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Collagenase for Wound Debridement in the Neonatal Intensive Care Unit: A retrospective case series

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Abstract

Background/Objective—The use of collagenase for enzymatic wound debridement has been studied extensively, and has been established as the standard of care for non-healing and necrotic wounds in individuals for which surgical intervention is not an option. Collagenase has been shown to be effective in the adult population, but has been studied in a limited capacity in infants and neonates. The purpose of this study was to investigate the use of collagenase in the neonatal intensive care unit (NICU).

Methods—Retrospective chart review of infants and neonates admitted to the NICU at Arkansas Children's Hospital in a 1-year time period with non-healing wounds that utilized collagenase for wound healing. A total of six wounds were identified: 5 surgical wound dehiscence, and one IV infiltrate.

Author Disclosure

Consent for Publication

The authors declare full consent for publication of the manuscript.

Conflict of Interest

The authors declare no conflict of interest for this study. This manuscript is original work.

Human Research Statement

The study was approved by the Institutional Review Board and conducted in accordance with the ethical standards of all applicable national and institutional committees. Waiver of informed consent was granted as data collection was performed through retrospective chart review only.

Results—Prior to the use of collagenase, five of the six wounds were treated with an alternative dressing. Once collagenase was initiated, three of these wounds reached complete granulation and closure in less time than in the episode of prior therapy. The number of days to reach 100% granulation once treated with collagenase was 5–18 days (mean=12.2 days). Surgical intervention for the debridement and closure of these wounds was not required, providing cost-savings to the patient. Daily wound care was completed with negligible pain recordings.

Conclusions—The results suggest that the use of collagenase for enzymatic debridement can be beneficial, safe, and effective for the treatment of non-healing and necrotic wounds in infants and neonates.

Keywords

santyl; collagenase; wound debridement; neonatal

INTRODUCTION

Pediatric wounds are a potential complication in the care of medically fragile children. Common causes of these wounds are trauma, burn, adverse pressure, surgery, surgical wound dehiscence, and IV infiltrate.^{1,2} The use of collagenase for enzymatic wound debridement has been studied extensively, and has been established as the standard of care for chronic, non-healing wounds in individuals for which surgical intervention is not an option.^{3,4} A large percentage of wounds initially treated to promote autolytic debridement have difficulty progressing through the natural stages of wound healing, especially for individuals with significant medical complications in which surgical strategies for wound debridement are not possible or are unfavorable. In these situations, significant amounts of nonviable tissue develop, thus impeding the wound healing process.^{1,5} Clostridium collagenase (Santyl) is the only FDA approved enzymatic debriding ointment.⁶ Collagenase selectively targets collagen debris in necrotic tissue that is bound to the wound bed, without affecting keratin, fat, or fibrin.^{3,4,5} Increased rate of wound healing, less days to healing, promotion of cell migration, increased selectivity, less pain to the patient, and decreased overall need for surgical intervention are outcomes associated with the use of collagenase Santyl for wound debridement.^{3,4,7} The use of collagenase (Santyl) has occasionally produced a transient erythema in surrounding tissues when the ointment has been applied outside the wound area, with one case of systemic hypersensitivity reported after 1 year of collagenase treatment.⁸

The use of collagenase for wound care has been examined largely in the adult population,^{3–9} and in a limited number of studies in the pediatric population. A study by Ozcan et al in 119 children (78 treated with collagenase and 41 with surgical debridement) with partial-thickness burn wounds established the safety and effectiveness of collagenase in subjects 3.2+/- 3 years of age, noting similar outcomes as those documented in adult studies, and asserting that collagenase should be the treatment of choice for eschar removal in this population with burn injury.¹⁰ Use of collagenase in the neonatal population was first documented in two cases by Tiras et al. The case series suggested that collagenase use was associated with expedient eschar removal, enhancement of granulation tissue formation, and prevention of scar formation.¹¹ Erdevi et al noted positive results in treatment of thrombotic

necrosis of the second digit of a neonate, negating the need for surgical intervention.¹² Karagol et al documented the use of the enzymatic ointment for necrotic tissue removal of a wound on the pinna of the ear in a preterm neonate with a significant medical history.¹³

Collagenase is the enzymatic debridement product of choice in individuals with wounds containing yellow slough or eschar with significant bacterial bioburden, in lieu of surgical intervention.^{3,4} Individuals that are not candidates for surgical intervention can include those that are extremely medically fragile or on anticoagulant therapy.^{3,4} A large portion of individuals in the Neonatal Intensive Care Unit (NICU) are medically fragile and may be on anticoagulant therapy. At Arkansas Children's Hospital, when the previously listed conditions are present, collagenase is routinely considered and the method of choice for physical therapists performing wound care in the NICU, with appropriate approval and order by a Licensed Independent Practitioner (LIP). The purpose of this retrospective case series was to examine the effectiveness of collagenase to treat chronic or necrotic wounds in five patients (with six wounds) in the NICU.

