Published Abstracts regarding Safety and Efficacy studies for Microporous Polysaccharide Hemospheres (MPH) absorbable Hemostatic Agent

Note: MPH is the primary hemostatic agent used in Bleed-X Vet Clotting Powder

Abstract One

Control/Tracking Number: 04-A-299-ISMICS
12/21/2003 A4-103

Microporous Polysaccharide Hemospheres, A Plant Based Topical Hemostatic Agent, For Bleeding Control Of The Sternum

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Introduction: Profuse bleeding after sternotomy is routinely controlled with bone-wax (BW). Unfortunately, bone-wax may cause non-union of the sternum and infections. Microporous Polysaccharide Hemospheres (MPH), a resorbable plant based hemostatic agent, offers a novel technique to control sternal bleeding during cardiac operations. This study evaluates the efficacy and safety of MPH as a topical hemostptic first time in human use.

Methods: Eighty patients with beating heart revascularisation were included in this prospective randomized trial. In 40 patients (pts; group-MPH) the MPH (Medafor Inc., Minneapolis, MN) was applied directly after sternotomy. The other 40 pts (group-BW) were treated with standard use of BW. The two groups did not differ in demographic and intraoperative data (age: 68.5±6.4 vs. 67.6±7.6years; grafts: 2.9+/-.0.6 vs. 3.2±0.8). All patients were operated with an activated-clotting-time of >350 sec and Protamine was given after revascularisation was completed.

Results: Satisfactory bleeding control of the sternum was achieved in 37 pts (93%) with MPH and in 39 pts (98%) with BW. Application of BW was rated easier, but destruction of sternal spongiosa in osteoporotic bone was more common using BW (p<0.05). The intraoperative decrease of Hemoglobin (Hb) was not significant (n.s.) between the groups (MPH: Hb preop 13.0±1.3mg/dl to Hb postop 10.5±1.5mg/dl vs. BW: Hb preop 12.9±1.6mg/dl to Hb postop 9.9±1.6mg/dl). Autologous transfusion (cell-saver) (MPH: 194±150ml vs. BW: 268±245ml), allogenic blood-units (MPH: 2 pts vs. BW: 3 pts) and postoperative blood loss (MPH: 880±460ml vs. BW: 830±520ml) did not differ significantly. We observed no allergic reaction, no reoperation due to graft failure and no death in either group. There was one resternotomy due to sternal instability in each group. Only in group-BW two wound-healing problems occurred (n.s.).

Conclusion: MPH can be applied safely and effectively and can replace bone wax.
Abstract Two

Use of Microporous Polysaccharide Particles in Prolonged Vascular Access Bleeding After Hemodialysis

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Introduction: Post dialysis prolonged bleeding from needle puncture of dialysis access can be a major problem in certain patients. Prolonged access bleeding can be due to excessive anticoagulation, uremic coagulopathy, high venous resistance in the access, inadequate hemostasis due to frail skin and tissue overlying the graft, etc. Common measures to stop bleeding are to manually hold the graft site or to use a specially designed clamp. All of these measures, due to prolonged application of pressure, can run the risk of graft clotting. Prolonged access bleeding also results in worsening anemia, increased requirement of iron preparation and epogen and a significant loss of time in the dialysis unit; all of which in turn increase the risk and cost of the dialysis treatment.

Methods: We have used sterile Microporous Polysaccharide Particles manufactured by Medafor, Inc. Minneapolis, MN, 55421) in 20 dialysis patients (one time each) who are considered by dialysis nurses to have prolonged access bleeding. The Microporous Polysaccharide is a bio-inert polymer material consisting of flowable microporous particles synthesized to a controlled porosity and spherical diameter, from raw materials derived from plants.

When applied to actively bleeding areas, the particles act as molecular sieves that rapidly absorb the fluid component of blood. The controlled porosity of the particles excludes platelets, red blood cells, and serum proteins, which are then concentrated on the surface of the particles. This activity produces an “instant gelling” followed by the formation of a fibrin mesh.

