The Renal effect of Prophylactic Aminophylline therapy after cardiac surgery in infants

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Acute kidney injury (AKI)

- Common complication among children requiring critical care
- Associated with substantial morbidity and mortality

Lafrance JP, Miller DR, J Am Soc Nephrol 2010  
Zappitelli M, et al., Kidney Int 2009  
Bellomo R, et al., Intensive Care Med 2004  
Dent CL, et al., Crit Care 2007  
Baskin E, et al., Ren Fail 2005  
AKI and CHD

- AKI is especially common in patients with congenital heart disease
- Prevalence of AKI following pediatric cardiac surgery ranges from 28% to 52%

Zappitelli M, et al., Kidney Int 2009
Bellomo R, et al., Intensive Care Med 2004
Dent CL, et al., Crit Care 2007
Li S., et al., Crit Care Med 2011
Increased risk for AKI

- Nephrotoxin exposure
- Uncorrected or residual heart defects
- Low cardiac output state
- Sepsis
- Open heart surgery requiring cardiopulmonary bypass (CPB)
  - which has been associated with a higher prevalence of AKI, likely due to renal ischemia-reperfusion injury
Aminophylline (AMP)

• **Pharmacologic effect**
  – **B**-agonistic effect
  – non-specific adenosine receptor antagonist
  – type IV phosphodiesterase inhibitor

• **Clinical effect**
  – well established bronchodilator
  – positive chronotropic and inotropic effect

• **Systemic capillary leak syndrome (SCLS)**
  – adjunct **diuretic** and **anti-inflammatory** effect
Aminophylline (AMP)

- Potential adjuvant AKI therapy
- Clinically, it has been used to increase urine output and augment diuresis in patients with
  - heart failure
  - perinatal asphyxia
  - neonatal apnea, respiratory distress
  - contrast-induced nephropathy
  - diuretic-refractory fluid overload
  - tacrolimus-induced AKI

Dragunow M, Pharmacol Biochem Behav 1990
We found limited literature about the renal effect of aminophylline after cardiac surgery.

We hypothesized that Aminophylline would be associated with an improvement in both creatinine clearance and urine output in children with AKI in postoperative status.
Objectives

✓ To assess the effect of aminophylline on renal function in infants with AKI in the setting of congenital heart disease.
Methods

• Retrospective review
• Infants under 3 months of age
• Who underwent open heart surgery
• Isolated VSD
• From Jan 2011 to Dec 2014
• Classification
  – AMP Group: Those who used AMP after surgery
  – Control Group: Those who did not use AMP
• **Preoperative Assessment**
  
  – age (day)
  – body weight (Kg)
  – Height (cm)
  – BSA (m$^2$)
  – S-Cr
  – creatinine clearance (CrCl)
• Intraoperative and postoperative data
  – CPB (cardiopulmonary bypass) time
  – ACC (aortic cross clamp) time
  – duration of mechanical ventilation (MV)
  – duration of ICU stay
  – duration of hospital stay
  – mortality

• Postoperative assessment of renal failure
  – Serial s-Cr, CrCl at 24, 48, 72, and 96 hrs
  – hourly urine output (UO. ml/kg/hr.)
Periop. management of AKI in CNUH

- in infant ( < 3 months)
  - Modified Ultrafiltration after CPB weaning
  - Furosemide iv (0.1~0.3 mg/kg/hr)
  - AMP iv (0.2-0.7 mg/kg/h)
    - ACC time > 60min, BW < 3.5kg, others
  - in Refractory AKI: CRRT
RESULTS
# Preoperative assessment

<table>
<thead>
<tr>
<th></th>
<th>AMP Group (n=41)</th>
<th>Control Group (n=23)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>45 (13 ~ 89)</td>
<td>56 (25 ~ 85)</td>
<td>0.07</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>5.5±7.0</td>
<td>4.8±0.8</td>
<td>0.62</td>
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<tr>
<td>Height (cm)</td>
<td>56.1±3.9</td>
<td>56.9±3.9</td>
<td>0.46</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>0.24±0.28</td>
<td>0.27±0.29</td>
<td>0.06</td>
</tr>
<tr>
<td>preop. S-Cr. (mg/dl)</td>
<td>0.26±0.11</td>
<td>0.24±0.07</td>
<td>0.315</td>
</tr>
<tr>
<td>preop. Cr Cl</td>
<td>120.4±66.4</td>
<td>124.5±57.5</td>
<td>0.808</td>
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### Intraoperative assessment

<table>
<thead>
<tr>
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<th>AMP Group (n=41)</th>
<th>Control Group (n=23)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>CPB time (hour)</td>
<td>89.6±65.7</td>
<td>68.7±31.5</td>
<td>&lt;0.001</td>
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<tr>
<td>ACC time (hour)</td>
<td>64.1±29.1</td>
<td>45.0±19.6</td>
<td>&lt;0.001</td>
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<tr>
<td>MV duration (days)</td>
<td>3.0±1.7</td>
<td>3.5±1.8</td>
<td>0.269</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>14.2±14.0</td>
<td>6.2±2.6</td>
<td>0.003</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>25.1±19.4</td>
<td>24.0±15.1</td>
<td>0.241</td>
</tr>
<tr>
<td>Mortality, n(%)</td>
<td>1 (2.4)</td>
<td>0 (0)</td>
<td></td>
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</tbody>
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s-Cr. Level in AMP Group over Time
Creatinine clearance over Time
Conclusions

• Level of serum creatinine was higher in patients with aminophylline at subsequent times

• Urine output tends to be higher after 60 hrs postoperatively.

• Aminophylline has positive diuretic effect after open heart surgery.

• Further prospective study of aminophylline in the setting of oliguric AKI in the pediatric patients is needed.
Thank you for your attention!