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Treatment of Dehisced, Thoracic Neonatal Wounds With Single-Use Negative Pressure Wound Therapy Device and Medical-Grade Honey

A Retrospective Case Series

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ABSTRACT

PURPOSE: The purpose of this study was to report on our experience with a portable, single-use negative pressure wound therapy device used in combination with activated active Leptospermum honey (ALH) in the treatment of colonized or infected, dehisced, thoracic wounds in neonates with complex congenital heart disease.

DESIGN: Retrospective, descriptive study.

SUBJECTS AND SETTING: We reviewed medical records of 18 neonates and reported on findings from 11; the remaining 7 were not included secondary to incomplete records, transfer to a different institution prior to wound healing, or death. The median age of our patients was 12 days (range, 2 days to 5 weeks); their mean gestational age was 34 weeks. All of the neonates had acquired postoperative wound dehiscence that were colonized or infected and were treated in the neonatal intensive care unit (NICU) at Cohen Children's Medical Center (New Hyde Park, New York), a regional perinatal center with a level 4 NICU.

METHODS: Wound cultures were obtained on all patients prior to treatment commencement. All cultures were repeated on day 4 of treatment. Systemic antibiotics were administered as necessary. No complications were observed related to the use of negative pressure wound therapy device and ALH. All patients were followed until discharge home or transfer to another facility. The pain scores during placement and removal were acceptable (between 1 and 3; median = 2) using the Neonatal Infant Pain Scale. Staff and parents indicated that the combination of ALH and the negative pressure wound therapy device did not interfere with daily care and parental bonding.

CONCLUSIONS: Use of ALH and a single-use negative pressure wound therapy device was successful in this series of 11 neonates with complex congenital heart disease.

KEY WORDS: Dehiscence, Honey, Negative pressure wound therapy, Neonate.

INTRODUCTION

Advances in medical technology have enhanced neonatal patients' survival. Congenital heart disease (CHD) occurs in approximately 1% of live births; it is the leading cause of mortality from birth defects.[1] Approximately a quarter of the 40,000 children born with CHD annually in the United States require intervention in the first year of life.[2] In the 60 years since the first successful repair of a congenital heart defect using cardiopulmonary bypass in 1953, the accurate diagnosis and effective treatment of even the most complex congenital heart lesions have become standard practice.[2] Critical CHD is often lethal in the absence of treatment, and effective surgical, catheter, and medical therapies in the first 1 to 2 weeks of life have extended life expectancy. Survival rate of preterm babies born at 23 weeks' gestation averages 17% to 20%, but they tend to have multiple comorbid conditions such as patent ductus arteriosus (PDA) requiring surgical ligation. Up to 50% of neonates entering our neonatal intensive care units (NICUs) leave with a scar owing to planned or urgent surgical procedures. Median sternotomy and lateral thoracotomy are 2 approaches commonly used for correction of congenital cardiac conditions. Less than 5% of children undergoing congenital cardiac surgery repair via medial sternotomy or lateral thoracotomy experience subsequent wound dehiscence.[3]

Surgical wound dehiscence is defined as separation of opposed or sutured margins following a surgical procedure; it typically occurs between postoperative days 4 and 14.[4,5] Wound dehiscence in neonatal patients presents unique challenges. Prematurity, immunocompromised status, hemodynamic instability, edema, and poor nutritional status may compromise wound healing in neonates. In addition, lack of a robust stratum corneum, elevated risk for epidermal stripping, increased percutaneous absorption, and small size limit product choices for the neonatal open wounds.[5] Dehisced cardiac wounds can be a portal entry for infections; increasing morbidity and the need for further debridement or related procedures prolong hospital stays by as much as 10 to 21 days.[6] As a result, aggressive use of antibiotics was traditionally advocated by cardiac surgeons.[6] However, in the era of antibiotic stewardship,

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practitioners are aware of antibiotics overuse and potential systemic and local side effects and their toll on the neonatal immune system. In addition, we now recognize critical contribution of bacterial bioburden and medical biofilm on wound dehiscence, nonhealing status, and resistance to systemic antibiotic treatments.[7]

