Caffeine

Newborn use only

2020

<table>
<tr><td>Alert</td><td>Caution with dosing: Caffeine citrate 2 mg = caffeine base 1 mg</td></tr>
<tr><td>Indication</td><td>1. Treatment of apnoea of prematurity.
2. Weaning from mechanical ventilation.
3. Prevention of post-operative apnoea.</td></tr>
<tr><td>Action</td><td>Competitive inhibition of the actions of adenosine at cell surface receptors.
Enhancement of respiratory effort and regularisation of breathing patterns through stimulation of central inspiratory drive and increased sensitivity of chemoreceptors to carbon dioxide.
Increase in respiratory centre output, smooth muscle relaxation and cardiac output.
Improvement in the contractility of the diaphragm and hence increasing the force of contraction and decreasing muscular fatigue.</td></tr>
<tr><td>Drug type</td><td>Central nervous system stimulant, respiratory stimulant.</td></tr>
<tr><td>Trade name</td><td>Cafnea (caffeine citrate), Auspman (Caffeine base)</td></tr>
<tr><td>Presentation</td><td>Caffeine citrate IV 40 mg/2 mL vial
Caffeine citrate oral 25 mg/5 mL solution
Caffeine base IV 50 mg/5 mL ampoule
Caffeine base oral 10 mg/mL solution</td></tr>
<tr><td>Dose</td><td><u>Caffeine citrate</u>

<table>
<tr><th></th><th>Loading dose</th><th>Maintenance dose
24 hours after loading dose</th><th>Post-Op apnoea
(single dose)</th></tr>
<tr><td>IV</td><td>20 mg/kg</td><td>10 mg/kg (range 5−20mg/kg) daily</td><td>10 mg/kg</td></tr>
<tr><td>Oral</td><td>20 mg/kg</td><td>10 mg/kg (range 5−20mg/kg) daily</td><td>10 mg/kg</td></tr>
</table>
Maintenance dose may be increased or decreased as per the clinical need.

<u>Caffeine base</u>

<table>
<tr><th></th><th>Loading dose</th><th>Maintenance dose
24 hours after loading dose</th><th>Post-Op apnoea
(single dose)</th></tr>
<tr><td>IV</td><td>10 mg/kg</td><td>5 mg/kg (range 2.5−10 mg/kg) daily</td><td>5 mg/kg</td></tr>
<tr><td>Oral</td><td>10 mg/kg</td><td>5 mg/kg (range 2.5−10 mg/kg) daily</td><td>5 mg/kg</td></tr>
</table>
Maintenance dose may be increased or decreased as per the clinical need.</td></tr>
<tr><td>Dose adjustment
Therapeutic hypothermia
ECMO
Renal impairment

Hepatic impairment</td><td>
Safety not demonstrated.
Not applicable
Current evidence is not enough to specify dose adjustment, but caution required in the context of renal impairment as caffeine is 86% renally excreted. Consider therapeutic drug monitoring.
No information.</td></tr>
<tr><td>Maximum dose</td><td>Loading dose: caffeine citrate in trials varied between 20 and 80 mg/kg.

Maintenance dose caffeine citrate in trials varied between 3 and 20 mg/kg/day. [1]</td></tr>
<tr><td>Total cumulative dose</td><td></td></tr>
<tr><td>Route</td><td>IV
Oral</td></tr>
<tr><td>Preparation</td><td><u>ORAL SOLUTION</u>
No dilution is required.

<u>IV INFUSION</u>
<u>Caffeine citrate</u>
Draw up 2 mL (40 mg) of caffeine citrate and add 3 mL sodium chloride 0.9% or glucose 5% to make a final volume of 5 mL with a concentration of 8 mg/mL.
<u>Caffeine base</u></td></tr>
</table>

	Draw up 2 mL caffeine base (20 mg) and add 8 mL sodium chloride 0.9% or glucose 5% to make a final volume of 10 mL with a concentration of 2 mg/mL.
Administration	IV: Infuse • loading dose over at least 30 minutes • maintenance over 10 minutes. ORAL: Solution may be administered without feeds, however consider giving with feeds to reduce gastric irritation.
Monitoring	Heart rate, number and severity of apnoea episodes and assess for agitation. Consider withholding dose if HR > 180 bpm. Cardiorespiratory monitoring should continue for at least 5-7 days after the cessation of caffeine treatment for apnoea. Therapeutic drug monitoring is usually not necessary. [2] Trough concentrations may be taken one hour before the next dose is due but should only be done if using high doses or toxicity is suspected. Monitoring of serum drug concentration should be determined on approximately day 5 of therapy. Standard caffeine dosing of a 20 mg/kg load followed by 5 mg/kg once daily results in serum concentrations of 5–20 mg/L (26-103 micromol/L). Supratherapeutic levels 20-60 mg/L (103 – 308 micromol/L) offer potential increased effect. Levels >60 mg/L (>308 micromol/L) are considered the toxic range. [3]
Contraindications	Contraindicated in infants with hypersensitivity to methylxanthines or citrate.
Precautions	Use with caution in infants with impaired renal or hepatic function, seizure disorders, cardiovascular disease or congenital heart disease.
Drug interactions	Fluconazole and verapamil may decrease caffeine elimination. Phenytoin may increase caffeine elimination. Caffeine antagonises the effects of benzodiazepines. Other methylxanthines (theophylline, aminophylline) should not be used concomitantly.
Adverse reactions	Arrhythmia (ventricular), flushing, tachycardia, vasodilatation, functional cardiac symptoms. Increased left ventricular output & increased stroke volume, hypotension. Agitation, irritability, restlessness, sleep disturbances, seizures (with toxic doses). May relax the lower oesophageal sphincter & increase gastric acid secretion leading to increased episodes of gastro-oesophageal reflux, gastritis, vomiting. Urticaria, alterations in serum glucose, diuresis, tachypnoea.
Compatibility	Fluids: Glucose 5%, Glucose 10%, Glucose 50% and sodium chloride 0.9%. Y-site: Dopamine, fentanyl, heparin, amino acid solutions and fat emulsions.
Incompatibility	Fluids: No information. Y-site: Aciclovir, frusemide, glyceryl trinitrate and ibuprofen lysine.
Stability	Caffeine citrate: Discard unused portion. Caffeine base: IV − discard unused portion. Oral solution − store at room temperature.
Storage	Store below 30 °C
Excipients	Cafnea Injection and oral solution contain citric acid monohydrate and sodium citrate. The injection contains no preservatives. Auspman caffeine oral solution – glycerol, potassium sorbate, hydrochloric acid.
Special comments	Half-life in neonates: 72−96 hours (range 40−230 hours decreasing with advancing corrected gestational age). [4, 5] Time to peak serum concentration: Within 30 minutes to 2 hours in oral administration. Caffeine may not reach subtherapeutic levels until 11 to 12 days post cessation [6].
Evidence	Refer to full version.
Practice points	Refer to full version.
References	Refer to full version.

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Original	9/11/2015

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