MONOGRAPH

AMINOPHYLLINE

Scope (Staff):	Medical, Pharmacy, Nursing, Anaesthetic Technicians
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Compatibility	Monitoring

DRUG CLASS

Aminophylline is a bronchodilator used intravenously in children with severe acute asthma who are receiving maximum treatment with inhaled bronchodilators. Possible effects include bronchial smooth muscle relaxation, anti-inflammatory effects, increase in diaphragm contractility and central nervous system (CNS) stimulation[1,3]

Aminophylline is a chemical complex which when administered disassociates to release the active drug theophylline.[1,2]

Aminophylline is a High Risk Medicine with a narrow therapeutic range and requires careful administration and monitoring as toxicity can occur even at therapeutic levels.[2]

INDICATIONS AND RESTRICTIONS

Intravenous aminophylline is indicated in severe acute asthma to reverse airway obstruction unresponsive to combined treatment of inhaled short acting beta-2 agonist and systemic corticosteroids.

Only intermittent IV dosing can be administered in general ward areas for children > 1 year of age.

Continuous IV infusion is restricted to Paediatric Critical Care (PCC). The infusion can be commenced in ED Resus where a patient is to be transferred to PCC.

Refer to Clinical Guideline: Asthma (acute) - Assessment and Management on the Ward for recommendations on the assessment and management of children with acute asthma in general ward areas.

See Formulary One

CONTRAINDICATIONS[2,3]

- Hypersensitivity to aminophylline, theophylline and ethylenediamine or any of the components of the formulation
- Concomitant use of oral theophylline (relative contraindication – discuss with consultant)

PRECAUTIONS

Children under 12 month of age, cardiac disease, hypertension, hyperthyroidism, peptic ulcer, epilepsy, hepatic impairment, fever, smoker, sepsis, pulmonary oedema, concomitant drugs which inhibit or enhance theophylline metabolism[2].

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- Aminophylline 250 mg/10 mL ampoule

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS1,7

Neonates: Limited data for apnoea of prematurity, caffeine citrate is the preferred agent. Contact pharmacy for advice[1]

Dosing in Overweight and Obese Children: Calculate dose using Ideal Body Weight

Loading doses should not be used if the patient is currently receiving aminophylline or theophylline.[4]

If patient is currently receiving or has received aminophylline or theophylline within 24 hours, obtain serum level prior to administering or omit the loading dose.

Age	Dose
≥ 1 month - < 12 months:	5 mg/kg
≥ 1 year - 18 years:	5 -10 mg/kg (maximum 500 mg)

Maintenance intermittent IV infusion doses:

Age	Dose
≥ 6 weeks - < 6 months:	3 mg/kg every 6 hours
≥ 6 months - < 12 months:	4 mg/kg every 6 hours
≥ 1 year - < 9 years:	6 mg/kg (maximum 500 mg) every 6 hours
≥ 9 years - < 12 years:	5 mg/kg (maximum 500 mg) every 6 hours
≥ 12 years - 18 years:	3 to 4 mg/kg (maximum 500 mg) every 6 hours

Maintenance continuous IV infusion doses (PCC only):

Age	Dose
≥ 6 weeks - < 6 months	0.5 mg/kg/hour
≥ 6 months - <12 months:	0.7 mg/kg/hour
≥ 1 year - < 9 years:	0.9 – 1.1 mg/kg/hour
≥ 9 years - < 12 years:	0. 7 mg/kg/hour
≥ 12 years - 18 years:	0.5-0.7 mg/kg/hour

The maintenance dosage of aminophylline must be individualised based on serum theophylline concentrations and clinical response including respiratory status, heart rate and blood pressure (BP).

Therapeutic Drug Monitoring

Aminophylline requires therapeutic drug monitoring, see Monitoring

Renal impairment:

- No dosage adjustment necessary[1]

Hepatic impairment:

- Dose reduction and frequent monitoring of serum theophylline concentration are required in patients with decreased hepatic function[1].

ADMINISTRATION

Aminophylline is a vesicant – administer via a central line if available. If extravasation occurs, stop infusion and disconnect (leave needle / cannula in place. Gently aspirate extravasated solution. Initiate hyaluronidase antidote.

Intermittent IV doses

Dilute to a concentration of 1 mg/mL with a compatible IV fluid. May be administered undiluted (25 mg/mL) if fluid restricted.

Administer loading dose over 30 minutes. Do not exceed 25 mg/minute.[3]

Administer subsequent maintenance doses over 20 minutes.[4]

Continuous IV infusion

Dilute to a concentration of 1mg/mL of compatible IV fluid and administer at an age specific rate as above.[4]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*[6]

Compatible fluids: Glucose 5%, glucose 10%, glucose in sodium chloride solutions, Hartmann's, Ringer's, sodium chloride 0.9%[6]

Only commonly used drugs are listed below. This is not a complete list of incompatible drugs. Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

INCOMPATIBLE drugs: adrenaline (epinephrine), amiodarone, atracurium, azathioprine, benzylpencillin, , cefepime, ceftriaxone, ciprofloxacin, clindamycin, dobutamine, haloperidol lactate, hydralazine, insulin (short- acting), magnesium sulfate, methadone, midazolam, morphine sulfate, moxifloxacin, mycophenolate mofetil, noradrenaline (norepinephrine), ondansetron, pentamidine, pethidine, phenobarbital (phenobarbitone), prochlorperazine mesilate, promethazine, sodium ascorbate, thiamine, vancomycin, verapamil

MONITORING

Monitor serum potassium before commencement[2] and with each theophylline level. Serum potassium levels may decrease (this effect may be compounded by concurrent high salbutamol use) and should be checked at the same time as the theophylline levels and corrected. See Potassium monograph.

