How is an intravenous aminophylline dose converted to an oral aminophylline or theophylline dose?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals

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Background

Theophylline is a bronchial smooth muscle relaxant used in the treatment of asthma and other respiratory diseases (1). Theophylline is only available as an oral formulation; for intravenous (IV) treatment aminophylline, a salt of theophylline, is used.

When changing a patient’s therapy from IV aminophylline to oral therapy with either theophylline or aminophylline, the bioavailability and the salt equivalence should be considered (1). The bioavailabilities of oral and IV aminophylline are summarised below (2):

<table>
<thead>
<tr>
<th>Dosage Form of aminophylline</th>
<th>Bioavailability</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV aminophylline</td>
<td>100%</td>
</tr>
<tr>
<td>Oral liquids</td>
<td>100%</td>
</tr>
<tr>
<td>Oral tablets and capsules (immediate release)</td>
<td>100%</td>
</tr>
<tr>
<td>Oral tablets and capsules (enteric coated)</td>
<td>Incomplete and unpredictable, with no clinical indication for use.</td>
</tr>
<tr>
<td>Oral tablets and capsules (extended release)</td>
<td>90-100% depending on the product.</td>
</tr>
</tbody>
</table>

The salt factor for aminophylline is approximately 0.8, i.e. the amount of a labelled dose of aminophylline which is theophylline is about 80% (1;3).

It is often not possible to achieve a dose that is exactly the same when converting from IV to oral therapy. The nearest practical dose should therefore be used. This is rarely a problem since pharmacokinetic and drug assay variability mean that measured theophylline levels are often not the same as predicted levels anyway. The aim is to achieve a dosage regimen that is likely to maintain concentrations within a range that is safe and effective for the individual (4). When treatment is changed from intravenous (IV) to oral therapy, the maintenance infusion should be stopped and oral therapy should be begun immediately (2). The following conversions assume that the patient is on the correct IV aminophylline dose.

**Answer**

Converting IV aminophylline to oral aminophylline:

1. Convert the hourly infusion rate to the total amount administered in 24 hours by multiplying the hourly dose by 24. (4)
2. Divide this total amount by the dosing interval for oral administration, e.g. 2 for twice a day. It is assumed that the oral product is completely absorbed, i.e. the bioavailability is 100% (4).

For example:

If the IV aminophylline dose is 35mg/hr and the dosing interval for oral aminophylline is every 12 hours, i.e. twice a day, divide the total daily dose of 840mg by 2. This gives the equivalent oral dose to be 420mg twice a day.

\[
\frac{35\text{mg}}{2} \times 24 = 420\text{mg}
\]
A suitable aminophylline dosing regimen could be Phyllocontin Continus® 225mg, 2 tablets (450mg) twice a day (5).

Converting IV aminophylline to oral theophylline:

1. The oral dose of aminophylline should be calculated as above, i.e. multiply the hourly dose by 24.
2. In order to calculate the equivalent theophylline dose, multiply this total aminophylline dose by 0.8, which is the salt correction factor (1). It is assumed that the oral product is completely absorbed.

For example:

If the IV aminophylline dose is 35mg/hr, then the total daily dose is 840mg. The oral theophylline dose is 840mg x 0.8 = 672mg daily.

A suitable theophylline dosing regimen could be Uniphyllin Continus®, 300mg in the morning and 400mg in the evening.

An alternative method has been suggested:

1. Multiply the mg/hour of intravenous aminophylline by 10, to obtain the theophylline dose to be given every 12 hours (6).

For example:

If the IV aminophylline dose is 35mg/hr, the dose to be administered every 12 hours is 350mg. A suitable theophylline dose regimen could be Nuelin SA 350mg bd (5).

Summary

♦ When converting from IV aminophylline to the oral dose, the bioavailability and salt factor must be considered. The salt factor for aminophylline is approximately 0.8 (salt factor = fraction of labelled dose which is theophylline).
♦ The total daily dose of IV aminophylline is the same for oral aminophylline (assuming bioavailability is 100% for the oral product).
♦ If IV aminophylline is changed to oral theophylline, then the total daily dose of IV aminophylline should be multiplied by 0.8.
♦ Alternatively, multiply the hourly aminophylline dose by 10, to obtain the theophylline dose to be given every 12 hours.
♦ When converting from IV to oral therapy, it may not be possible to exactly match the doses. The nearest practical dose should therefore be used and adjusted according to blood levels.

Limitations

Other factors that affect theophylline clearance such as drug interactions, whether the patient is a smoker or has congestive heart failure should also be considered when suggesting doses (1). These are not discussed within this Q+A. It is assumed that the patient has been stabilised on the IV aminophylline dose for at least 48 hours (reaching steady state levels) before starting oral therapy (7). It is also assumed that the patient is on the correct IV aminophylline dose before converting to oral therapy.

Calculating IV aminophylline to oral doses are only estimates. The rate of absorption can vary between brands (5).
References


Quality Assurance

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Search strategy

- Medline: *AMINOPHYLLINE/ and exp ADMINISTRATION, INTRAVENOUS/ and *THEOPHYLLINE/ and exp ADMINISTRATION, ORAL/
- Internet Search (www.google.co.uk); (converting IV aminophylline +oral; aminophylline to theophylline)
- Clinical expert (Catherine Rigby, Specialist Therapeutic Drug Monitoring Pharmacist, Northwick Park Hospital), November 2013.