While topical antimicrobial agents are commonly used in adult patients, the risk of adverse side effects in neonates is significant. Structurally and functionally immature skin enhances percutaneous absorption of topical products.[8] Common topical antimicrobials such as silver- or iodine-based products can be toxic to a neonate, induce systemic illness, cause cutaneous burns, and provoke an allergic reaction. Polyhexamethylene biguanide or methylene blue/gentian violet–based antimicrobials have not undergone adequate testing to determine efficacy and safety in the neonatal population.[8]

Evidence is sparse; nevertheless, ALH has been used successfully in neonates with various chronic wounds.[9] My clinical experiences strongly suggest that the effects of negative pressure wound therapy (NPWT) can be amplified by concomitant use of active Leptospermum honey (ALH). Research suggests that many dehisced wounds fail to close because they remain in an inflammatory stage of wound healing.[7] The wound healing properties of ALH have been described in multiple publications.[19-23] Active Leptospermum honey possesses hygroscopic properties that increase local lymphatic flow, replenish proteases, and support autolytic debridement by slough removal, increased oxygen perfusion, and decreased edema.[19] Because ALH is acidic (pH range, 3.2-4.2), it promotes a more acidic pH in the bed of colonized or infected wounds that tend to have a more alkaline environment, supporting coliform and other potentially pathogenic bacterial reproduction and biofilm formation.[19,20] Restoration of a more acidic environment also minimizes available nutrition required for bacterial reproduction. Acidity and increased oxygen diffusion promote fibroblast migration, proliferation and organization of collagen, and angiogenesis. It stimulates immunomodulation by upregulation of tumor necrosis factor α, IL-1β, IL-6, and prostaglandin E_2 from monocytes.[19,20] The ratio of pro/anti-inflammatory modulators produced by ALH may decrease production of free oxygen radicals; this is particularly important in preterm babies who have an impaired ability to destroy oxygen radicals. Research suggests that ALH has antifungal, antiviral, and antibacterial activities against multiple gram-positive and gram-negative species known to colonize the wound surface and impair healing.[19-25] Upon contact with wound exudate, glucose oxidase in ALH produces hydrogen peroxide at a concentration that inhibits bacterial growth without compromising new granulation tissue. A literature search identified several clinical studies examining the use of ALH in pediatric populations. Simon and colleagues[26] described successful wound closure with ALH in the pediatric hematology-oncology population, and Amaya[27] reported positive wound healing with ALH in 115 neonatal and pediatric patients.

Negative pressure wound therapy enhances wound closure by removing interstitial fluid and infectious organisms, decreasing edema, and promoting perfusion, angiogenesis, and granulation tissue formation.[10-20] It targets both macro- and microenvironment of the wound bed. The microstrain induces cellular micro deformations, which promote cellular migration, growth factors release, cell proliferation, and approximation of wound edges. On the macro level, the dressing provides moist, closed wound healing environment. Until recently, a single form of vacuum-assisted closure system was available; it comprised a canister, suction mechanism, and wound filler (such as black polyurethane foam, white polyvinyl alcohol foam, or black foam bonded with silver). We found this type of device bulky difficult to apply to a wound in a small neonate. Based on clinical experience in our facility, multiple concerns have been raised related to uses of traditional NPWT delivered via a vacuum-assisted closure system. They are (1) ingrown granulation tissue, which causes pain upon foam removal and disturbance of the healing process; (2) difficult application and removal of NPWT dressings with an increased risk for medical adhesive–related skin injury (epidermal stripping and pain); (3) application of higher negative pressure with an increased risk for potential hemodynamic instability; (4) inconsistency in troubleshooting when the system alarms; and (5) parent's apprehension in handling a baby when the unit is present.