METHODS

Patient population

Before starting the study, permission was received from the University of Arkansas for Medical Sciences Institutional Review Board and the director of the Neonatal Intensive Care Unit (NICU). An initial screen of medical records for NICU admissions for a 1 year period was conducted. A chart review was performed on five patients who presented with non-healing wounds treated with collagenase during their admission to the NICU at Arkansas Children's Hospital. A total of six wounds were identified: 5 surgical wound dehiscence, and one IV infiltrate. Each patient presented with a complex medical history and required close monitoring in the NICU. Table 1 presents demographic data and other infant characteristics.

Intervention

During the NICU admission, a physical therapist assessed and performed wound care including application of collagenase (nickel-thick), a moist cover layer (saline-soaked or petroleum impregnated gauze) to achieve enzymatic activation for optimal results⁸, and adherent dressing (transparent adhesive film, tape, or self-adherent soft silicone dressing). Dressings containing silver or iodine should be avoided, as they inactivate collagenase.⁸ For some patients, once debridement was completed, the collagenase was discontinued and an alternative dressing was applied.

Data Collection

Wound size (length, width, and depth) and percent granulation tissue in the wound bed were assessed at each treatment. Initial wound measurements (Table 1) reflect the size of the wound when collagenase was initiated. Data collection included the number of days of an alternative debridement treatment or dressing and the number of days to full granulation tissue once the collagenase was applied. The total number of treatments were reported in Table 2. Pain assessments (mean values reported in Table 2) were completed at each treatment utilizing either the Neonatal Pain and Sedation Scale (N-PASS) or the Revised-

Face, Legs, Agitation, Cry, Consolability (r-FLACC) scale depending on the patient's adjusted age and cognitive capability. Both scales have been shown to be reliable and valid in assessing pain in their studied population.^{14,15}

RESULTS

The mean day of life for infants and neonates assessed was 65.8 days. See Table 1 regarding chronological and adjusted ages. Prior to the use of collagenase, five of the six wounds were treated with an alternative dressing. In addition, none of the patients included in this review were being actively treated, nor had they been treated with antibiotics for wound infection. Table 2 presents a summary of wound care treatment and the number of days to one hundred percent granulation once the collagenase was applied. Full closure was obtained by five of the six wounds; patient 2 discharged from the NICU prior to reaching closure. The number of days to reach 100% granulation for the five wounds followed through full closure was 5–18 days with a mean of 12.2 days. Figure 1 provides a graph of the time course of wound healing for each patient once the collagenase was applied.

DISCUSSION

This retrospective study is similar to the case series of Tiras et al.¹¹ who suggested that collagenase use was associated with expedient eschar removal and enhancement of granulation tissue formation. All of the infants and neonates reviewed in the case series were able to achieve full healing without the need for surgical intervention which is similar to the case described by Erdeve et al.¹²

Each of the patients involved in this study had multiple diagnoses and significant medical status changes throughout their hospital stay. Oxygenation levels, circulatory compromise, and overall nutrition can play a significant role in wound healing. Wound healing can be limited with decreases in oxygenation, tissue perfusion, and decreased nutrition.⁵ For instance, in Patient 4 there was an apparent decline and plateau in improvement of wound A, which correlated with a period of significant medical status decline. The remaining four patients maintained a stable medical status throughout wound treatment and thus presented with a positive progression rate from the initial to final treatment.

Daily wound care was completed with negligible pain recordings. Patients 4 and 5 presented with higher averages (0.6 and 0.35 respectively) than patients 1–3 (averaging 0); however, these pain ratings were noted to be related to possible medication withdrawal or other medical procedures completed simultaneously with standard wound care.

Complete granulation was achieved by 5 of the 6 wounds reflected in this study; Patient 2 was discharged prior to achieving 100% granulation, but she did return for follow-up 2 months later with a closed wound and minimal scar tissue formation at the wound site. The remaining 5 wounds were followed through complete healing. Patient 4's wound B was also treated with collagenase despite having 95% granulation for uniformity of wound dressings.

Five of these wounds were treated with an alternative dressing prior to the initiation of collagenase. Alternative therapies and products used prior to use of collagenase include, but

are not limited to, wet to dry dressing, xeroform, adaptic, and various forms of cover dressings (foam, dry gauze, tegaderm). It is pertinent to note that once collagenase began, three of these wounds reached complete granulation and closure in less time than the total number of days the initial intervention was used. Patients 3, 4 and 5 were treated with an alternative dressing once 100% granulation was achieved. Additional wound care studies are needed in the infant population, as well as to examine the efficacy and cost of continuing collagenase as the primary dressing once one hundred percent granulation tissue has been achieved.

The results of our retrospective study suggest that the use of collagenase for enzymatic debridement can be beneficial for the treatment of chronic and necrotic wounds in the medically fragile infant population. In addition, surgical intervention for the debridement and closure of these wounds was not required, providing cost-savings and promoting a safer environment for the patient.

