

A Clinical Guideline for the use of Intravenous Aminophylline in Acute Severe Asthma in Children

For Use in:	Paediatric High Dependency Unit or Intensive Care, Emergency Department
By:	Medical and Nursing Staff
For:	Children with Acute Life-Threatening Asthma
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This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

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Version and Document Control:

Version Number	Date of Update	Change Description	Author
1.1	23/04/2020	Reviewed with no clinical changes, as the drugs mentioned in document are specific, and unlikely to change	Dr I. Rose and Dr C. Kavanagh

This is a Controlled Document

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Quick reference

Escalation of Care for Acute Severe or Life-Threatening Asthma

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Objective

- To ensure the safe use of intravenous aminophylline in either the High Dependency Unit or Intensive Care Unit for children and resus Emergency Departments with acute severe or life threatening asthma.
- To provide appropriate instruction for the preparation of intravenous aminophylline solutions.
- To highlight problems with intravenous aminophylline use and suggest solutions if problems arise.

Broad recommendations

- Intravenous aminophylline should only be used if indicated, which will be informed by the patient's clinical condition. It can be used in patients with acute severe asthma or life-threatening asthma.
- Patients receiving intravenous aminophylline should be nursed in either a high dependency unit or an intensive care unit.
- Patients receiving intravenous aminophylline have continuous ECG monitoring and regular monitoring of electrolytes and blood gases.

Background

Aminophylline is a xanthine derivative. It is given for its theophylline activity which causes direct relaxation of bronchial smooth muscle relieving bronchospasm. The bronchodilatory effect of theophylline is minimal if bronchospasm is not the cause. The bronchodilatory effect may be via inhibition of selected phosphodiesterases, which produces an increase in intracellular cyclic AMP. Theophylline also directly stimulates the medullary respiratory centre.

It provides relief of severe bronchospasm associated with asthma and for the treatment of status asthmaticus. It must be prescribed and monitored carefully.

In cases of acute severe or life threatening asthma it can be given as an intravenous loading dose and continued as an intravenous infusion. This must only occur in a high dependency unit or an intensive care unit.

If a patient is receiving intravenous salbutamol **and** intravenous aminophylline, then treatment in an intensive care unit is recommended. If only using one agent, then it can be given in HDU.

This policy offers advice on intravenous aminophylline dosing and monitoring in patients with life threatening asthma.

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Indications for Use

Intravenous aminophylline should only be prescribed in acute severe asthma unresponsive to nebulised bronchodilators and life threatening asthma.

Consideration should be given to commencing intravenous salbutamol instead of aminophylline. Both can be used together, but if a child needs both, then this should be undertaken in an intensive care unit.

The risk of toxicity is high as there is a narrow therapeutic index. Aminophylline levels should be checked whilst the infusion is running on at least a daily basis.

Care should be taken in patients who are already receiving theophylline based products. In this scenario, a loading bolus of aminophylline would not be recommended.

Due to the immaturity of aminophylline metabolic pathways in children under the age of 1 year, particular attention to dosage selection and frequent monitoring of serum aminophylline levels are required when aminophylline is prescribed to children in this age group.

Caution is also recommended in patients undergoing influenza immunisation or who have an active influenza infection or febrile illness.

Dosing of Aminophylline

Recommended dosing would be:

- An initial loading dose of aminophylline 5mg/kg (max. 500mg) over 20 minutes. This should be omitted if the patient is already taking an oral theophylline.
- This would be followed by an intravenous infusion of aminophylline at a dose rate of 1mg/kg/hr in 1month-12year olds or 0.5-0.7mg/kg/hr in 12-18year olds.

Aminophylline has a narrow therapeutic index; therefore, cautious dosage determination is essential.

Therapeutic serum concentrations of aminophylline are considered to range from 5-15mcg/mL and levels greater than this are often associated with toxic effects.

Serum theophylline levels should be checked every 12 hours while the infusion is running. Serum potassium level should be checked at the same time.

First order pharmacokinetics, therefore doubling the rate of infusion should result in a doubling of the plasma level. In extreme cases, consider a bolus: a 1mg/kg bolus should increase the plasma level by about 2mcg/mL.

Monitoring of Aminophylline levels:

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Level <5mcg/mL = increase the dose by 50% and recheck in 6 hours.

Level 5-14mcg/mL = continue current dose.

Level 15-20 mcg/mL = half the infusion rate.

Level > 20mcg/mL STOP infusion and recheck in 6 hours.

