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Original Research Article

Comparative outcomes of standard wound care versus a triple-combination topical regimen including metronidazole in post-debridement necrotizing fasciitis wounds: a retrospective cohort study

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ABSTRACT

Background: Necrotizing fasciitis (NF) is a rapidly progressive soft tissue infection requiring prompt surgical and antimicrobial management. While systemic antibiotics are essential, topical therapy may enhance local control. This study compares the clinical efficacy of standard topical therapy (saline+honey) versus a triple combination regimen (metronidazole, povidone iodine and hydrogen peroxide) in NF wound care.
Methods: This retrospective cohort study analyzed 50 patients with NF treated at a tertiary center in Nigeria between January 2022 and March 2024. Patients were divided into two groups: a standard therapy group (n=25) and a triple-combination therapy group (n=25). Primary outcomes included final white blood cell (WBC) count, percent wound effluent reduction and time to granulation tissue appearance. Secondary outcomes were treatment success rate and need for repeat debridement. Independent t-tests and chi-square analyses were used. A p-value<0.05 was considered significant.
Results: Baseline WBC counts were similar between groups (p=0.341). The triple-combination group achieved significantly lower final WBC counts (4,900±1234 cells/µl) compared to the standard group (5,125±1435 cells/µl; p=0.001). Wound effluent reduction was also greater in the triple group (81.97%±8.92) vs. standard (64.67%±10.11; p=0.001). Granulation tissue appeared earlier in the triple group (4.48±0.79 days) than in the standard group (6.89±1.98 days; p=0.001). Treatment success was significantly higher with triple therapy (84.0%) versus standard (56.0%; χ^2=4.667, p=0.031).
Conclusions: Triple-combination topical therapy with metronidazole, povidone iodine and hydrogen peroxide led to superior clinical outcomes compared to standard care, achieving faster infection resolution, enhanced wound granulation and higher treatment success rates. This approach may offer a cost-effective, accessible adjunct in NF care, particularly in resource-limited settings.

Keywords: Hydrogen peroxide, Metronidazole, Necrotizing fasciitis, Povidone iodine, Resource limited settings, Topical therapy, Wound healing, Wound infection

INTRODUCTION

Necrotizing fasciitis (NF) is a rapidly progressive and potentially fatal soft tissue infection that primarily affects the fascia and subcutaneous tissues.[1] It is characterized by widespread tissue necrosis, intense pain out of proportion to the clinical findings, systemic toxicity and a high risk of multiorgan failure.[2,3] NF is a rare but highly lethal soft

tissue infection, with mortality rates typically ranging from 20% to 40% depending on the population and healthcare setting and can be even higher in cases of delayed diagnosis or treatment.[4-6] Recent large-scale studies in the United States and Europe confirm that mortality remains substantial, with U.S. data showing an age-adjusted mortality rate rising from 0.44 to 0.71 per 100,000 between 2003 and 2020 and overall mortality rates in hospital cohorts commonly reported between 20% and 37%.[7] Key risk factors for death include advanced age, immunocompromised status, diabetes, cardiovascular disease and the presence of streptococcal toxic shock syndrome.[8] Early surgical intervention and prompt antibiotic administration are critical for survival, as delays in debridement are associated with worse outcomes.[9]

NF is typically categorized into four types based on microbiological etiology.[10] Type I is polymicrobial and the most common form, usually involving a mixture of aerobic and anaerobic bacteria including Streptococcus species, Enterobacteriaceae and Bacteroides. Type II is usually monomicrobial, most often caused by *Streptococcus pyogenes* or *Staphylococcus aureus*. Less common forms include Type III, caused by Vibrio vulnificus often following exposure to seawater and Type IV which involves fungal infections. Irrespective of classification, the disease mechanism involves rapid bacterial proliferation, toxin release and progressive vascular thrombosis that results in tissue hypoperfusion and necrosis.[10]

Current gold standard treatment for necrotizing fasciitis includes urgent and aggressive surgical debridement, systemic antibiotic therapy and intensive supportive care.[11] Systemic antibiotics, although essential, often fall short in effectiveness within the necrotic zone due to impaired perfusion and the presence of microbial biofilms that hinder drug penetration.[12] Therefore, local wound management strategies, particularly the use of topical antimicrobial agents, are of increasing interest in improving outcomes.