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References

1. Sussman, C., Bates-Jensen, B. Wound Care: A Collaborative Practice Manual for Health Professionals. Philadelphia: Wolter Kluwer Lippincott Williams & Wilkins; 2012.
2. McCulloch, J., Kloth, L. Wound Healing: Evidence-Based Management. Philadelphia: F.A. Davis; 2010.
3. Shi L, Carson D. Collagenase Santyl ointment: a selective agent for wound debridement. J Wound Ostomy Continence Nurs. 2009; 36(6 Suppl):S12–6. [PubMed: 19918145]
4. Ramundo J, Gray M. Collagenase for enzymatic debridement: a systematic review. J Wound Ostomy Continence Nurs. 2009; 36(6 Suppl):S4–11. [PubMed: 19918148]
5. Schultz GS, Sibbald RG, Falanga V, et al. Wound bed preparation: a systematic approach to wound management. Wound Repair Regen. 2003; 11(Suppl 1):S1–28. [PubMed: 12654015]
6. Mosher BA, Cuddigan J, Thomas DR, Boudreau DM. Outcomes of 4 methods of debridement using a decision analysis methodology. Adv Wound Care. 1999; 12(2):81–8. [PubMed: 10326360]
7. Waycaster C, Milne CT. Clinical and economic benefit of enzymatic debridement of pressure ulcers compared to autolytic debridement with a hydrogel dressing. J Med Econ. 2013; 16(7):976–86. [PubMed: 23701261]
8. Smith & Nephew, Inc. Collagenase Santyl: application process. Collagenase Santyl. 2014
9. Milne CT, Ciccarelli AO, Lassy M. A comparison of collagenase to hydrogel dressings in wound debridement. Wounds. 2010; 22(11):270–4. [PubMed: 25901516]
10. Ozcan C, Ergün O, Celik A, Cördük N, Ozok G. Enzymatic debridement of burn wound with collagenase in children with partial-thickness burns. Burns. 2002; 28(8):791–4. [PubMed: 12464480]
11. Tiras U, Erdeve O, Karabulut AA, Dallar Y, Eksioğlu HM. Debridement via collagenase application in two neonates. Pediatr Dermatol. 2005; 22(5):472–5. [PubMed: 16191005]
12. Erdeve O, Atasay B, Arsan S. Collagenase application for amputation in a preterm. Pediatr Dermatol. 2007; 24(2):195–6. [PubMed: 17461824]
13. Karagol BS, Okumus N, Dursun A, Karadag N, Zenciroğlu A. Early and successful enzymatic debridement via collagenase application to pinna in a preterm neonate. Pediatr Dermatol. 2011; 28(5):600–1. [PubMed: 21854418]

14. Hillman BA, Tabrizi MN, Gauda EB, Carson KA, Aucott SW. The Neonatal Pain, Agitation and Sedation Scale and the bedside nurse's assessment of neonates. *J Perinatol.* 2015; 35(2):128–31. [PubMed: 25144158]
15. Malviya S, Voepel-Lewis T, Burke C, Merkel S, Tait AR. The revised FLACC observational pain tool: improved reliability and validity for pain assessment in children with cognitive impairment. *Paediatr Anaesth.* 2006; 6(3):258–65.

Figure 1. Days to 100% Granulation. Days of treatment on x-axis with percentage of granulation on the y-axis.

Table 1

Patient Demographics. Wound size recorded as length $\times$ width $\times$ depth in centimeters.

PATIENT	1	2	3	4	5
Chronological Age	1 mo, 26 days	15 days	6 mo, 14 days	1 mo, 14 days	20 days
Adjusted Age	N/A	N/A	5 mo	14 days	N/A
Diagnosis	39 wk TNB, CDH, CVA	39 week TNB, MMC, ventriculomegaly, hydrocephalus, IVH	34 wk PTNB, IUGR	36 wk PTNB, caudal regression syndrome, sacral agenesis, imperforate anus, MMC, hydrocephalus, Arnold-Chiari malformation, RDS,	38 wk TNB, MMC, microcephaly, ventricular dilatation, Arnold Chiari malformation
Wound Type	surgical incision dehiscence; CDH repair	surgical incision dehiscence; MMC repair	IV infiltrate	surgical incision dehiscence; MMC repair with skin expansion site at flank	surgical incision dehiscence; MMC repair
Wound Location	abdomen	lower back	anterior scalp	A: lower back B: right flank	lower back
Wound Size	$0.7 \times 3.8 \times 0$	$3.5 \times 0.8 \times 0.4$	$1.8 \times 1.2 \times 0.2$	A: $1.5 \times 1.5 \times 0.1$ B: $2 \times 2 \times 1$	$2 \times 0.8 \times 0.1$

Term Newborn (TNB), Congenital Diaphragmatic Hernia (CDH), Cerebrovascular Accident (CVA), Myelomeningocele (MMC), Intraventricular Hemorrhage (IVH), Intrauterine Growth Restriction (IUGR)

Wound History and Progression.

Pain reported is an average over the treatment episode (N-PASS or r-FLACC scales)

Table 2

PATIENT	1	2	3	4		5
				A	B	
Day of Alternative Dressing	30	1	28	42	38	7
Number of Treatments (once collagenase initiated)	20	7	19	16	13	14
Days to 100% Granulation	13	n/a*	14	18	5	11
Pain Reported (average)	0	0	0	0.6		0.35

* Patient 2 discharged from the hospital prior to attaining 100% granulation. 90% achieved by 7th treatment with collagenase.