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Safety and Efficacy of Locally Manufactured Hypochlorous Acid Solution in the Management of Acute and Chronic Wounds in a Tertiary Public Hospital in the Philippines: A Single Arm Validation Study

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Chronic non-healing wounds represent a prevalent concern encountered at the Surgery Out-Patient Department of Valenzuela Medical Center, constituting a substantial portion of in-patient referrals from various medical specialties like Internal Medicine for collaborative management. Consequently, several institutions have established dedicated Wound Care Clinics, although such specialized facilities remain scarce across the Philippines. Compounded by the escalating incidence of conditions like Diabetes Mellitus, Immunosuppression, Peripheral Vascular Disease and Malnutrition which hinder wound healing, the challenge persists in effectively addressing the substantial patient load. Chronic wounds necessitate prolonged treatment periods, imposing significant financial burdens on patients seeking care at outpatient facilities. At our institution, we employ Hypochlorous (HOCl) Acid solution as one of the irrigating solutions for both acute and chronic non-healing wounds. Widely recognized in the medical field for its antiseptic properties, this solution finds versatile applications, including as nasal and pharyngeal sprays, intra-operative peritoneal lavage solutions, ocular solutions, hemodialysis solutions, peritoneal dialysates, intravenous fluids, fogging solutions for airborne pathogen sterilization, and as a topical treatment for wound care patients. This study endeavors to furnish substantial data on the effectiveness, cost-efficiency, and clinical safety of utilizing locally manufactured HOCl Acid in the management of non-healing wounds.

Index Terms—Acute Wounds, Chronic Wounds, Hypochlorous Acid, Wound Care

I. INTRODUCTION

The human body's immune system exhibits a remarkable ability to produce Reactive Oxygen Species (ROS), which are highly reactive chemicals pivotal in deactivating viruses and inducing cell death through various mechanisms. These include phagocytosis, loss of intracellular contents, reduced uptake of nutrients and oxygen, inhibition of protein synthesis, chlorination of amino acids, diminished DNA synthesis, decreased adenosine triphosphate production, and oxidation of sulfhydryl enzymes and amino acids [27].

The mitochondrial membrane-bound enzyme nicotinamide adenine dinucleotide phosphate-oxidase (NADPH) serves as a key catalyst for ROS generation. Upon neutrophil activation, respiratory bursts generate hydrogen peroxide (H2O2), and the activated granule enzyme myeloperoxidase (MPO) converts H2O2 to Hypochlorous Acid in the presence of chloride and hydrogen ions. Consequently, Hypochlorous Acid emerges as one of the most effective and prevalent oxidizing agents.

The physiological functions of Hypochlorous Acid extend both intracellularly and extracellularly. Extracellularly, it facilitates pathogen deactivation and taurine chlorination, while intracellularly, it induces oxidation, inhibits mature virions, and supports interleukin-6 depletion. Moreover, it stimulates mucosal cells in the respiratory tract and activates responses of the innate immune system. Its antibiofilm and antimicrobial properties are particularly effective against pre-existing biofilms commonly encountered in chronic wounds. Notably, Hypochlorous Acid serves as a natural biocide, exhibiting anti-bacterial, anti-fungal, anti-viral (including efficacy against COVID-19), anti-spore, and anti-prion activities. Current clinical evidence indicates that HOCl surpasses other widely recognized antiseptic solutions such as Chlorhexidine, Povidone Iodine, Gentamicin, Bacitracin, and Cefazolin in potency.

Hypochlorous acid topical solutions have undergone extensive examination through various in vitro and in vivo studies on microflora, correlating with the microbiological profile of chronic non-healing wounds. These investigations consistently

demonstrate a notable reduction in the growth of specific cultures, including Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, Candida albicans, and Escherichia coli. Remarkably, the efficacy of HOCl, as generated by neutrophils, is exemplified by its ability to swiftly neutralize 150 million E. coli bacteria within milliseconds, requiring only 2 x 10 log -7 mol HOCl.

