Efficacy of Microporous Polysaccharide Hemospheres on Liver Punch Biopsies in Porcine Model

Ereth, MH; Schrader, LM; Dong, Y; Henderson, JL; Nuttal, GA; Oliver, WC
Transfusion, Coagulation and Cardiopulmonary Bypass Research Group
Department of Anesthesiology, Mayo Clinic Rochester, MN

Abstract

**Purpose:** Microporous Polysaccharide Hemospheres (MPH) are a novel topical hemostat made entirely from purified potato starch. MPH activates the clotting cascade and hyperconcentrates platelets and coagulation proteins while enhancing a hemostatic plug that is not easily displaced. This study evaluated the efficacy of MPH in facilitating hemostasis in animals undergoing liver punch biopsies.

**Methods:** Mayo’s Institutional Animal Care and Use Committee approved all procedures. Livers were exposed in six animals and a 6-mm diameter by 5-mm deep biopsy punch was used to create 6 bleeding wounds (2 in each of three lobes). Either Gelfoam or MPH was applied to the wound with digital pressure for one minute. In the MPH group, a piece of Parafilm was used to cover the powder and hold pressure. The wounds were evaluated at one minute for adequate hemostasis, slight bleeding (oozing), or active bleeding. If active bleeding was observed, a second application was administered. Each site was observed for up to 10 minutes. The time to hemostasis was recorded with hemostasis within 5 minutes considered efficacious and the number of applications within 10 minutes recorded.

**Results:** A total of 36 biopsy punches were made with 19 each of MPH and Gelfoam. Within five minutes, 16 out of 18 (89%) punch sites in the MPH group and 9 out of 18 (50%) punch sites in the Gelfoam group achieved adequate hemostasis.

**Conclusion:** MPH provided more consistent hemostasis of active bleeding sites with a smaller number of applications on pig liver biopsies than did Gelfoam. Due to the promising results of this study, further investigation into the capabilities of MPH is warranted.

**Introduction**

Successful hemostasis is critical in minimizing perioperative morbidity and mortality associated with general surgical procedures. During surgical procedures when control of bleeding by conventional methods is not possible, the use of surgical hemostats as an adjunctive is common. Although there are several products available, surgeons remain in need of a method that can attain the goal of superior hemostatic safety and efficacy, ready and easy to use, formation of durable hemostasis in a large wound, and pose no risk to blood-borne disease. Microporous Polysaccharide Hemospheres (MPH) are a powder-like device recently cleared for market by the US Food and Drug Administration as a topical hemostatic agent. This novel polysaccharide material is formed into tightly engineered particles with closely controlled porosity and spherical diameters. When applied to actively bleeding area, these particles act as molecular sieves that rapidly absorb the fluid component of blood thereby concentrating platelets, fibrinogen and other proteins on their outer surfaces. This activity produces a gelled clot formation followed by the development of an endogenous fibrin mesh. This study was conducted to evaluate the efficacy of MPH beads compared to Gelfoam in aiding hemostasis of actively bleeding 6-mm biopsy punch wounds on pig livers.
Methods and Materials

Animals

All animal procedures were reviewed by Mayo’s Institutional Animal Care and Use Committee before implementation, to ensure compliance with NIH, USDA, and AAALAC guidelines. The pig model was selected as the experimental species because of its similarity to humans when monitoring and measuring physiological responses during the procedure. Six female Yorkshire white pigs weighing 32-38 kg were studied.

Procedure

After induction, pigs were placed in the supine position. Animals were maintained in a surgical plane of anesthesia throughout the procedure. Following a laparotomy and exposure of the liver, a 6-mm diameter biopsy punch was used to create two 5-mm deep punches in each of three liver lobes for a total of 6 punches per animal. Due to a uni-lobed anatomical anomaly, one animal had all six biopsy punches made in one lobe. All sites were created, treated and evaluated individually. One defect in each lobe was treated with each hemostat, resulting in 3 Gelfoam- and 3 MPH-treated sites per animal. Sites were then covered with MPH or Gelfoam and one minute of manual pressure. Parafilm was used to cover the powder and apply pressure in the MPH group. The wound was observed after pressure release for adequate hemostasis. If active bleeding or continued oozing was observed during the one-minute observation time, a second application of assigned treatment was administrated in the same manner as the first application until complete hemostasis was reached. Complete hemostasis was defined as no active bleeding. This process continued until hemostasis was achieved, or 10 minutes had elapsed. If 10 minutes elapsed without achieving hemostasis, the treatment was considered a failure and the investigator used any other method to stop bleeding.