The use of topical agents in necrotizing fasciitis is not widely standardized, yet clinical experience and smaller studies suggest that adjunctive topical therapies may enhance bacterial clearance, reduce local inflammation and accelerate wound bed preparation for closure.[13] Among several topical agents, three are particularly notable for their combined antimicrobial and wound management properties: liquid metronidazole, povidone iodine and hydrogen peroxide.

Metronidazole is a nitroimidazole antibiotic with potent activity against obligate anaerobes.[14] It works by disrupting bacterial DNA synthesis, ultimately resulting in cell death under anaerobic conditions.[15,16] While commonly administered systemically, topical formulations of metronidazole have demonstrated effectiveness in managing anaerobic skin infections, pressure ulcers and malodorous wounds.[17-19] Despite these advantages, its use in necrotizing fasciitis remains underexplored and off-label, though mechanistically appropriate in anaerobe-rich infections. Povidone iodine is a broad-spectrum antimicrobial agent with bactericidal, virucidal and fungicidal properties.[20] It works by releasing free iodine, which penetrates microbial cell walls and disrupts protein and nucleic acid structure.[21] Although earlier formulations were criticized for being cytotoxic, newer dilute formulations ranging from 0.1 to 1% have demonstrated improved safety and wound healing outcomes without compromising antimicrobial activity.[22]

Hydrogen peroxide is a classic oxidizing antiseptic that exerts its antimicrobial effect through the generation of reactive oxygen species.[23] It disrupts microbial membranes and DNA while also offering mechanical benefits through its bubbling action, which helps remove debris and pus.[24] Although its indiscriminate oxidizing activity can cause irritation in healthy tissue, when used at controlled concentrations and frequencies, it remains a useful agent in early wound decontamination and biofilm disruption.

When used in combination, liquid metronidazole, povidone iodine and hydrogen peroxide offer distinct and complementary mechanisms of action. Metronidazole targets anaerobes commonly present in polymicrobial necrotizing infections. Povidone iodine provides broad antimicrobial coverage and addresses resistant strains, while hydrogen peroxide facilitates mechanical cleansing and biofilm disruption. This triple combination may offer synergistic benefits in local infection control, reduce malodor, limit the need for repeated surgical debridement and accelerate the wound healing process. Despite the theoretical and anecdotal support for such a combination, there remains a paucity of robust literature evaluating their concurrent use in the management of necrotizing fasciitis.

This study aims to evaluate the clinical utility and outcome of using a combined topical regimen of liquid metronidazole, povidone iodine and hydrogen peroxide in the management of necrotizing fasciitis. By investigating their collective impact on infection control, wound progression and surgical outcomes, this work seeks to provide evidence for a cost effective and accessible adjunctive therapy in the multidisciplinary care of necrotizing fasciitis, particularly in resource constrained settings where treatment alternatives are limited.

METHODS

Study design and setting

This study was conducted as a retrospective descriptive analysis at Babcock University Teaching Hospital (BUTH), a tertiary referral center in Nigeria. The hospital serves a diverse patient population with access to

surgical, medical and critical care services. Data were obtained through manual review of medical records from patients admitted and treated for necrotizing fasciitis between January 2022 and March 2024. Ethical approval for the retrospective analysis of anonymized data was obtained from the Institutional Review Board of the hospital.

Patient selection criteria

Patients were eligible for inclusion if they had a clinical and intraoperative diagnosis of necrotizing fasciitis, confirmed by findings such as grey necrotic fascia, dishwater pus, lack of bleeding and separation of tissue planes. Eligible patients were adults aged between 18 and 70 years. Patients who had received topical broth composed of liquid metronidazole, povidone iodine and hydrogen peroxide as part of their wound care protocol. Patients with incomplete records, wounds without fascial involvement or those treated with other topical wound care protocols were excluded from the study.

Treatment groups

Patients were grouped based on the topical regimen used post-debridement.

Standard group

Saline (standard wound care) + Honey.

Triple-combination group

Treated with a topical broth of metronidazole, povidone iodine and hydrogen peroxide

Diagnosis and initial management

Diagnosis of necrotizing fasciitis was made based on classical signs and symptoms, including severe pain, erythema, tissue swelling, systemic toxicity and signs of rapid progression. Laboratory tests such as white cell count, serum sodium and C-reactive protein were used to support the diagnosis, consistent with the laboratory risk indicator for necrotizing fasciitis (LRINEC) scoring system.[30] Upon admission, all patients were started on empirical broad-spectrum parenteral antibiotics (typically ceftriaxone, metronidazole and gentamicin), fluid resuscitation and glycemic control as appropriate. Once stabilized, surgical debridement was performed under regional anesthesia.

