.

FOR GASTROINTESTINAL BLEEDING
QUADRUPLE STRENGTH continuous IV infusion
<table>
<tr><th>Infusion strength</th><th>Prescribed amount</th></tr>
<tr><td>1 mL/hour = 0.2 units/kg/hour</td><td>10 units/kg argipressin and make up to 50 mL</td></tr>
</table>

Draw up 0. 5 mL/kg argipressin (10 units/kg) and dilute in 50 mL sodium chloride 0.9% or glucose 5% = 0.2 units/kg/mL solution.
Infusing at a rate of 1 mL/hour = 0.2 units/kg/hour.
</td></tr>
<tr><td>Administration</td><td>Continuous intravenous infusion via a central line. Use with caution via a peripheral line.</td></tr>
<tr><td>Monitoring</td><td>
Continuous heart rate, ECG and blood pressure monitoring required.
The pressor response should be carefully monitored and may require the weaning of other vasopressors.
Assess urine output and peripheral perfusion frequently.
Monitor water balance and serum sodium.
Observe IV site closely for blanching and extravasation.
For diabetes insipidus:
The dose of this is titrated (usual dose range 0.0005 to 0.001 units/kg/hour (0.5 to 1.0 milliunits/kg/hour), aiming for:
• urine output 2–4 mL/kg/hour,
• neutral fluid balance,
• maintain plasma sodium 145–150 mmol/L
Aqueous IV argipressin has a half-life of 20–30 minutes, so a change in infusion rate is reflected 1 hour later.
</td></tr>
<tr><td>Contraindications</td><td>Hypersensitivity to argipressin.</td></tr>
<tr><td>Precautions</td><td>Use in hypotension:
Argipressin causes water retention and hyponatraemia.</td></tr>
</table>

	May cause ischaemia related to infusion site. Acute ECG or biochemical evidence of myocardial ischaemia. Previously documented chronic and/or severe liver dysfunction (INR > 2, direct bilirubin > 50 micromol/L) or clinical evidence of portal hypertension. Documented or high suspicion of mesenteric ischaemia. **Use in diabetes insipidus:** The mainstay of initial therapy is accurate fluid and electrolyte management. ADH administration should only be considered after a reasonable period of observation establishes that DI is persistent (at least 4–6 hours, but preferably longer in acute situations). Early or over vigorous ADH administration may provoke cerebral oedema, Prior to starting the infusion, it is advisable to allow the patient to drift into a slightly negative fluid balance. This can be easily achieved by not replacing all the previous hour(s) urine output. Once the argipressin infusion has commenced, continue the fluid regimen of replacement of previous hour's losses plus insensible losses. **Use in gastrointestinal bleeding:** There are few reports of argipressin use for gastrointestinal bleeding in newborns. The dose regimen is unclear and other agents may be more effective.
Drug Interactions	Noradrenaline (norepinephrine) and heparin—when used with argipressin may decrease the antidiuretic effect of argipressin.
Adverse Reactions	Causes water retention and hyponatraemia. Early or over vigorous administration may provoke cerebral oedema, Cardiac complications include coronary ischaemia, myocardial infarction, ventricular arrhythmias (ventricular tachycardia and asystole) and severe hypertension. Other reported adverse effects include severe GI ischaemia leading to bowel necrosis, hyponatraemia, anaphylaxis, bronchospasm, urticaria, angioedema, rashes, venous thrombosis, local irritation at injection site and peripheral vasoconstriction leading to cutaneous gangrene.[1,2]
Compatibility	Fluids: Glucose 5%, sodium chloride 0.9% Y-site: Amiodarone, pantoprazole (EDTA-free).
Incompatibility	Fluids: No information. Y-site: Diazepam, furosemide (frusemide), indometacin, phenytoin.
Stability	Diluted solution: Discard remainder after use. Change infusion solution every 24 hours
Storage	Ampoule: Store below 25°C.
Special Comments	Administration via a central line is preferred as extravasation may cause tissue necrosis.
Evidence summary	Refer to Full version.
References	Refer to Full version.

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