Chronic non-healing wounds are characterized by a prolonged inflammatory phase during wound healing, which precedes the proliferative and regenerative stages. Various factors contribute to this delay, including systemic influences such as metabolic diseases like diabetes mellitus, systemic conditions like rheumatic diseases, chronic illnesses such as HIV, advanced age, malnutrition or inadequate diet, alcoholism, and medications like steroids. Additionally, local factors such as wound depth, edema, location, and necrosis further complicate healing processes. However, all chronic wounds exhibit a common feature: an escalation in both the quantity and diversity of microflora, necessitating the use of broad-spectrum antimicrobial agents. Hypochlorous Acid emerges as a valuable agent in wound care due to its ability to stimulate skin fibroblast and keratinocyte cell migration, as evidenced by wound healing assays.

One of the primary procedures performed by Wound Care Specialists or General Surgeons is wound debridement, which involves the removal of devitalized tissues from the wound bed. Surgical debridement entails the meticulous removal of necrotic debris using a sterile scalpel or scissors. Conversely, autolytic debridement involves introducing moisture to the wound bed and facilitating the enzymatic breakdown of sloughs.

Current solutions incorporate stabilized Hypochlorous Acid, serving as a biocide that effectively eliminates pathogens without harming healthy tissues. This limitation is founded on the time/pressure relationship for tissue damage, wherein increased pressure correlates with greater tissue damage, and prolonged contact exacerbates tissue injury [25].

II. SCOPE AND SIGNIFICANCE

The study enrolled subjects aged 18 years and above, admitted to the hospital and assessed by the Department of Surgery, male and female, with or without co-morbidities, within a timeframe of 6 months. Patients excluded from the study are those with documented Peripheral Arterial Occlusive Diseases, individuals who are immunocompromised (HIV+), and those diagnosed with pathologic dermatologic lesions.

Upon completion of the study, the researchers evaluated the effectiveness of irrigating HOCl solution by evaluating the percentage of wound size regression and the quality of discharge within 4 weeks of treatment initiation. Cost-effectiveness will be gauged by the rate of wound size regression. Faster wound recovery is anticipated to result in fewer outpatient department (OPD) visits over a shorter treatment duration, thereby reducing complications associated with chronic wounds such as sepsis and amputation as well as the overall cost of wound care. Any adverse reactions were also documented.

The primary objective is to establish the clinical safety and efficacy of locally manufactured Hypochlorous Acid Solution for the management of acute and chronic wounds. Specific objectives include determining the percentage of wound regression, average time to full recovery in weeks, and assessing the quality of wound discharge at the conclusion of treatment.

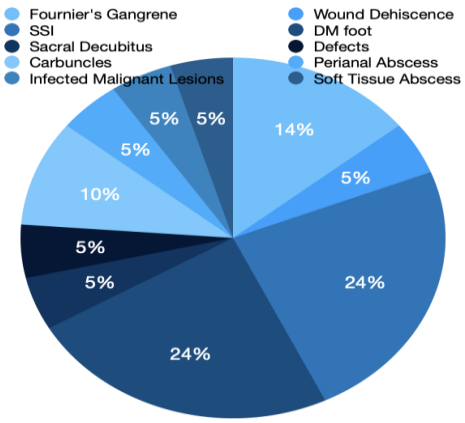
III. METHODOLOGY

The study adopted a single-arm design, with data collection conducted at the Department of Surgery of Valenzuela Medical Center in Karuhatan, Valenzuela City, Philippines. Progress for each subject was meticulously documented during every wound dressing session, commencing from the initial wound assessment until the completion of 4 weeks of treatment or until the wound achieved full healing. Wound care procedures were administered by the Wound Care Specialist or Surgery Resident Physician, and informed consent was obtained from all patients participating in the study. Data analysis involved evaluating reductions in healing time and wound size for each group.

