Safety of intraperitoneal fucoidan solution in healthy adult horses undergoing exploratory celiotomy and jejunojejunostomy: Clinical findings.

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Introduction and Hypotheses

Postoperative (PO) intraabdominal adhesions are a common and frustrating complication following abdominal surgery for horses and often result in euthanasia of the patient. Efficacy studies in several different animal models of PO adhesions have shown that intraperitoneal (IP) fucoidan solution prevents adhesion formation[1]. The customized fucoidan used in the current study is a high molecular weight polymer that readily dissolves in physiologically normal solution producing a solution with a lower viscosity than water. It is thought that fucoidan prevents adhesion formation by providing a temporary physical lubricant and barrier during the early stages of peritoneal repair. Advantages of fucoidan solution over viscous sodium carboxymethylcellulose gel (CMC) include easier preparation and handling compared with CMC prepared in the practice. CMC is available from compounding pharmacies; however, IP use of such a preparation of CMC was shown to increase adhesions compared with untreated horses[2]. Advantages of fucoidan over heparin are that it only has 1/10th the anti-coagulant effect of heparin on a weight to weight basis and has not been shown to have any anti-coagulant effect at clinical doses. The effects of IP fucoidan on PO clinical findings in a clean-contaminated model have not been evaluated. The purpose of the current study was to evaluate the clinical-related safety of fucoidan solution in horses. (Pathology-related safety of fucoidan solution was also investigated during this study and these data are presented in a separate abstract at these proceedings.) Our hypotheses were that following celiotomy and anastomosis in horses: (1) IP fucoidan solution would not influence heart rate, rectal temperature, colic, PO reflux, incisional infection or septic peritonitis compared with Lactated Ringer's Injection USP (control LRS); and (2) IP fucoidan solution would not influence hematology, chemistry or coagulation profiles compared with control LRS.

Materials and Methods

Twelve horses donated to the veterinary teaching hospital for reasons unrelated to the gastrointestinal tract or abdomen were used. Horses were block randomized and assigned to 1 of 2 experimental groups: (1) fucoidan solution and (2) control LRS (n=6 per group). Fucoidan solution and control LRS were prepared by mixing 50 mL of Fucoidan Concentrate containing 2.5 g of Fucoidan (ARC Equine Standard) and 50 mL of LRS, respectively, into a 5 L bag of LRS & warming to body temperature before surgery.

All procedures were IACUC approved. Horses were treated perioperatively with flunixin meglumine & antimicrobials. A brief abdominal exploration was performed through a 20-cm ventral midline celiotomy incision. At jejunal segments 10 and 5 arcuate vessels oral to the ileum, a 1-cm full thickness circumferential wedged segment was resected and an anastomosis performed using 2-0 polyglactin 910 in 2-layer simple continuous pattern (Figure 1). Prior to closure of the linea alba, 5 L of fucoidan solution or control LRS were infused into the abdomen. The body wall was routinely closed.

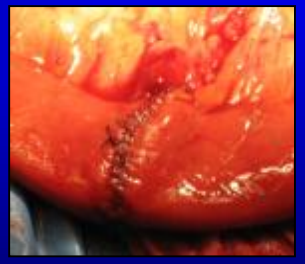

Figure 1. Resection & jejunojejunostomy site.

Postoperatively, feed was gradually reintroduced over 48 hours. A physical examination was performed every 12 hours. Horses were monitored for signs of colic & checked for PO reflux (> 1 L, POR) q 8 h. The incision was subjectively graded for edema, pain on palpation, drainage, and dehiscence. A complete blood count, plasma chemistry, and coagulation profile were performed preoperatively and on days 1, 2, 6, and 10 postoperatively. Horses were euthanized on day 10 postoperatively. An ANOVA was used to compare data between groups. A p value < 0.05 was considered statistically significant.