Negative pressure wound therapy has been used extensively in pediatric and adult populations with complex abdominal, orthopedic, and trauma wounds. Chariker and colleagues[28] presented a series of 24 pediatric traumatic wounds that achieved flap closure and healing with NPWT (via primary closure and secondary intention) in an average of 9 to 17 days, depending on wound type. Hutchison and Craw[29] described use of acellular dermal template and NPWT in 8 pediatric patients with complicated soft-tissue extremity wounds. Treatment was well tolerated and deemed integral to closing wounds in half the time (3.5 days vs 6.8 days); none of the study participants required flap surgery. Baharestani[13] summarized use of NPWT in pediatric patients (ranging from neonates to adolescents) with sternal wounds, pressure injuries, burns, and various abdominal wounds. This article supports the use of NPWT in the neonatal and pediatric population with specific recommendations, while urging caution in general when a traditional NPWT device is in use. In the last 5 years, a disposable, compact and ambulatory, canister-less version has emerged that addresses some of the aforementioned concerns (NPWT-PICO; Smith and Nephew Healthcare, Hull, United Kingdom). The system is a self-contained, comparatively light, battery-operated unit.[9,15] The top film layer possesses a high moisture vapor transmission rate, enhancing evaporation of exudate that is absorbed by the middle layer. An inner silicon contact layer and border around the device allow fluid to pass, preclude granulation tissue ingrowth, and ensure atraumatic removal and avoidance of epidermal stripping and pain. Absorptive middle component can absorb and retain up to 300 mL of exudate, more than most neonatal thoracic wounds ever produce. Available literature recommends considering lower pressure setting in pediatric population as compared to adults to minimize risks of dehydration, fluid loss, blood pressure swings, and electrolyte imbalances; negative pressures ranging from 50 to 75 mm Hg have been recommended when NPWT is used in neonates.[13] The purpose of this study was to describe our experience with the use of medical-grade honey combined with a single-use negative pressure wound device in the treatment of colonized or infected dehisced thoracic wounds in neonates with complex CHD.

METHODS

This is a single-center, retrospective chart review study; data were collected between 2014 and 2016 and recorded on a standardized form developed for purposes of this study. We searched for medical records of neonates undergoing surgery for cardiac disease/PDA repair from our computerized Neonatal Information System (NIS5). Inclusion criteria were postoperative wound dehiscence following medial sternotomy or lateral thoracotomy. Exclusion criteria were (1) death prior to wound closure, (2) transfer prior to wound closure, and (3) incomplete data. The study protocol was reviewed by the institutional review board and was granted exemption based on category 4 (collection or study of existing de-identified data).

Clinical Management

The DIME (Debridement or Devitalized tissue/Inflammation, Infection/Moisture balance/Edge preparation) conceptual framework guided wound management.[30] Wound cultures were obtained prior to treatment with ALH and the single-use NPWT system. Debridement is an essential important pillar in this conceptual framework, and wounds covered with slough, exudate, or eschar were debrided via surgical, mechanical, enzymatic, or autolytic means as indicated. We relied on clinical signs and symptoms to separate simple colonization from infection. Wounds were diagnosed as infected if they exhibited erythema, warmth, increased exudate, or swelling, combined with systemic signs and symptoms (respiratory distress, hyperthermia, hypotension, hypoglycemia, and feeding intolerance). Infected wounds were treated with systemic antimicrobials.

Local treatment of the dehisced wounds, based on principles of maintaining a moist wound environment comprising ALH and NPWT. Active Leptospermum honey consists of 90% honey and 10% vegetable esters, creating a thinner consistency than other medical-grade honey formulations. The ALH gel was placed directly on wound bed to stimulate lymph flow, allow oxygen exchange, provide antimicrobial coverage as a treatment and prevention strategy, and promote granulation tissue growth. One neonate required surgical debridement, and 2 wounds required packing gauze along with the ALH due to significant depth. All wounds were covered with an NPWT device (PICO). We found that it also works well for wounds with more substantial depth as long as packing or hydrophobic gauze is used. The single-use NPWT device was centered on the wound with the pressure bevel pointing cephalad. To avoid skin irritation, a nonalcohol cyanoacrylate skin barrier was applied to the periwound area and allowed to dry completely. An airtight seal was ensured by placing adhesive strips over the dressing perimeter. The device was set to deliver −80 mm Hg continuous negative pressure. The first dressing change took place on the fourth day after NPWT was started. Subsequent dressing changes were on days 7, 10-11, and 14 and weekly thereafter until closure. Infants received partial swaddling and oral sucrose solution during dressing changes. Wound status was evaluated by the neonatal wound physician and a cardiac surgeon with each dressing change. Wound closure rates in centimeters were documented manually. Once wound cavity had complete or almost complete epithelialization, NPWT was discontinued. All wounds epithelialized completely. Following discharge, patients were seen in the follow-up clinic at least once, usually within 4 weeks of discharge.

