The effect of cryopoor plasma addition to adsorbed plasma to correct prothrombin time in dogs: an in vitro study

Hilvy Cheung, Karl Jandrey DVM, Julie Burges
Veterinary Medical Teaching Hospital, School of Veterinary Medicine, University of California, Davis

Introduction

- Anticoagulant rodenticide intoxication reduces activation of vitamin K dependent coagulation factors II, VII, IX, and X and is one of the most common toxicities in dogs that present to emergency veterinary clinics.
- The mechanism of toxicity is inhibition of vitamin K reductase and vitamin K epoxide reductase, which play an essential role in recycling of vitamin K. This leads to decreased carboxylation or activation of the specific coagulation factors[1,2].
- Due to the short biological half lives of factors II, VII, IX, and X, patients often present to emergency clinics 2.5 days after rodenticide ingestion with nonspecific clinical signs including lethargy, pale mucous membranes, and inappetence, as well as more severe signs of coagulopathies including hemoabdomen and hemothorax[3,4].
- Current treatments may include: vitamin K supplements, activated charcoal, hospitalized care, and transfusion of blood products[5,6].
- Cryopoor plasma, which is the byproduct of plasma processing of cryoprecipitate, has been shown to contain similar concentrations of the vitamin K-dependent coagulation factors when compared to fresh frozen plasma[7].
- Cryopoor plasma is less expensive than fresh frozen plasma and may offer clinicians another potential treatment option for rodenticide toxicity.

Objective

Determine if increasing amounts of cryopoor plasma added to barium adsorbed canine plasma is as effective as fresh frozen plasma to correct the prothrombin time and the concentrations of vitamin K dependent coagulation factors II, VII, IX, and X.

Methods and Materials

Phase 1: Determine protocol to adsorb canine plasma
- Canine fresh frozen plasma was acquired through the UC Davis Veterinary Blood Bank.
- Completed different trials with various forms and concentrations of barium to maximize the increase in PT and PTT.
- Oral barium sulfate suspension at a dose of 200mg BaSO₄ per mL of fresh frozen plasma adsorbed the plasma of vitamin K dependent coagulation factors.

Phase 2: Determine the optimal transfusion value
- Mix cryopoor plasma and fresh frozen plasma at various doses to mimic those below, including, and above that often used clinically (10mL-20mL of FFP/10 kg BW) for the treatment of rodenticide intoxication[8].
- Each sample will be analyzed at the UC Davis VMTH for PT, INR, FTT, and fibrinogen.
- Frozen samples will be sent to the Comparative Coagulation Lab at Cornell University Animal Health Diagnostic Center for complete analysis of the concentrations of coagulation factors II, VII, IX, and X.

Preliminary Data

Phase 1: Determine protocol to adsorb canine plasma

<table>
<thead>
<tr>
<th>Contents</th>
<th>PT</th>
<th>FTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original plasma</td>
<td>13.6</td>
<td>14.5</td>
</tr>
<tr>
<td>Adsorbed plasma</td>
<td>13.6</td>
<td>14.5</td>
</tr>
<tr>
<td>Fresh-frozen plasma</td>
<td>13.6</td>
<td>14.5</td>
</tr>
<tr>
<td>Cryopoor plasma</td>
<td>13.6</td>
<td>14.5</td>
</tr>
</tbody>
</table>

Table 1: Anticoagulant rodenticides commonly ingested by dogs

Adapted from Murphy, N.E. 2002

Discussion

- An adsorption protocol using oral barium sulfate suspension has been confirmed to adsorb plasma of vitamin K dependent coagulation factors.
- Based on preliminary data, the addition of fresh frozen plasma and cryopoor plasma to adsorbed plasma does improve PT and PTT.
- Increasing amounts of volume added of fresh frozen plasma and cryopoor plasma correlates with a greater correction in coagulation times.

Limitations

- In vitro study may not correlate to a clinical application due to the complicated physiology of coagulation and rodenticide intoxication.
- In our preliminary data, Factor X appears to continually be adsorbed following removal of plasma.

Future Directions

- Six additional mixing trials using different fresh frozen plasma and cryopoor plasma will be added to adsorbed plasma to complete phase 2 to determine the optimal transfusion value of cryopoor plasma in comparison to fresh frozen plasma.
- Then, statistical analysis will be completed to determine the optimal transfusion value and correlate it with clinically relevant transfusion doses for cryopoor plasma.
- In the future, we hope to use this data to design a clinical trial for the use of cryopoor plasma to treat canine anticoagulant rodenticide intoxication.

Acknowledgements

Thank you to Marjory Brooks, Sean Owens, UC Davis Veterinary Blood Bank, and Cornell University Animal Health Diagnostic Center for making this project possible. Funding provided by the Emergency and Critical Care Research Endowment and Boehringer-Ingelheim Animal Health.

References


Hilvy Cheung • hchyung@ucdavis.edu • 510.396.4002 • www.linkedin.com/in/hilvycheung
UC Davis School of Veterinary Medicine / c/o 2021