Evaluation of the Potential Adverse Effects Associated with Calcium Carbonate Precipitate During Continuous Venovenous Hemofiltration (CVVH)

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Abstract

Purpose: This study evaluated the potential adverse effects associated with exposure to calcium carbonate precipitate in Acusol 35 Solution (Acusol 35) during CVVH. Methods: 14 dogs were anesthetized, instrumented, and random was negative control articles (n=8) followed by CVVH for determination of pH, subvisible particle counts, and presence of visible particles. Cardiovascular Measurements: Arterial pressure, pulmonary arterial pressure, central venous pressure, heart rate, and cardiac output were monitored before and during CVVH. Stroke volume, systemic vascular resistance, and pulmonary vascular resistance were calculated.

Background

The clinical use of Acusol 35 Solution has been associated with occasional formation of visible, white, calcium carbonate precipitate in the tubing set during continuous renal replacement therapy (CRRT).

Methods

- Test article: Accusol 35 Solution (Baxter, lot 08J0870G) pH-adjusted and not previously subjected to a therapy simulation.
- Negative control article: Accusol 35 Solution (Baxter, lot 08J0870G) pH-adjusted but not previously subjected to a therapy simulation.
- Positive control article: Sephadex G-50(2) beads (Sigma-Aldrich, catalog #: G50300-50g. dry diameter 100 to 300 mm) suspended in 0.9% Sodium Chloride.

Table 1. Negative Control and Test Articles

<table>
<thead>
<tr>
<th>Beads</th>
<th>Acid</th>
<th>pH</th>
<th>Subvisible Particles (counts/ml)</th>
<th>Visible Particles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accusol 35</td>
<td>1.0</td>
<td>7.4±0.02</td>
<td>&lt;0.01</td>
<td>Absent</td>
</tr>
<tr>
<td>Test Article</td>
<td>0.5</td>
<td>7.4±0.02</td>
<td>&gt;0.5</td>
<td>Present</td>
</tr>
</tbody>
</table>

CV parameters remained stable throughout CVVH. No meaningful toxicological differences were observed between the test and negative control articles.

Clinical Pathology: No meaningful toxicological differences were observed between the test and negative control articles.

Histopathology: No adverse effects were observed on CV parameters, blood gases, and lung histology as compared with Acusol 35 containing no visible particles that were within EP specification.

Conclusions

Under the conditions of this study, continuous veno-venous hemofiltration performed on anesthetized dogs for six hours using Accusol 35 Solution containing visible and sub-visible particles (≤10 μm at approximately 36-times higher than the maximum concentration reported by the governing European Pharmacopoeia monograph titled “Solutions for Haemofiltration and for Haemodialfiltration”), no adverse effects were observed on CV parameters, blood gases and electrolytes, and lung histology as compared with Accusol 35 containing no visible particles and sub-visible particles that were within EP specification.

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