Application: At the end of the dialysis the needle is withdrawn half way. The particles are then poured on the puncture site and a band-aid is applied on the puncture site. The needle is then withdrawn fully and folded gauze is applied on the top of the band-aid to maintain the manual pressure until the bleeding has stopped.

Results: Retrospectively the data was reviewed in 20 patients who had received microporous particle for prolonged bleeding. Application of Microporous Polysaccharide Particles along with manual pressure reduced the bleeding time from average 35 minutes to 5 minutes (p=0.0001) in this group. No breakthrough bleeding or infection was noted during seven days of post procedural follow up. Among the 20 patients, the average age was 65, 45% were diabetic, 65% were female, 40% had a primary fistula, and 60% had a graft.

The average baseline post dialysis access bleeding time in this group at baseline was 35 minutes (range 20 minutes to 90 minutes).

Conclusion: Use of Microporous Polysaccharide Particles along with manual pressure significantly reduced the post dialysis bleeding in high-risk patients. No side effects were noted in this short-term study.
Abstract Three

Dermatologic Surgery
Volume 30 Page 908 - June 2004
Volume 30 Issue 6 A4-108

Hemostasis in Mohs Micrographic Surgery
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Background. Microporous polysaccharide hemospheres consist of controlled-porosity spherical particles manufactured from bioinert plant polysaccharide. Microporous polysaccharide hemospheres facilitate hemostasis by rapidly absorbing the fluid component of blood, concentrating platelets and clotting factors to accelerate blood clotting.

Objective. The objective was to compare a microporous polysaccharide hemisphere bandage and electrocautery in achieving hemostasis.

Methods. Twenty-four patients with a total of 48 stages of Mohs micrographic surgery were included. Patients were stratified by whether or not they were taking anticoagulant medications. Within each group, patients were randomized to receive either the microporous polysaccharide hemisphere bandage or electrocautery. Outcomes included bleeding through the dressing (early time point) and active bleeding upon dressing removal (late time point).

Results. Nineteen patients not taking anticoagulants had 40 stages, of which 18 received the study bandage and 22 received electrocautery. The remaining 5 patients on anticoagulants had 8 stages, of which 4 received the study bandage and 4 received electrocautery. In both total and subgroup analysis, there was no increase in the incidence of active bleeding upon dressing removal (p>0.05).

Conclusion. The microporous polysaccharide hemisphere study bandage showed no increased incidence of active bleeding upon dressing removal compared to electrocautery.
Do Microporous Polysaccharide Hemospheres (MPH) Enhance Surgical Site Infection In A Rat Model?
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Introduction: Hemostatic agents are commonly used to stop bleeding in a variety of surgical procedures. Depending on the type of agent used, residual material may remain at the surgical site for several days or even months, promoting foreign body reactions (1). A new hemostatic powder device, Microporous Polysaccharide Hemospheres (MPH; Medafor, Inc., Minneapolis, MN 55430, USA), may alleviate foreign body reaction due to its degradation properties. Derived entirely from plant starch, MPH has the potential to be broken down by amylase within hours of application. This study was designed to determine if MPH would enhance infection in a surgical wound, and to compare the infection rate of MPH to Gelfoam and Control.

Methods: An intrabdominal incision was placed in 120 Wister Outbred Rats and the study wounds were contaminated with Escherichia coli (2). The study wounds were randomly treated with Control (n=40), MPH (n=40) or Gelfoam (n=40) and closed with one 4-0 VICRYL suture. Following a 72-hour survival, the animals were sacrificed and a tissue sample of the study wound was dissected and cultured for E. coli growth. Colony forming units per gram of tissue (cfu/g) were calculated for each animal and compared between groups.

Results: A homogenate culture of the tissue revealed no difference between the Control and MPH groups, but a significant difference between the Gelfoam group and the Control and/or MPH groups. Clinical infection was defined as having greater than 1.0x10^5 cfu/g. When comparing groups, Gelfoam had 87% clinical infection, whereas Control and MPH had 14% and 24%, respectively.