IV. RESULTS

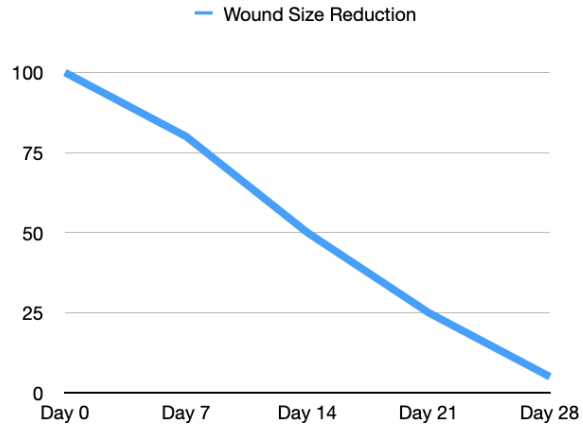
In this single-arm validation study, 20 complicated wound patients were selected and categorized based on the type of wound they presented with. The categorization included conditions such as Fournier’s gangrene, wound dehiscence, surgical site infection, diabetic foot ulcers, sacral decubitus pressure injuries, post-surgical wound defects, carbuncles,

perianal abscesses, infected malignant lesions, and other types of soft tissue abscesses. The following chart illustrates the incidence of these various types of wounds observed in the study.



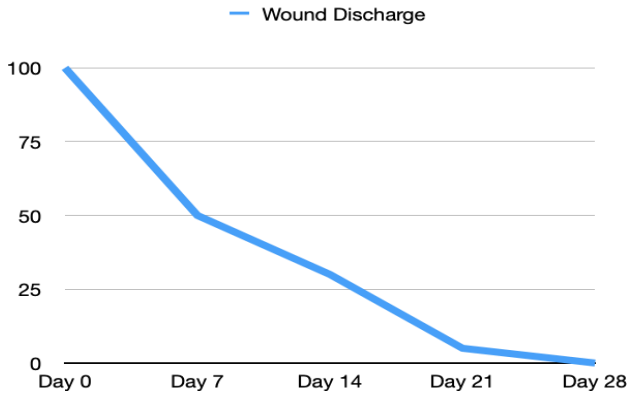
A. Effect on wound size reduction and time to full recovery

The treatment of chronic non-healing wounds with Hypochlorous Acid irrigating solution resulted in a significant reduction in wound size from Day 0 of application to Day 14 of observation. HOCl was applied once daily and the circumference of the wound was measured. The y-axis represents the size in centimeters, while the x-axis indicates the duration of HOCl solution usage in these patients. The data in the following graphs demonstrate wound size reduction of up to 20% as early as week 1 of usage, with nearly 95% reduction observed by week 4.



B. Effect on wound discharge

Given that heavy exudative discharge is a characteristic of chronic non-healing wounds, the elimination of biofilms on the wound bed was monitored from weeks 1 to 4 (x-axis) through qualitative measurement (heavy, moderate, light, no discharge). The mean data was obtained from the average day when the wound beds exhibited light or almost zero discharge. The graph illustrates that reduction in exudative discharge was observed as early as Day 3 of usage.



V. Case Series Documentation

Index Patient I is a case of a 35-year-old female who underwent a Caesarian Section procedure at a tertiary government hospital. During a follow-up visit at the Outpatient Department (OPD) of the Obstetrics and Gynecology (OBYNE) department, the patient was found to have wound dehiscence at the surgical site, exposing the deep fascia. Consequently, the patient was referred to the Surgery Department for co-management. Daily wound care was provided for a duration of 4-8 weeks, resulting in a remarkable 98% regression of the wound with robust skin granulation observed.

Index Patient II is a case involving a 50-year-old male who presented at the Emergency Department (ED) due to severe perianal pain. Upon admission, the working impression was a perianal abscess. The patient underwent incision and drainage at the Operating Room (OR), followed by post-operative wound care at the bedside. The wound was irrigated with HOCl daily until discharge. Subsequently, the patient followed up on Postoperative Day (POD) 14, showing 95% wound closure.

Index Patient III involves a patient admitted with Fournier's Gangrene who underwent one episode of wound debridement under anesthesia. Following this procedure, the patient received daily wound care for a duration of 2 weeks. Significant improvement of the wound was noted during this period, with granulation observed on the wound bed, approximating 95%.

