# Evaluation of a Novel Polyethylene Glycol-Based Incisional Sealant in 100 Horses

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## ABSTRACT

Wounds and post-operative surgical sites in horses are a concern for equine veterinarians due to environmental factors, and owner and patient compliance with bandaging. The purpose of this study was to evaluate a new polyethylene glycol hydrogel applied as a liquid bandage in 100 horses with various injuries and or surgical procedures. After application of the polyethylene glycol (PEG) based hydrogel, the incision sites were evaluated either at a follow-up exam or through client comments during a follow-up phone call. Incision sites healed adequately and wounds healed exceptionally well according to the owner comments, and there were no adverse events reported. Eighty nine percent (89%) of owners were satisfied to very satisfied with the outcomes after using the product. The liquid bandage allows visualization of the wound, unlike traditional bandages, and eliminates the need to rebandage. This study suggests that the novel hydrogel liquid bandage causes no adverse events and is beneficial to incisional healing due to its protective barrier properties and ability to use in hard-to-bandage locations and may be an attractive option to traditional bandages for equine veterinarians.

## INTRODUCTION

Wounds and post-operative surgical sites have always been a concern for the equine veterinarian. Unlike physicians, equine practitioners have very limited control over postoperative convalescence, patient compliance with keeping bandages in place, and environmental factors such as flies, dirty stalls, and pasture conditions. For protection against environmental factors, equine veterinarians use bandages, incisive surgical drapes, N-Butyl cyanoacrylate, and biological agents to cover surgical sites and wounds.[1] A new polyethylene glycol (PEG)-based hydrogel polymer was developed for wound protection. The liquid bandage polymerizes into a gel in approximately 90 seconds and covers the sutured area or the wound.

Polyethylene glycol (PEG) derivatives with molecular weights of 10 kilo Dalton (kDa) and higher are extensively used in medical devices and as drug carriers in pharmaceuticals

applications[2,3] because they have proven to be generally safe and non-toxic. [4]The polymer tested in this study has previously been tested *in vitro* with a lack of significant or relevant safety concerns.[5]

*In vitro* studies using this polymer have demonstrated the elution kinetics and compatibility of a variety of active pharmaceutical ingredients (APIs).[5] Cytotoxicity studies (ISO 10993-5) demonstrated no cytotoxicity or cell lysis, and ASTM 10993-4 hemolysis studies demonstrated the article to be non-hemolytic and non-thrombogenic. [5] Extensive *in vivo* safety studies of the polymer in multiple animal models, including rabbits, mice, horses and dogs, have demonstrated the polymer causes no significant adverse events and no relevant pathological findings. [5-10] A study in 11 horses (n=20 legs) using the polymer for injection into the navicular bursa demonstrated no significant adverse effects.[10] SutureSeal™, the same liquid bandage form of the polymer used in this study, has been used topically in over 1,000 companion animals after surgery and to cover wounds with no adverse effects reported. [5,8,9]

In this study, the liquid bandage was evaluated on a variety of wounds in 100 horses in a clinical setting from September 2012 to December 2012. The wounds ranged from surgical incisions, and those allowed to heal by second intention after liquid bandage application.

## MATERIALS AND METHODS

### *PEG polymer test article*

The SutureSeal™ formulation (Medicus Biosciences; San José, California) is comprised of three compounds: one containing 8 nucleophilic groups (8-arm-PEG 20K amine), the second also containing 8 nucleophilic groups and 8 degradable acetate groups (8-arm-PEG 20K amine acetate) and the third containing 4 electrophilic groups (4-arm-PEG 20K amide ester) in a stoichiometric ratio; a buffer and a viscosity enhancer. The polymer was designed to be degraded in 2-weeks by selecting degradable acetate groups, numbers of crosslinking sites and the polymer concentration in the solution. All reactive PEG materials were purchased from JenKem Corp, Plano, Texas. The firmness, adhesion, and elastic modulus of the polymer were characterized by a Texture Analyzer (TA.XT.plus) with Exponent software (v6.0) using various probes. The sterile solid components in the injection kit were applied at the target site as a liquid biopolymer, which solidifies at a pre-set time of 90-120 seconds and adheres to the tissue.

### *Study Design*

One hundred horses with either surgical incisions or other wounds were enrolled in the case study to test the novel liquid bandage. The horses were divided into to 4 groups: Group 1 (n = 54) consisted of primary closures with +/- bandage placement over the site; Group 2 (n = 29)

were horses that had celiotomies; Group 3 (n = 9) horses had surgical intervention but all had areas were allowed to heal by second intention; Group 4 (n = 10) were horses that had crytorchidectomies and scrotal ablations.

In all groups, the sterile liquid was mixed and spread over the incisional or wound area with a brush tip applicator. The solution turned into a solid gel in approximately 90 seconds thus covering the sutured area or the entire wound. The hydrogel was formulated to degrade in 14 days.