Conclusion: In this rat infection model, using E. coli as an inoculum, MPH does not increase infection when used as a hemostat for surgical wounds compared to Control. Gelfoam, a frequently used hemostatic agent, significantly enhances infection when compared to MPH and/or Control. Because hemostatic agents can be potentiators of infections, this study suggests that MPH would be beneficial during surgical procedures where risk of bacterial infection exists.

References:
2. Kaiser AB, Kernodle DS: Low-inoculum model of surgical wound infection. JID. 1992;166:393-96
Evaluation Of Microporous Polysaccharide Hemospheres As A Novel Hemostatic Agent In Open Partial Nephrectomy: Favorable Experimental Results In The Porcine Model

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PURPOSE: Microporous polysaccharide hemospheres (MPH, Medafor, Minneapolis, Minneapolis) are a novel hemostatic agent made from purified plant starch. MPH activates the clotting cascade and hyperconcentrates platelets and coagulation proteins, while enhancing a hemostatic plug. We evaluated the hemostatic efficacy of MPH compared with standard surgical technique in a porcine open partial nephrectomy model.

MATERIALS AND METHODS: Standardized lower pole partial nephrectomy was consecutively performed in each kidney of 12 female pigs. Each pig was randomized to two groups, namely treatment with MPH application or control with the conventional surgical technique (oxidized cellulose with bolster sutures). The right kidney was harvested one half-hour after hemostasis was achieved and the left kidney was harvested after seven days.

RESULTS: Mean animal and resected renal tissue weight were comparable. Ischemic and hemostasis times were significantly decreased in the MPH treated group (2.67 and 4.67 minutes, respectively) vs. the control group (8.33 and 7.75 minutes, respectively) (each p = 0.004). Blood loss was equivocal (0.88 gm in the treatment group vs. 2.09 gm in the control group, p = 0.07). No hemostatic complications were noted in either group. No evidence of residual foreign material was found in the MPH group at one week.

CONCLUSIONS: MPH provided rapid, effective and durable hemostasis in the porcine open partial nephrectomy model. Additional experimental and clinical evaluation is warranted to define the role of MPH assisted partial nephrectomy in humans.
Abstract Six

Comparative Safety and Efficacy of Topical Hemostatic Agents in A Rat Neurosurgical Model

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Neurosurgery: October 2008 - Volume 63 - Issue 4 - p 369-372

Abstract

OBJECTIVE: Adequate hemostasis is extremely important in neurosurgery, commonly requiring the use of topical hemostatic agents. Apart from variable efficacy, the residual presence of these agents may cause foreign body reaction, infection, and delayed bone growth. This study compares the safety and efficacy of commonly used agents with a newly approved agent, MPH-Arista (microporous polysaccharide hemospheres; Medafor, Inc., Minneapolis, MN).

METHODS: A brain tissue defect was created in 228 Wistar outbred rats, and either no agent (negative control), MPH-Arista, Surgicel (oxidized cellulose; Ethicon, Inc., Somerville, NJ), Avitene (microfibrillar collagen; Alcon, Inc., Humacao, PR), FloSeal (gelatin matrix thrombin sealant; Baxter Healthcare Corp., Deerfield, IL), or kaolin (positive control) was implanted. Time to hemostasis was documented. The animals were sacrificed at different intervals up to 28 days, and presence of residual material and foreign body reaction was determined.

RESULTS: MPH-Arista, Avitene, FloSeal, and Surgicel performed better (defined as complete hemostasis within 1 minute) than control (no treatment). Residual material was not present at any time with Arista, markedly contrasting with the presence of residual material in 100% of lesions in the Avitene, FloSeal, and Surgicel groups on Day 14. Avitene and FloSeal also demonstrated a propensity for causing granuloma formation, whereas Arista and Surgicel showed no such evidence.