A total of 36 biopsy punches were made with 18 applications each of MPH and Gelfoam. The successful hemostasis rate in 5 min and 10 min was recorded for analysis. Any sites that did not show bleeding or oozing at the time of initial pressure release were considered to achieve hemostasis within 1 minute. The total number of applications needed to reach hemostasis within 10 minutes was also recorded.

MPH after achieving hemostasis
(excess material removed)
Discussion

In this study, 89% of MPH-treated wounds reached successful hemostasis within 5 minutes. We chose to not use the time to hemostasis as a primary endpoint because it is often difficult to determine the exact time of complete hemostasis. We felt there would be more validity in results associated with the ability to achieve hemostasis within a certain time frame. By focusing on the ability to achieve hemostasis within 5 or 10 minutes, we reduce the potential of biasing our findings. The concern of the medical community is not necessarily the exact time in which hemostasis can be achieved, but rather whether or not it can be achieved within a reasonable amount of time, comparable to other products.

The way in which the product was applied during the study was similar to how we felt it would be done in a human surgical setting. For the MPH-treated group, residual product from failed applications was wiped away with gauze before reapplication. For Gelfoam-treated sites in which the oozing or bleeding emerged along the edges of the hemostat, the original application was removed and another one applied. This was done because once bleeding occurs around the Gelfoam, it was difficult to reestablish the clean interface between product and tissue. For those in which the oozing or bleeding lifted up only through the center of the hemostat, an additional Gelfoam pad was placed on top of the previous application.

MPH hemostatic beads may be an excellent solution for topical bleeding (internal and external) in the operating room, emergency room and intensive care unit. Determining the safety and efficacy of MPH hemostatic beads in achieving hemostasis in a controlled environment will allow for use in variable bleeding situations such as traumatic lacerations, epistaxis, and other internal operative uses. In the future, cardiac, vascular, and orthopedic surgery subjects may also be able to benefit from this simple hemostatic application which may limit transfusion requirements.

Results

<table>
<thead>
<tr>
<th></th>
<th>MPH (n=18)</th>
<th>Gelfoam (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful Hemostasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 min</td>
<td>16 (89%) *</td>
<td>9 (50%)</td>
</tr>
<tr>
<td>&lt;10 min</td>
<td>18 (100%)</td>
<td>17 (94%)</td>
</tr>
<tr>
<td>Failed</td>
<td>0 (0%)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Total Applications</td>
<td>12 (67%)</td>
<td>4 (22%)</td>
</tr>
<tr>
<td>2</td>
<td>5 (28%)</td>
<td>7 (39%)</td>
</tr>
<tr>
<td>3</td>
<td>1 (5%)</td>
<td>4 (22%)</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Failure</td>
<td>-</td>
<td>1 (6%)</td>
</tr>
</tbody>
</table>

*p<0.05 (Fisher’s Exact Test)

Within 5 minutes, 89% of MPH-treated sites and 50% of Gelfoam-treated sites achieved complete hemostasis. Within 10 minutes, 100% of MPH-treated sites and 96% of Gelfoam-treated sites achieved complete hemostasis. One Gelfoam site failed to achieve complete hemostasis within the 10 minutes.

With only one application, 67% of the MPH-treated wounds and 22% of the Gelfoam-treated wounds achieved complete hemostasis. It took two applications to achieve complete hemostasis in 28% of MPH- and 39% of Gelfoam-treated wounds. It took three applications to achieve complete hemostasis in 5% of MPH- and 22% of Gelfoam-treated wounds. Eleven percent of Gelfoam-treated wounds required 4 to achieve hemostasis. Overall, 95% of MPH-treated wounds were able to reach hemostasis with two applications compared to 61% of Gelfoam-treated wounds. (p<0.05)
Summary
Microporous Polysaccharide Hemospheres (MPH) provided more consistent hemostasis of active bleeding sites with a smaller number of applications on pig liver biopsies. The use of MPH may represent an advancement in the management of surgical bleeding.