Administration Details for Intravenous Aminophylline

Intravenous Aminophylline can be diluted with either 5% glucose or 0.9% sodium chloride solutions.

Aminophylline for peripheral administration:

- Remove 20 mLs from a 500mL bag of diluent (5% glucose or 0.9% sodium chloride solution) and discard.
- Add 500mg (20mLs) Aminophylline (25mg/mL preparation) to this bag.
- This will create a solution of 1mg/mL.
- The infusion rate 1mg/kg/hr. =1mL/kg/hr.

Aminophylline for central venous administration:

- Draw up 20mL (500mg) of Aminophylline (25mg/mL preparation) into a 50mL syringe and make up to 50mL with diluent (5% glucose or 0.9% sodium chloride)
- This will create a solution of 10mg/mL.
- The infusion rate 10mg/kg/hr. =1mL/kg/hr.

Nurses should state on the drug chart the exact time of administration.

Administration of infusion should be via a syringe pump.

Set the volume to be infused on the syringe pump to prevent overdose.

The line must always be primed with the diluted aminophylline infusion to prevent any delay in the patient receiving the medication.

Monitoring of Intravenous Aminophylline

1. Patient needs to be nursed in a High Dependency Unit or Intensive Care Unit.
2. Continuous cardiac ECG monitoring is needed.
3. Initial observations every 5 minutes for the first 10 minutes (pulse, respiratory rate, BP, oxygen saturation).
4. Observations every 15 minutes thereafter.
5. Minimum of 12 hourly U&Es to monitor potassium levels.

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6. Adverse effects include: muscle tremors (especially the hands), tachycardia, nausea and vomiting, headaches, agitation and hyperactivity, palpitations, feelings of warmth.
7. High doses can cause peripheral vasodilatation resulting in hypotension.
8. Overdose can result in chest pain, SVT and pulmonary hypertension.
 - Reduce infusion rate if develop lactic or metabolic acidosis, tachycardia, arrhythmias, tremor, severe hypokalaemia, hyperglycaemia or hypophosphatemia.

Discontinuing Intravenous Aminophylline Infusion

Criteria for reducing intravenous bronchodilator therapy:

- Normal respiratory effort.
- Normal ability to speak.
- Reduction in oxygen requirement.

The elimination half-life of aminophylline is 3-5 hours

Reduce the intravenous aminophylline dose by 50% of the original dose every 6 hours.

Following cessation of infusion, aminophylline will be cleared within 72 hours.

Patients should receive inhaled or nebulised salbutamol every 2 hours and ipratropium every 4 hours whilst weaning off intravenous bronchodilators. Rebound bronchospasm can occur 24-48 hours after stopping intravenous aminophylline, so patients need observed in hospital for this time period.

Clinical audit standards

- All children over the age of 2 years with acute severe or life threatening asthma receiving intravenous aminophylline should initially have a loading dose unless they are already taking an oral theophylline and then as an intravenous infusion of aminophylline if needed.
- Patients requiring intravenous aminophylline are nursed in a High Dependency unit or Intensive Care Unit.
- Patients requiring intravenous aminophylline have continuous cardiac ECG monitoring.
- Patients requiring intravenous aminophylline have a minimum of 12 hourly U&Es to monitor potassium levels.
- Medical notes should reflect review of the dosing regimen.

Summary of development and consultation process undertaken before registration and dissemination

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The authors listed above drafted this guideline on behalf of the regional High Dependency Care Forum and the Children's Critical Care Group who have agreed the final content. During its development the guideline has been circulated for comment. Comments were addressed and incorporated if appropriate.

This version has been endorsed by the Clinical Guidelines Assessment Panel.

References

1. Aminophylline hydrate Solution for Intravenous Infusion – Mercury Pharma. Summary of Product Characteristics [04/01/16] on Electronic Medicines Compendium: (accessed on 12/02/17 via www.medicines.org.uk/)
1. BNF for children, January 2017
2. British Thoracic Society, Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. Available from url: <https://www.brit-thoracic.org.uk/document-library/clinical-information/asthma/btssign-asthma-guideline-2016/>
2. Singhi S, Grover S, Bansal A, Chopra K. Randomised comparison of intravenous magnesium sulphate, terbutaline and aminophylline for children with acute severe asthma. *Acta Paediatrica* 2014; 103(12); 1301-1306.
3. Yung M and South M Randomised control trial of aminophylline for acute severe asthma. *Arch Dis Child* 1998;79:405-410