CONCLUSION: Each of these hemostatic agents was effective in controlling bleeding in the majority of standardized neurosurgical lesions. MPH (Arista) degrades more rapidly than Surgicel, Avitene, and FloSeal and does not result in any foreign body reaction.
Abstract Seven

Microporous Polysaccharide Hemospheres Provide Effective Topical Hemostasis in a Human Modified Bleeding Time Incision Model

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Summary
Topical bleeding from surgical and traumatic wounds contributes to substantial blood loss and patient morbidity. Several topical hemostatic agents are available which either provide clotting components (e.g., fibrin glues) or provide a surface for clotting to be stimulated (e.g., collagen, gelatin sponge, oxidized cellulose). A new microporous polysaccharide hemosphere (MPH) product (Medafor Inc, Minneapolis, MN) works by a unique mechanism. The polysaccharide microspheres have a porous surface that effectively absorbs water and low molecular weight compounds from blood, concentrating platelets and clotting proteins at the bead surface, thereby enhancing endogenous clotting mechanisms.

We investigated the efficacy of this topical hemostat in a modified bleeding time study in human subjects. Twenty-nine healthy human volunteers had two small surgical incisions placed on their non-dominant forearm. One site was treated with the MPH and the other site acted as control. Time to hemostasis and quality of wound healing was evaluated.

The MPH treated wounds stopped bleeding five minutes faster (84 seconds on average, compared to 381 seconds) than the control site (p<0.001). Immediate hemostasis was achieved in 23 out of 29 (79%) of the subjects treated with MPH. Wound healing, as measured by length of scar and width of induration at seven days showed no significant difference between the MPH-treated group and the control.

In conclusion, this novel topical hemostatic agent (MPH) significantly speeds thrombosis of skin lacerations with no visibly apparent inhibition of wound healing. Investigations of the application of MPH technology for topical hemostasis in surgical wounds and traumatic bleeding continue.

Introduction
Topical bleeding represents a major cause of blood loss in surgical and non-surgical trauma patients. This can lead to blood transfusions with their inherent risk of complications (transfusion reactions and transfusion transmitted disease) as well as significant expense. To circumvent the need for transfusion, several hemostatic agents have been developed and fall into two categories: those that add clotting elements to generate clots (fibrin sealants and thrombin glues), and those that act as a surface on which endogenous coagulation factors react to generate clots (e.g., gelatin foam, microfibrillar collagen, oxidized regenerated cellulose). These agents have varying degrees of efficacy, some carrying a potential risk of infection or allergic reaction, adhesion formation, prolonged preparation time, and considerable expense.

MPH (Medafor Inc, Minneapolis, MN) is a novel microporous polysaccharide hemosphere product that promotes blood clotting by a unique mechanism. It is made from purified potato starch and formed into 30-100 micron spheres with a microporous surface. These pores, applied
directly onto an actively bleeding wound, act to rapidly dehydrate blood and concentrate clotting proteins, red blood cells, and platelets to promote instantaneous clot formation. At the same time the microsphere surface also promotes clotting. The polysaccharide microspheres are quickly degraded by endogenous amylase and pyrase, leaving no substance to act as a nidus for infection or adhesion formation. The raw material and production costs make MPH considerably less expensive than other hemostatic agents. In addition, thrombo-elastograph (TEG) analysis demonstrates that when MPH was added to citrated blood, clot formation was faster.

Materials and Methods
The study design and protocol were reviewed and approved by the institutional research board. Twenty-nine healthy volunteers gave written informed consent. Exclusion criteria included: age less than 18 years, pregnancy, ongoing infection, history of bleeding/clotting diathesis, use of anticoagulant medications, any bruises, scars or recent cuts on the area of forearm to be studied. The average age of volunteers was 36 years and 77% were male.