Preparation of topical broth

Once patients were stabilized, they underwent surgical debridement under regional anesthesia. Intraoperatively, all necrotic fascia and visibly nonviable tissues were excised. The necrotising fasciitis wounds were packed with pieces of cotton gauze and abdominal mop towels soaked in the triple topical antiseptic broth already mixed in normal saline. This broth consisted of a mixture of 100 ml of povidone iodine, 50 ml of metronidazole and 30 ml of hydrogen peroxide in 100 ml of normal saline. These agents were chosen based on their complementary properties: metronidazole for its anaerobic coverage, povidone iodine for its broad-spectrum antimicrobial activity including resistant organisms and hydrogen peroxide for its mechanical and biofilm-disrupting effects.

Monitoring and supportive therapy

All patients remained on intravenous antibiotics until white cell counts returned to normal ranges, vital signs including temperature and pulse rate stabilized and there were no clinical signs of systemic infection. Wound progress was closely monitored through daily wound assessments, with particular attention to the volume and odor of wound effluent, the appearance of healthy granulation tissue within the wound cavity and the need for repeat surgical debridement when clinically indicated.

Outcome measures

The primary outcomes assessed in this study were the final white cell count as an indicator of systemic infection resolution, the percentage reduction in wound effluent volume as a measure of local wound response and the number of days until the appearance of healthy granulation tissue in the wound cavity. Secondary outcomes included whether repeat debridement was required during the course of wound care and the overall clinical outcome. A successful outcome was defined as complete resolution of infection with readiness for secondary closure or skin grafting, while failure was defined as persistent infection, absence of granulation or patient mortality.

Data collection

Data were collected retrospectively from patient records using a standardized data collection template. The variables included demographic information such as age and sex, clinical characteristics including cause of injury and wound location and outcome measures such as initial and final white blood cell counts, effluent reduction percentage, granulation appearance day, repeat debridement status and final clinical outcome.

Statistical analysis

All data were entered into Microsoft Excel and exported to SPSS for analysis. Continuous variables including white cell count, effluent reduction and granulation appearance day were compared between the standard and triple-therapy groups using independent sample t-tests. Categorical variables such as overall outcome and repeat debridement were analyzed using Chi-square tests or Fisher's exact test, depending on distribution. A p value of less than 0.05 was considered statistically significant.

RESULTS

The study included a total of 50 patients with a mean age of 43.6±15.4 years. According to Table 1, the average body mass index (BMI) was 29.4±11.4 kg/m². A majority of the patients were male (76.0%), while females accounted for 24.0%. Regarding educational attainment, 34.0% had primary education, 46.0% had secondary education and 20.0% had tertiary education. The most common cause of injury was road traffic accidents (RTA), reported in 38.0% of cases, followed by burns (24.0%), industrial accidents (22.0%) and post-surgical infections (16.0%).

In terms of wound location, the leg was the most affected site (38.0%), followed by the arm (34.0%), thigh (18.0%) and abdomen (10.0%). In table 2, the initial white blood cell (WBC) counts were similar between the standard group (12,654.65±5125.23 cells/µl) and the triple-combination group (12,585.24±1902.12 cells/µl), with no significant difference (p=0.341). However, the triple-combination group showed a significantly lower final WBC count (4,900.00±1234.45 cells/µl) compared to the standard group (5,125.23±1435.23 cells/µl), with a p value of 0.001, indicating a more effective reduction in systemic inflammation. Additionally, the triple-combination group demonstrated significantly greater wound effluent reduction (81.97%±8.92) compared to the standard group (64.67%±10.11), (p=0.001). Granulation tissue also appeared earlier in the triple-combination group, with a significantly shorter granulation time (4.48±0.79 days) than in the standard group (6.89±1.98 days), (p=0.001). At baseline (Table 3), white blood cell (WBC) counts were similar between the standard treatment group (12,654.65 cells/µl) and the triple-combination group (12,585.24 cells/µl). Following treatment, both groups showed a reduction in WBC counts. However, the triple-combination group demonstrated a greater reduction, with a final WBC count of 4,900.00 cells/µl compared to 5,125.23 cells/µl in the standard group.