Instrument

Pain was assessed via the Neonatal Infant Pain Scale (NIPS).[31] Six physiologic indicators are used to assess pain in full-term and premature infants; they are facial expression, crying, breathing, movement or position of arms and legs, and state of arousal. Scores vary from 0 to 7, where 0 indicates no pain and 7 indicates highest possible pain; a score of 3 to 4 indicates mild to moderate pain, and scores greater than 4 indicate severe pain. The instrument has undergone extensive psychometric testing and has been found to have strong construct and concurrent validity, excellent test-retest, and interrater reiablity.[31,32]

Data Analysis

Descriptive analyses were used to report findings.

RESULTS

Chart review identified 18 neonates who underwent surgical management of complex cardiac disease, and 11 were included in this retrospective review. Seven were excluded due to incomplete record data, transfer to referring institution prior to complete wound healing, or death. Six were male and 5 were female; their median age was 12 days (range, 2-35 days), and their mean gestational age was 34 weeks.

Management included attention to the infection/inflammation component of the DIME framework.[30] Wound cultures were obtained prior to commencement of treatment with ALH and the single-use NPWT device. Two of 11 wounds were found to be colonized, 5 were deemed infected, and 4 had no growth (Table). Systemic antibiotics were used as clinically indicated (prior sepsis, pneumonia, or clinical deterioration without a clear source). I also observed that 7 of 11 patients were on antibiotics at the time of dehiscence; nevertheless, wound cultures were positive in 7 neonates. Most of the wounds dehisced between 4 and 10 days (median = 6 days).

During the course of treatment, we relied on clinical signs and symptoms to separate simple colonization from infection. Five wounds that were deemed infected had erythema, warmth, increased exudate, and swelling along with systemic instability (such as respiratory distress, hyperthermia, hypotension, hypoglycemia, and feeding intolerance) (Figure 1). Wounds deemed colonized did not have systemic deterioration or local signs of infection (Figure 2). All colonized and infected wounds were recultured after 4 days of treatment, and 5 exhibited no growth. All patients achieved 100% granulation tissue on this regimen; no secondary debridement was required once a combination of ALH and one-time use NPWT treatment was applied.

Debridement is also an essential pillar of the DIME framework. Wounds that are covered with slough, exudate, or eschar will not heal until wound bed is prepared for granulation tissue growth and further epithelialization. One of our patient's wound required surgical debridement (Figure 1), 2 were mechanically debrided (Figures 3 and 4) by using a monofilament designed to retain dead tissue and bacteria (Debrisoft Lolly; Lohmann-Rauscher GmbH & Co, Milwaukee, Wisconsin), and one was enzymatically debrided with Collagenase (Smith and Nephew Healthcare, Hull, United Kingdom) for 3 days prior to treatment commencement (Figure 2). We also used autolytic debridement during ongoing treatment, because hyperosmolar ALH helps increase lymph flow, donates moisture, and likely modulates inflammatory cell response that may enhance macrophage presence along with supportive function of NPWT.[16]

Complete epithelialization was obtained in all wounds. Treatments using the NPWT device ranged from 7 to 20 days; the mean time was 11 days or 2 single-use units per patient. The time to complete wound closure ranged from 12 to 29 days (mean = 18 days). All patients tolerated treatment well; no