Modified Bleeding Time
The primary outcome of this study was time to hemostasis as measured by a modified bleeding time analysis. With patients in the sitting position the volar surface of the non-dominant forearm was swabbed with alcohol and the skin was allowed to dry. Two Surgicutt (International Technidyne Corporation, Edison, NJ) devices were used simultaneously to produce two incisions (5 mm x 1 mm deep) in the skin 5 cm below and parallel to the antecubital fossa. MPH was applied to either medial or lateral incision sites with different subjects to avoid site-specific differences in bleeding time. After blotting off excess blood from both sites with gauze, a single dose of approximately 25 mg dry MPH beads was directed into the study incision (no sham substance was placed in the control site). Immediately following application of MPH, gentle pressure was applied over both sites for 30 seconds. A second investigator with a stopwatch recorded the time to hemostasis at both sites. At 15 second intervals the quality of bleeding from each site was visually evaluated and scored based on degree of bleeding until hemostasis was reached. Bleeding time was evaluated for up to 10 minutes, and in case of failure (defined as the wound not achieving hemostasis after 10 minutes) the investigator used other methods to stop bleeding (typically additional pressure over the wound).

The study subjects remained in the procedure area for 15 minutes after bleeding stopped to observe for any re-bleeding or reactions to the MPH beads. No complications occurred in our study subjects. The secondary outcome was determination of any differences in wound healing between the control and treatment group.

At seven days following application, subjects returned for visual inspection of the two scars. Measurements of scar length, width of skin induration, and whether the scar was raised or not was noted. Two subjects did not return for follow-up.

Results
Application of MPH beads to a bleeding time incision demonstrated a dramatic reduction in bleeding time in humans. In all but two of the subjects, MPH application caused immediate hemostasis. This degree of hemostasis was never observed at the control site, where the fastest time to hemostasis was 180 seconds. In 4 out of 29 subjects, MPH-treated wounds attained immediate hemostasis, but had slow oozing thereafter. In none of the subjects were any side effects from MPH treatment observed.
Time to hemostasis was significantly lower at the MPH treated site with an average time to hemostasis of 84 seconds (95% CI: 32-136), compared with 381 seconds (95% CI: 334-428) for the control site (paired t-test, P<0.0001). In addition, the 95% confidence interval for differences between the two groups was between 216-378 seconds. Thus, treatment with MPH decreased bleeding time by five minutes (297 ± 81 seconds) compared to the control site. Analysis of wound healing at seven days revealed no statistical difference in size of scar or skin induration. Scar size was 3.8 mm (95% CI: 3.5-4.1) at the control site and 3.8 mm (95% CI: 3.6-4.1) at the MPH site. Similarly, the width of induration of the skin was 1.5 mm (95% CI: 1.4-1.7) and 1.8 mm (95% CI: 1.2-2.4) for control and experimental sites, respectively (p=NS).

Discussion
Microporous polysaccharide hemospheres dramatically reduced time to hemostasis in a human bleeding time model. The addition of MPH to the wound resulted in an immediate cessation of bleeding. Gentle pressure alone had no similar effect on control sites. There was no visible difference in wound healing or scar formation between the control and study sites. Delayed slight oozing did occur in four of the MPH sites. This may be due to ineffective application. In one subject the MPH treated site oozed for greater than 10 minutes whereas the control site clotted in 3 minutes.

It is unclear whether this represents an effect of the MPH or possible anatomic difference between the two sites on this subject’s forearm, such that a larger venule may have been lacerated by the incision. Bleeding from traumatic and surgical wounds represents an important cause of patient morbidity. Significant blood loss may require blood transfusion with the inherent risk of transfusion-transmitted disease, and added expense. Several other topical hemostatic agents, including fibrin glues and thrombin, have limited efficacy, may be difficult to use, have allergic or infectious potential, and are expensive. Other products, which serve as a substrate to activate thrombosis and hemostasis, demonstrate variable efficacy, difficulty with application and decreased efficacy in heparinized patients. The MPH technology (MPHTM, Bleed-XTM, ) represents a series of hemostatic agents with a novel mechanism of action. In addition to providing physical support for clot formation, the MPH absorbs water from the local environment and hyper-concentrates platelets and coagulation factors. This instantly places platelets and clotting proteins in direct contact, promoting thrombus formation. The MPH beads swell as they dehydrate the blood, further acting as a hemostatic plug. The product is made from purified plant starch and has virtually no infective or sensitization risk and is relatively inexpensive.