Results

No difference was observed between experimental groups for heart rate or rectal temperature (Figure 2A) pre-operatively or during the 10 day study period. No difference was observed between groups in the number of colic episodes. Two horses in the fucoidan solution and three horses in the LRS control group that had POR. The volume of POR was greater for the horses in the fucoidan group (23 L from day 1 to 4; and 139 L from day 2 to 5) compared with the control LRS group (9.5 L within the first 24 hours of surgery; 4 L on day 3; and 5 L within the first 72 hours of surgery) and all horses recovered normally. There were no signs at necropsy indicating the cause of the POR. The reflux and feces were negative for Salmonella spp. One control horse developed an incisional infection. There were no signs of peritonitis in any horse. There was no difference between experimental groups for fibrinogen concentration, platelet count, activated partial thromboplastin time, gamma glutamyl transferase, aspartate aminotransferase, or creatinine concentration. A difference between groups was determined at several time points for leukocyte and neutrophil counts (Figures 2B and 2C), antithrombin III (Figure 2D), prothrombin time (Figure 2E), and hematocrit (Figure 2F).

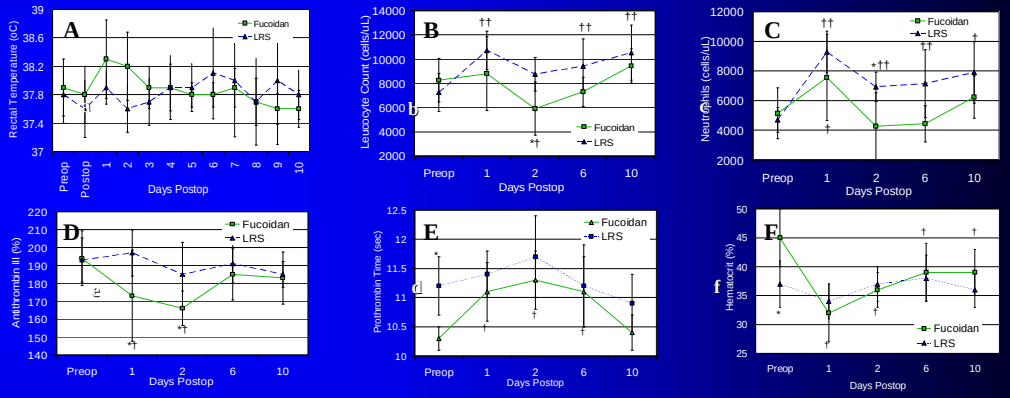

Fig 2. Effect of fucoidan solution and Lactated Ringer's Injection USP (control LRS) on selected clinical parameters following resection and jejunojejunostomy in horses. (A) rectal temperature, (B) leucocyte count, (C) neutrophil count, (D) antithrombin III, (E) prothrombin time, and (F) hematocrit. * statistically significant between fucoidan and control LRS; † fucoidan, †† control LRS, statistically significant compared with own group's preoperative value (ANOVA, $p < 0.05$).

Discussion

With the exception of POR, fucoidan had no impact on clinical signs. We are uncertain of the importance of POR in horses administered IP fucoidan solution. POR had not been found in a foal abrasion model investigating the use of fucoidan solution for adhesion prevention and we have not found POR to be a feature of clinical cases in which fucoidan solution has been used (unpublished data). POR is commonly seen as a PO complication and the occurrence rate in our study was not different compared to that seen clinically following jejunojejunostomy. IP fucoidan solution did have an influence at some time points on several laboratory values compared with control LRS; however, values were generally within normal limits. Although fucoidan is a sulphated polysaccharide (as is heparin), treatment with fucoidan did not negatively impact any of the coagulation parameters.

Conclusions

Fucoidan solution was safely administered IP during celiotomy and anastomosis in horses. Fucoidan solution represents an alternative option to CMC and heparin in cases where adhesions are a likely complication, and is simple to use in a clinical setting. Fucoidan solution appears to act as a physical barrier between damaged peritoneal tissues and may be appropriate for use in horses during abdominal surgery.

References

1. Yamout S, et al: Proc 2007 ACVS Ann Mtg, Chicago, USA; 2. Klohnen A, et al: Proc 2008 ACVS Vet Symp, San Diego, USA