TABLE.
Patients' Demographics and Wound Details

Pt	M/F	Gestational Age, wk	Weight, g	Condition	Wound	Infected/Colonized/ Clean	Debridement Prior to NPWT	Days w/ NPWT	Granulation %	Complete Closure, d
1	M	36	2516	Coarctation of aorta; right AA	Sternal	Colonized	Collagenase 3 d	12	100	17
2	M	34	2340	Coarctation of aorta	Sternal	Clean	NO	9	100	16
3	M	34	1975	Hypoplastic right heart	Sternal	Colonized	NO	18	100	25
4	F	34	2200	Ebstein's anomaly	Sternal	Clean	NO	9	100	14
5	F	36	2388	Hypoplastic left heart	Sternal	Infected	NO	15	100	19
6	M	40	2915	Tetralogy of Fallot	Sternal	Clean	NO	11	100	14
7	F	39	3003	AV canal	Sternal	Clean	NO	8	100	15
8	M	36	2789	VSD	Sternal	Infected	NO	8	100	13
9	F	27	690	Patent ductus arteriosus	Thoracotomy	Infected	Mechanical	b	100	12
10	F	39	2980	Hypoplastic left heart	Sternal	Infected	Mechanical	16	100	25
11	M	37	2685	Hypoplastic left heart	Sternal	Infected	Surgical	20	100	29

Abbreviations: AA, AA_ Aortic Arch; AV, atrioventricular; F, female; M, male; NPWT, negative pressure wound therapy; VSD, Ventricular Septal Defect.

adverse events occurred. No instances of medical adhesive skin injuries (periwound skin stripping or irritation) occurred. Pain scores were monitored during dressing changes and were found to be low (median = 2, with range of 1-3) on the NIPS.

DISCUSSION

Eleven neonatal patients with dehisced cardiac surgical wounds had successful wound closure using a combination therapy of ALH gel and a portable, single-use, canister-less NPWT device. I believe that combination of these 2 products supported the healing cascade synergistically. Negative pressure wound therapy promoted wound contraction, stimulation for cell growth, exudate containment, and physical protection for vulnerable wound bed. Honey supported continuous wound debridement, exudate clearance, increased oxygenation, contributing to fibroblast and endothelial cells growth, and provided antimicrobial defense as either an actual topical antimicrobial treatment or a preventive element in clean or colonized wounds. Wound cultures were obtained prior to commencement of treatment. All colonized and infected wounds were recultured on the fourth day of treatment, and 5 exhibited no growth after 4 days (we attribute this mostly to honey and NPWT effects), as we know that systemic antibiotics are not always active in place of wound surface biofilm.[24]

We found no maceration of surrounding skin with the single-use NPWT device, which contrasts with occasional occurrences using the traditional unit. Dressings remained on the wounds for as long as 7 days. No disturbances in vital signs, blood pressure, NIPS score, electrolyte status, and urination occurred upon commencement or during combination therapy. We found the single-use NPWT system was comparatively lightweight and compact. Interviewed staff described the device as easy to apply and remove, as well as simple to maintain. No

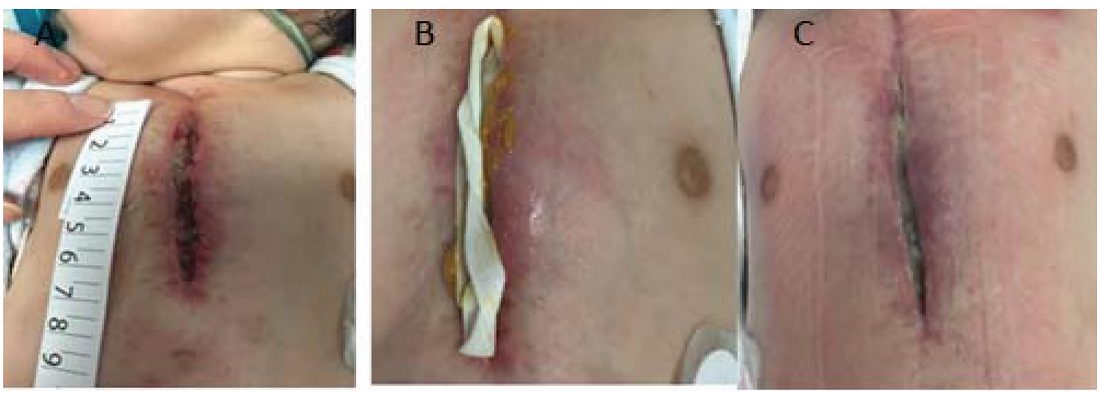

Figure 1. Case 11. Progression of wound to closure. (A) Day 3 of dehiscence. Postsurgical debridement. (B) Wound packed with honey and packing tape and PICO was placed. (C) Day 17.