Conclusion
Microporous polysaccharide hemospheres (MPH) effectively accelerated time to hemostasis in this model of bleeding in healthy adults. In addition, this agent appears to have no negative impact on visible wound healing at seven days. The use of MPH may represent an important advancement in the management of topical bleeding with significant advantages over other hemostatic agents.
Abstract Eight

Hemostatic Powder Use For Thyroid Surgery

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Purpose:
In thyroid surgery leaving a drain lodge is a routine technique. There was no alternative technique for using drainage until today. In this study without usage drain, hemostatic powder is used and observed prospectively.
Method:In this study we investigated 10 patient who had a surgical operation due to thyroid pathology finding in 2005 August – October. One patient was male the others nine were female. Average age was 46 (22-46). Two of them had Base Dow Graves, Two of them papillary CA, one of them solitary thyroid nodule. Five of them had multinodular goiter (MNG). Total thyroidectomy was applied to the patient with Solitary nodule and MNG .1 gm Microporous Polysaccharide Powder applied to all the patient’s thyroid lodge for hemostasis (Pictures 1, 2). Without applying drainage tubes skin and lower skin was closed (Picture 3). Cases were investigated while patients were hospitalized for seroma and wound infection.

Findings:
Hospitalization period was an average of 1.1(1-3) days. After the surgery period one patient developed a hematoma but the other eight patients did not have any complications. All the patients were examined by neck ultrasound scanning in the postoperative period and the thyroid lodge was investigated. It was seen that two patients had 3cc, four patients had 1cc, one patient had 20cc liquid and two patients had no liquid. One patient developed a neck hematoma and during ultrasonography scan a 40cc hematoma developed but with conservative treatment the patient was sent home in 3 days. None of the patients developed wound infection.

Results:Hemostatic powders have been used largely in abdominal parts of the body. But no study had been done regarding thyroid surgery and use of hemostatic agents. This prospective small study showed that hemostatic powders can be an alternative for drainage tube use. There should be more controlled randomize studies done in order to understand of comparison between drainage use or hemostatic powder use.
Abstract Nine

Use of MPH in ENT Surgery

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Introduction: MPH is a microporous hemostat that acts as a molecular sieve, when applied to the bleeding area. It rapidly absorbs the fluid components of blood, producing a coagulation of the cellular blood components. We used MPH in the prevention of bleeding after soft tissue surgery in the fields of ENT (parotidectomy, neck dissection, and tonsillectomy). In a small pilot study we compared the rate of post-haemorrhage in patients, who underwent tonsillectomy or parotidectomy.

Material/Methods: We compared two groups of patients in every kind of surgical procedure. In one group (20 patients) no hemostat was used, in the other group (20 patients) MPH was applied to the surgical wound. The rate of post-haemorrhage events was documented and in the parotidectomy groups the amount of blood and wound secretion was compared.

Results: Tonsillectomy: There was no after-bleeding in the MPH group, while two cases of post-haemorrhage were seen in the group without use of MPH. Parotidectomy: There was no post-haemorrhage in the MPH-group, but two cases of after bleeding in the non-MPH group with needed surgical intervention. The average amount of blood and wound secretion in the MPH group was significantly lower (38 ml over two days) compared to the non-MPH group (118 ml over two days).

Conclusion: The use of MPH as a wound cover after soft tissue surgery in ENT seems to be an excellent method to prevent post-haemorrhage events and to reduce postoperative wound secretion. These results will be proven in a larger collective study of patients (50 in every group).