Aminophylline is monitored therapeutically in terms of plasma-theophylline concentrations.[4] This is because aminophylline is a chemical complex which when administered disassociates to release the active drug theophylline.[1,2]

Theophylline level should be monitored in all patients continuing beyond loading dose of aminophylline. Obtain level 30 minutes after the end of loading dose and every 12 hours thereafter (wait 30 minutes after completion of intermittent dose before taking the level).

Target theophylline level is **5-15 microgram/mL**[1]. Higher therapeutic concentration **(10-20 micrograms/mL)** may be necessary to achieve satisfactory clinical response. However, this should be weighed against the increased risk of adverse effects.

Dosage adjustment should be based on both serum theophylline concentration[8] and clinical response, with dosage increases being up to a maximum of 25%. Do not increase dose unless the patient is still symptomatic, and the aminophylline is being tolerated. Refer to dosage adjustment table below.

Theophylline level can be requested from Path West Biochemistry as required (24 hours / 7 days). The minimum collection volume is 0.3 mL into either a lithium heparin (plasma; green top) or clotted whole blood (serum; red top) tube. The sample can be collected either as venous or capillary blood. For more information, refer to Path West Test Directory

Steady state theophylline concentration[8]	**Dose adjustment**
< 9.9 microg/mL	If tolerated, but symptoms remain, increase dose by 25%. Recheck level.
10 - 14.9 microg/mL	Maintain dosage if tolerated. Recheck level at 24 hour intervals. If symptoms not controlled, consider additional medications for management.
15 - 19.9 microg/mL	Reduce dose by 10% to improve safety margin even if dose is tolerated. A higher level of 15-20 microg/mL may be maintained at the discretion of a consultant in severe cases
20 - 24.9 microg/mL	Decrease dose by 25%. Recheck level.
25 - 30 microg/mL	Stop infusion for 12 hours (ages 6 weeks to < 16 years) or 24 hours (ages ≥ 16 years) and decrease subsequent doses by at least 25%. Recheck level.
> 30 microg/mL	Stop dosing and treat overdose; If resumed, decrease subsequent dosage by at least 50%. Recheck level.

- Patients receiving aminophylline on general wards require close monitoring – the medical team must liaise with the ward shift coordinator / Clinical Nurse Manager and Hospital Clinical Manager to ensure adequate staffing levels. Medical staff may be required to remain on the

ward throughout the duration of the aminophylline infusion. This should be determined by the treating Consultant based on the individual patient's need.

- At a minimum continuous cardiorespiratory monitoring for all patients during infusion and for one hour following completion of the infusion.
- Assess and record heart rate, respiratory rate and BP every 15 minutes during the loading dose, and hourly thereafter for two hours. Assess for agitation / irritability.
- Rapid administration of aminophylline may cause CNS and cardiovascular effects such as bradycardia and severe hypotension.[1] The dose and rate of administration must be independently second checked by two authorised clinicians (medical, nursing staff or pharmacist).

ADVERSE EFFECTS

Common: nausea, vomiting, dizziness, headache, insomnia, tremor, irritability, restlessness, diuresis, sinus tachycardia[6]

Serious: atrial fibrillation and dysrhythmias are rare unless there is concurrent hypokalaemia; cardiac arrest, erythroderma, immune hypersensitivity reaction, intracranial haemorrhage, seizure[2, 6]

STORAGE

Store below 25°C. Protect from light[5]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **aminophylline**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Asthma (Acute) Assessment and Management on the Ward

Asthma – PCH Emergency Department Guideline

CAHS Allergy And Adverse Drug Reaction Management Policy

CAHS High Risk Medicines Policy

CAHS Medication Safety Policy

PCH Guidelines for Drug Dosing in Overweight And Obese Children 2 to18 Years Guideline

PCH Medication Administration Policy

PCH Smart Infusion Pumps and DERS Policy

Potassium monograph

Related external legislation, policies and guidelines

To access to the Manufacturer SDS for this product, use the following link to ChemAlert.

RCH Melbourne - Extravasation Guideline

References

1. Aminophylline Drug Information.UpToDate.Retrived February 2023,from Aminophylline: Pediatric drug information - UpToDate (health.wa.gov.au)
2. Clinical Pharmacology. Aminophylline 2023. Available from: Theophylline, Aminophylline Monograph - Clinical Pharmacology (health.wa.gov.au)
3. Australian Medicines Handbook. Australian Medicines Handbook. Accessed online February 2023. Available from: Aminophylline - Australian Medicines Handbook (health.wa.gov.au)
4. British National Formulary. Aminophylline: Royal Pharmaceutical Society; Accessed February 2023. Available from: MedicinesComplete — CONTENT > BNF for Children > Drug: Aminophylline (health.wa.gov.au)
5. Society of Hospital Pharmacists Australia. Australian Injectable Drugs Handbook: Aminophylline 2023. Accessed February 2023 Available from: AIDH - amiNOPHYLLine (health.wa.gov.au).
6. Micromedex 2.0 [Internet]. Thomson Reuters (Healthcare)Inc. 2019.
7. Australian Medicines Handbook, Pharmaceutical Society of Australia, Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists, Royal Australian College of General Practioners. AMH children's dosing companion [Internet]. Accessed online February 2023. Available from: Aminophylline - AMH Children's Dosing Companion (health.wa.gov.au)
8. Table adapted from: Cooney L, Hawcutt D, Sinha I. The Evidence for Intravenous Theophylline Levels between 10-20mg/L in Children Suffering an Acute Exacerbation of Asthma: A Systematic Review. *PLoS One*. 2016;11(4):e0153877. Published 2016 Apr 20. doi:10.1371/journal.pone.0153877

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