Group 1 (n = 54): Surgeons applied the polymer over sutured areas on either lacerations that were repaired or masses that were removed, and in a few elective surgeries. No bandages were used for 19/54 horses (35%) and bandages were placed on 35/54 horses (65%). When bandages were used, it was placed over the site primarily for compression of the area. Of the 35 cases involving bandages, no primary bandage layer was used over the wound in 30 cases (86%) and in 5 cases (14%) a primary bandage layer consisting of a telfa pad and cling gauze was placed, on top of the PEG hydrogel.

Group 2 (n = 29): Surgeons applied the polymer to the ventral midline celiotomy or right para-median celiotomy incisions. The surgeries consisted of 27 colic surgeries, 1 umbilical hernia repair, and 1 cystic calculi removal. All horses were recovered in a 16‘x16’ recovery stall with head and tail ropes to assist in recovery. Abdominal bandages were placed on two horses during the recovery period. All of the incisions were examined daily for the next 14 days for any excessive heat, pain, swelling or discharge. Only 24 horses were available for long-term evaluation. Five (5) horses were euthanized prior to discharge.

Group 3 (n = 9): Surgeons applied the polymer to primary wounds. Three of the nine wounds (33%) were in areas too difficult to bandage. The remaining six out of nine (67%) had wounds that were bandaged for compression. No primary bandage layer was used over these wounds.

Group 4 (n = 8): Surgeons applied the polymer in the inguinal area for incisions related to cryptorchid surgery with scrotal ablation. None of the horses were bandaged. The mild swelling associated with the procedure was managed with oral phenylbutazone at (2.2 mg/kg) orally every 12 hours for 10 days. All the horses were placed on trimethoprim/sulfamethoxazole double strength (960mg) dosed at 15mg/kg orally given twice a day for 5 days.

All the owners were contacted approximately 30 days after the surgery or injury to determine the satisfaction with the type of repair and to discuss any complications or comments associated with the PEG hydrogel polymer covering. Eight (8) horses were lost to follow-up evaluation. Therefore, 92 horses were evaluated in the study. The following scale was given to each owner to determine his or her satisfaction of the healed area:

5: Extremely Satisfied
4: Satisfied
3: Not satisfied but not dissatisfied
2: Dissatisfied with the hydrogel bandage
1: Caused the area to become more inflamed (increased redness, heat, or swelling )

RESULTS

Summarized results from the owner surveys conducted 30 days after application of the liquid bandage to the suture site or wound are shown in Table 1.

Table 1: Summary of owner survey scores 30 days after application of the liquid bandage.

| | Increased Inflammation 1 | Dissatisfied 2 | Not Satisfied but Not Dissatisfied 3 | Satisfied 4 | Extremely Satisfied 5 |
|---|---|---|---|---|---|
| **Group 1 (54)** | 0 | 3 | 3 | 48 | 0 |
| **Group 2 (24)** | 0 | 0 | 0 | 6 | 18 |
| **Group 3 (9)** | 0 | 0 | 0 | 0 | 9 |
| **Group 4 (5)** | 0 | 0 | 0 | 0 | 5 |
| **Total (84)** | 0 | 3(3.2%) | 3 (3.2%) | 54 (59%) | 28 (30%) |

Group 1 horses (hydrogel used to cover surgically created or traumatically created wounds that were sutured) healed without dehiscence or infection. The hydrogel did not interfere with the application or function of bandages in the horses that had bandages placed. The majority of clients in this group (48/54; 89%) were generally satisfied giving a score of 4 with the appearance of the healed wound and the healing process and felt that bandage changes were easier due to the covering of the wound. There were 6 out of 54 clients (11%) that were not completely satisfied with the results giving a score of 3 or 2. The primary complaint of dissatisfaction was the owner being required to change the bandages, rather than a complaint about the polymer. One owner commented that he was unsure whether hydrogel was present because he could not see the material on the suture site. However, the owner did state that he could feel that “something” was on the suture site.

Group 2 horses (hydrogel placed on the ventral midline celiotomies and right para-median celiotomy) healed with no evidence of complications. Twenty-four horses were available for

long-term evaluation and 5 horses were euthanized for reasons not related to wound healing. All of the owners in this group were satisfied with the healing of the incisions giving a score of 4 to 5 (18-score 5 and 6-score 4). The majority of the wounds had no evidence of complications and only 1 horse developed slight drainage from the incision line. This horse had 18 feet of small intestine removed and a large amount of saline was placed into the abdominal cavity prior to closing the incision. The incision line did get infected and dehiscence of the skin did occur and no organisms were isolated on culture of the incision site. On Day 4, an abdominal bandage and more polymer was placed over the opened incision. The area was granulated in approximately 14 days without any other complications. Another horse in this group presented for a second surgery and a right para-median incision was performed. An abdominal bandage was placed upon recovery and removed prior to discharge. The owner thought that the healing process was better the second time as compared to the first time. For the 5 horses that did not survive to discharge, 1 developed a myopathy immediately post operatively and gradually improved but not to the satisfaction to the owner's expectation and was humanely euthanized on Day 10 postoperatively. Three of the horses were euthanized due to continuous reflux for 5 to7 days duration. The last horse was euthanized due to early signs of laminitis.