Index Patient IV is a case of 51/M admitted due to giant carbuncle on the back measuring 30cm x 25cm in diameter and approximate depth of 5cm with history of uncontrolled DM. Patient underwent multiple series of wound debridement and application of HOCL as intraoperative irrigating and post-operative bedside solution. Marked improvement with good granulation was observed until Day 21 which subsequently subjected to split-thickness skin grafting for final skin coverage procedure.

Index Patient V is a case of 50/M admitted due to scrotal abscess. HOCL irrigating solution was used daily and marked improvement was noticed as early as 7th day of admission.

VI. DISCUSSION

All chronic wounds should be assumed to be contaminated, and the level of wound bioburden is a crucial factor in determining wound healing. Therefore, reducing the bioburden in every wound is an essential component of wound care. Biofilms contribute to bioburden through the dense and impervious glycocalyx matrix secretion they produce. Biofilms are the main cause of delayed chronic wound healing. Their formation is believed to create a self-perpetuating cycle, prolonging the presence of macrophages and neutrophils in the wound, which in turn impairs normal wound healing and potentially reduces the effectiveness of innate immunological responses. Treatment with HOCl affects biofilms by modifying their structure, facilitating access of HOCl and other bactericides to local bacteria, thereby potentially benefiting the treatment of chronic wounds. Biofilms can be degraded through debridement by exposing constituent bacterial flora, making treating agents more effective as the biofilm regrows.

Hypochlorous Acid offers efficacy with relatively low cytotoxicity. Its therapeutic index (TI), or antimicrobial effectiveness over cytotoxicity, is typically much higher than that of sodium hypochlorite or hydrogen peroxide for key bacterial pathogens. Since chronic wounds often do not progress through the proper physiologic stages of wound healing and become stagnant only at the inflammation stage, studies have shown complete antibiotic activity in in vitro studies against Pseudomonas aeruginosa, Staphylococcus aureus, and Candida albicans, with permissive effects on keratinocyte and fibroblast migration and replication.

In biological systems, hypochlorous acid is considered the most effective and most common oxidizing agent. It is one of the foremost endogenous molecules for effective phagocytosis of invading bacteria and viruses. HOCl exhibits high activity against all bacterial, viral, and fungal pathogens, including spores. Even in trace amounts, aqueous solutions of HOCl can kill pathogens within 30 seconds of exposure.

HOCl exhibits no cellular toxicity when used in clinically effective dosages. It has been widely reported that the human body regulates the levels of HOCl during the inflammatory response using its own 'antioxidant-defense' system based on

scavenger molecules, such as taurine and nitrites, which diminish or neutralize HOCl and protect against oxidative damage to cells.

VII. CONCLUSION

The efficacy of stabilized Hypochlorous Acid (HOCl) as an irrigating solution has been well-established in various types of chronic non-healing wounds, including Fournier's gangrene, wound dehiscence, surgical site infections, diabetic foot ulcers, sacral decubitus pressure injuries, carbuncles, perianal abscesses, infected malignant lesions, large post-surgical wound defects, and other soft tissue abscesses. This effectiveness has been demonstrated by reductions in the percentage of wound size, decreased time to full healing, and elimination of exudative discharge within a 4-week period in patients treated at a Tertiary Government Hospital in Karuhatan, Valenzuela City. Furthermore, no cytotoxicity related to the HOCl solution was observed or recorded during these treatments.

RECOMMENDATION

The authors recommend further studies on Hypochlorous Acid Irrigating Solution using control groups (such as a normal saline group, povidone-iodine group, chlorhexidine group, etc.). Additionally, the authors propose investigating the efficacy of Hypochlorous Acid Solution in treating various types of wounds, including partial thickness burns, post-appendectomy irrigation, peritoneal lavage for exploratory laparotomy, and as a solution for pre-surgical skin preparation. These suggestions are intended to undergo further clinical trials to expand our understanding of the applications and effectiveness of Hypochlorous Acid Solution in wound management across different clinical scenarios.

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