Combined treatment with ascorbic acid and N-acetylcysteine prevents contrast-induced nephropathy in high-risk patients with acute myocardial infarction undergoing percutaneous coronary intervention


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Disclosure Statement of Financial Interest

I, Marek Grygier DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
Background:

- Contrast-induced nephropathy (CIN) is a common cause of acute renal failure.

- Patients developing CIN have more complications, higher short- and long-term mortality, increased length of stay, and higher overall costs.

- CIN is typically defined as an increase in serum creatinine by either more than 0.5mg/dL or more than 25% from baseline within the first 2-3 days after contrast media administration.

- Pathophysiology of CIN is complicated and poorly understood.

- The incidence of CIN in general population is lower than 3%, but it can be as high as 50% or even more in patients with multiple risk factors.
Background:

- Patients with acute myocardial infarction undergoing percutaneous coronary intervention (PCI) are at high-risk of contrast-induced nephropathy.

- The most common and important prophylaxis for CIN is hydration.

- Oral and intravenous hydration should be encouraged.

- There are different protocols of fluids administration and it is necessary to reduce the rate and volume of infusion in patients with ventricular dysfunction.
Conflicting evidence suggests that administration of the antioxidant acetylcysteine (NAC) prevents the renal impairment, however NAC became a popular tool for CIN prevention.

NAC operates as a free-radical scavenger and a hemodynamic effect with improvement of renal blood flow and may be dose dependent.

CIN reduction can be achieved by a high-dose oral or mix (oral and IV) of NAC administration.

Some authors suggest NAC does not replace hydration prophylaxis, however in a recent meta-analysis Kelly et al. report that NAC is the most effective agent for preventing CIN in patients with renal failure, pointing out that this drug is more reno-protective than hydration alone.
Background:

- Ascorbic acid is an oxygen free-radical scavenger, but its role in CIN prevention is not clear.

- The REMEDIAL-Study did not show an advantage with IV ascorbic acid.

- On the contrary, a randomized placebo-controlled trial (Spargias et al.) of oral administration of ascorbic acid reported encouraging results and the same positive trend is confirmed by Kelly’s meta-analysis.

- There are no data on the usage of combination of NAC and ascorbic acid especially in patients with acute coronary syndrome.
Objectives:

The aim of our study was to examine the role of:

- combined treatment with NAC, ascorbic acid and fluids
- NAC with fluids
- and fluids alone

for the prevention of contrast induced nephropathy in high-risk patients undergoing primary angioplasty.
Material:

- A prospective, single-center, randomized trial in 152 consecutive patients with acute coronary syndrome and at least one risk factor of contrast nephropathy, undergoing emergency PCI was conducted.

- Contrast-mediated nephropathy was defined by an absolute increase of serum creatinine >=0.5mg/dl or relative increase of >=25% measured 2-5 days after the procedure.
Risk factors of contrast induced nephropathy (at least one should be present):

- documented history of chronic renal insufficiency (serum creatinine >1.2 mg/dl (106 μmol/l) and/or calculated creatinine clearance <60 ml/min)
- diabetes mellitus
- congestive heart failure NYHA III-IV
- hypotension or cardiogenic shock
- advanced age >75 years
- anemia (hematokryt < 39% ♂, <36% ♀)
- low ejection fraction in the past (EF<35%)
- chronic treatment with non-steroid anti-inflammatory drugs or steroids
Enrollment to the study
(assessment of the inclusion and exclusion criteria, written informed consent)

Randomization

**Grupa B (NAC):**
- NAC 1200mg i.v. in 250ml 0.9%NaCl
  (before PCI – within 5-10min.)
- NAC 1200mg p.o. 2 x daily - during 48h after PCI
- 50-125ml/h 0,9%NaCl i.v.
  from randomization till 12h after PCI

**Grupa C (NAC+ ascorbic acid):**
- NAC 1200mg i.v. in 250ml 0.9%NaCl
  + 3000 mg ascorbic acid i.v.
  (before PCI – within 5-10min.)
- NAC 1200mg p.o. + 2000mg ascorbic acid p.o. 2 x daily during 48h after PCI
- 50-125ml/h 0.9%NaCl i.v.
  from randomization till 12h after PCI

**Grupa A (placebo):**
- 50-125ml/h 0,9%NaCl i.v.
  from randomization till 12h after PCI
### Baseline patient demographics, clinical characteristics and procedural data.

<table>
<thead>
<tr>
<th></th>
<th>Group A (0.9%NaCl)</th>
<th>Group B (0.9%NaCl+NAC)</th>
<th>Group C (0.9%NaCl+NAC + Vit.C)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>67±9 (n=52)</td>
<td>66±6 (n=50)</td>
<td>65±8 (n=50)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Gender (male/female)</strong></td>
<td>34/18</td>
<td>30/20</td>
<td>31/19</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Diabetes mellitus</strong></td>
<td>32</td>
<td>28</td>
<td>29</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>40</td>
<td>38</td>
<td>41</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>42</td>
<td>38</td>
<td>36</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Peripheral vascular disease</strong></td>
<td>10</td>
<td>11</td>
<td>7</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Ejection fraction(%)</strong></td>
<td>45±10</td>
<td>43±8</td>
<td>42±11</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Serum creatinine (mg/dl)</strong></td>
<td>1.4±0.4</td>
<td>1.4±0.5</td>
<td>1.3±0.7</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Creatinine clearance (ml/min.)</strong></td>
<td>48±10</td>
<td>52±8</td>
<td>51±11</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Contrast volume (ml)</strong></td>
<td>180±21</td>
<td>165±16</td>
<td>170±18</td>
<td>NS</td>
</tr>
</tbody>
</table>
Incidence of contrast induced nephropathy:

- Group A (0.9% NaCl)
- Group B (0.9% NaCl + NAC)
- Group C (0.9% NaCl + NAC + Vit.C)

P = NS

P < 0.01

Contrast induced nephropathy (%)
Serum creatinine concentration (baseline and 3-5 days after PCI):

- Group A: P<0.01
- Group B: P=NS
- Group C: P=NS
Conclusions:

- Prophylactic administration of high-dose NAC and ascorbic acid offers better protection against contrast-mediated nephropathy in high-risk patients with acute coronary syndrome undergoing coronary intervention.
Thank you!