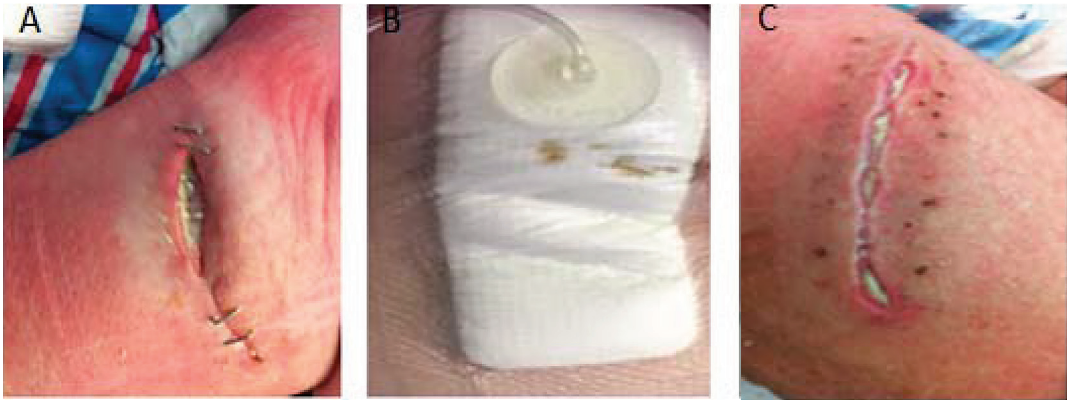

Figure 2. Case 1. Progression of wound to closure. (A) Status post Collagenase 3 days. Pre-NPWT/ALH. (B) PICO on. (C) Complete closure. NPWT indicates negative pressure wound therapy; ALH, active Leptospermum honey.

Figure 3. Case 9. Progression of wound to closure. (A) Day 2 of dehiscence. Premechanical debridement. (B) Remaining staples were removed and PICO was placed. (C) Day 9.

adverse events were associated with the use of this combination therapy. Our findings are consistent with those of Sharp,[25] who reported similar concerns with a traditional vacuum-assisted closure device and successful use of single-use PICO on 8 adult orthopedic patients. Issues with pain upon removal, site and size complexity, feasibility of use at home, and staff training issues in transferring patients to an area that does not routinely use NPWT led his team to the single-use NPWT device use. Sharp reported that all wounds healed, all patients reported decreased pain and more comfortable wear time using the single-use device, and all patients were able to be discharged earlier than anticipated based on experiences with the traditional unit. Neonatal nurses or physicians do not work with NPWT on daily basis. A need for specialized staff always arises if a traditional NPWT device is used. Maintenance and troubleshooting such a device always generate anxiety with my staff. We found improved confidence in our providers in their comfort and ability to work with a single-use NPWT device.

Limitations

This was a single-center, single-unit study of patients treated for congenital and acquired cardiac conditions. Patients were followed by a wound-certified intensive care unit physician and a consistent group of cardiac surgeons. Results may not be generalizable to every unit or all patients. Nevertheless, our sample represented a span of 3 years and patient diagnoses

Figure 4. Case 10. Progression of wound to closure. (A) Day 2 of dehiscence. Mechanical debridement completed and PICO was placed. (B) Status post 1 week of NPWT. (C) Day 18. NPWT indicates negative pressure wound therapy.

were varied. Data were collected retrospectively; in order to mitigate the risk for incomplete documentation of pertinent outcomes, we excluded patients with incomplete data. Perceptions concerning the ease of use of a device are subjective, and personal bias can influence such perceptions. A larger multisite trial, involving greater numbers and comparing traditional versus single-use NPWT devices, is recommended.

CONCLUSION

Findings suggest that the use of a single-use NPWT device and ALH facilitated dehiscent wounds closure in 11 neonates following complex cardiac surgery. Both components address immaturity of neonatal skin, support antimicrobial environment and moist wound bed preparation, and avoid cytotoxicity, all while decreasing the number of applications and pain upon placement and removal. In today's neonatal clinical practice, efficacy, safety, caretaker satisfaction, and portability are important elements. A combination of medical-grade honey and single-use NPWT checks all the boxes; therefore, I recommend considering this combination approach in treatment of dehisced wounds in neonates.

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