Group 3 horses (polymer was used for primary wound care [6 horses had habronemiasis, 1 horse had a dehisced wound, and the other 2 horses had mass removals that could not be closed]). The 6 horses that were treated for habronemiasis had their wounds injected with triamcinolone, covered with the hydrogel polymer and then bandaged to add compression to the wound. The other wounds included a surgically removed shoe boil on the elbow, squamous cell carcinoma removal on the sheath, and squamous cell carcinoma removed in the vulvar area. Five out of nine (5/9; 56%) owners reported being satisfied with the results of having the area covered with the PEG hydrogel polymer giving a score of 4 to 5. Four out of nine (4/9; 44%) owners reported not being happy with the initial outcome of the steroid injection and covering the wound giving a score of 2 to 1. All 4 horses returned and had the sites injected 3 more times every 2 weeks with 20 mg of triamcinolone. The last intralesional injection was done with the PEG hydrogel mixed with triamcinolone (20mg) instead of the phosphate buffered saline and covered with the PEG hydrogel/triamcinolone mix. The owners felt that the last injection with PEG hydrogel/triamcinolone mix helped the area heal better than the steroid injections alone giving the healing process a score of 5.

Group 4 (horses that had the scrotal ablation/cryptorchid surgery) had no complications associated with the hydrogel covering the incision lines. All the owners were very satisfied with the results of the procedure giving a score of 5.

## DISCUSSION

Dressings and bandaging are an important component of successful wound management. The ideal wound dressing would function like skin; to protect the area from trauma, thermoregulate, allow water and electrolytes to pass through, and allow oxygen and carbon dioxide exchange.[1] Various wound dressing are available for use in veterinary or human medicine and have been classified as adherent, hydrophilic, non-adherent absorbent or nonabsorbent, or biologic.[11] The physical attributes of bandages are to protect the wound from environmental debris, to absorb or allow excessive fluids to move from the injured site, and compression of the site. Most standard bandages consist of three layers. The primary layer is in direct contact to the wound or incision and should be sterile, maintain contact with the incision or wound, conform to the body surface, nonirritating or toxic, permit passage of exudates, and non-adherent.[1] The secondary layer has two major functions, to absorb or draw exudate from the wound and to provide cushioning to the area. The tertiary layer functions to secure the bandage.

Hydrogel dressings are available for use in equine medicine to either eliminate bandaging or as an additional component to bandaging. They are currently available as amorphous gel, in gel-impregnated gauze, or in a mesh-reinforced pad.[12] The new hydrogel dressing used in this study is a biodegradable, PEG-based hydrogel that has been developed for wound care in both human and veterinary medicine. The unique liquid-to-solid properties of the polymer allows for initial application as a thin liquid to cover wounds with rapid polymerization to a flexible solid form once it is on the wound. The polymer provides a protective barrier that remains in contact with the area and yet bends with movement. The polymer allows exudate to be removed, and air exchange to the wound.

The overall response by the owners was very favorable. Eighty nine percent (89%) or 82 out of 94 owners were satisfied to extremely satisfied with the outcome of using the polymer to cover their horses incisions or wounds. There was no infection or complications from using the polymer with or without a bandage. Out of the 94 horses used in the study, 6 owners (6.25%) were dissatisfied with the overall outcome of the procedure. However, none of the dissatisfaction was due to the use of the PEG hydrogel dressing, but were related to the burden of bandaging with traditional bandages used in in addition to the liquid bandage in their particular cases.

The use of the PEG hydrogel dressing on the incision site may be beneficial in helping the horse heal with and without a bandage. Previous studies have shown that the recovery room floor is a source of infection to a surgical site and the use of bandages and/or stents have decreased postoperative complications. [13,14] Horses may recover better without the added irritation of a bandage placed over the surgical site. The hydrogel could be applied first, the horse allowed to recover, and then the bandage can be placed after recovery to ensure good placement of the bandage, if desired.

Preliminary studies with PEG hydrogels have shown sustained, predictable drug delivery over several weeks both *in vitro* and *in vivo.*[15,16] In four horses in this study, the hydrogel dressing was mixed with triamcinolone due to their unresolved habronemiasis. The combination of the polymer and triamcinolone may have improved wound healing in these particular horses due to their habronemiasis. In addition to forming a protective barrier over wounds, the hydrogel polymer may be able to deliver therapies such as corticosteroids, water-soluble antimicrobials, growth factors and other medications that may further enhance wound healing. Further studies are required to explore the potential combination products.

## CONCLUSION

The PEG hydrogel liquid bandage caused no reported adverse events. Wounds and surgical incisions healed adequately and there were no obvious differences in wound healing whether the liquid bandage was applied alone or under a traditional bandage. Eighty-nine (89%) of owners were satisfied to extremely satisfied with the product. There were good outcomes in horses in which the polymer was mixed with triamcinolone. Additional studies will elucidate the potential benefits of using the polymer as a drug delivery vehicle.

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