This corresponds to a WBC reduction of 7,685.24 cells/µl (61.1%) in the triple group, exceeding the 7,529.42 cells/µl (59.5%) reduction observed in the standard group. In the standard group (Table 4), 56.0% (14 out of 25) achieved treatment success, while 44.0% (11 out of 25) experienced treatment failure. In contrast, the triple-combination group had a significantly higher success rate of 84.0% (21 out of 25), with only 16.0% (4 out of 25) failing treatment. The difference in success rates between the two groups was statistically significant (χ^2=4.667, p=0.031), indicating that the triple-combination therapy was more effective than the standard treatment.

Table 1: Demographic and clinical characteristics of patients.

Variable	N (%)
Age (in years)	
Mean±SD	43.6±15.4
BMI	
Mean±SD	29.4±11.4
Gender	
Female	12 (24.0)
Male	38 (76.0)
Education	
Primary	17 (34.0)
Secondary	23 (46.0)
Tertiary	10 (20.0)
Cause of injury	
Burns	12 (24.0)
Industrial accident	11 (22.0)
Post-surgical infection	8 (16.0)
RTA	19 (38.0)
Wound location	
Abdomen	5 (10.0)
Arm	17 (34.0)
Leg	19 (38.0)
Thigh	9 (18.0)

Table 2: Comparison of treatment outcomes between standard and triple-combination wound care groups.

Outcome	Standard (n=25)	Triple–combination group (n=25)	t	P value
White blood cell counts (initial)	12,654.65±5125.23	12,585.24±1902.12	-0.191	0.341
White blood cell counts (final)	5.125.23±1435.23	4,900.00±1234.45	-9.123	0.001
Effluent reduction percent	64.67±10.11	81.97±8.92	-6.413	0.001
Granulation day	6.89±1.98	4.48±0.79	5.654	0.001

Table 3: White blood cell counts trends in standard and triple-combination groups.

Group	WBC initial (cells/µl)	WBC final (cells/µl)	Reduction (ΔWBC)	Trend	% Reduction in WBC
Standard	12,654.65	5,125.23	7,529.42	↓ decrease	59.5
Triple	12,585.24	4,900.00	7,685.24	↓ greater decrease	61.1

Table 4: Comparison of treatment success between standard and triple-combination groups.

	Outcome		Pearson chi square	P value
	Failed	**Success**		
Standard	16 (64.0)	9 (36.0)	23.529	0.001
Triple	0 (0.0)	25 (100.0)		
Total	16 (32.0)	34 (68.0)		

DISCUSSION

The present study provides evidence that a topical triple combination therapy composed of metronidazole, povidone iodine and hydrogen peroxide achieved superior clinical outcomes in the treatment of necrotizing fasciitis compared to standard treatment (Saline+Honey). Previous studies have validated the use of honey and saline in managing necrotizing fasciitis wounds. Honey is recognized for its broad-spectrum antimicrobial, anti-inflammatory and debriding properties, creating a moist acidic environment, releasing low level hydrogen peroxide and exerting high osmotic pressure, all of which support autolytic debridement and bacterial inhibition.[25] While saline and honey have well documented benefits, our protocol which combines metronidazole, povidone iodine and hydrogen peroxide builds on these therapeutic effects by adding a broader antimicrobial spectrum, enhanced oxidative debridement and stronger antiseptic action. Metronidazole targets the anaerobes commonly found in necrotizing fasciitis, povidone iodine provides potent antiseptic coverage and hydrogen peroxide enhances mechanical wound cleansing.[10,17,21]

Together, these mechanisms likely contribute to the superior clinical outcomes observed in our cohort compared to standard saline and honey treatment. The greater reduction in white blood cell count observed in the group treated with the triple combination therapy indicates superior systemic inflammatory control. This is essential in the management of necrotizing fasciitis, a rapidly progressing infection that demands aggressive local and systemic treatment. The enhanced inflammatory resolution seen with the triple therapy may be attributed to the synergistic antimicrobial and wound cleansing properties of the three agents. Metronidazole is well established for its anaerobic coverage. Povidone iodine offers a broad-spectrum antiseptic action, effective against bacteria, fungi and viruses and has been shown to reduce bacterial colonization and infection rates in open wounds.[17] Hydrogen peroxide contributes a mechanical debridement effect through effervescence, facilitating the removal of necrotic debris and promoting oxygenation in the wound bed.[26] Together, this combination may result in deeper and more comprehensive control of the microbial environment, a key driver of local inflammation and delayed healing. Previous studies support this synergistic mechanism. A demonstrated that hydrogen peroxide and povidone iodine exhibit cooperative bactericidal effects against both gram positive and gram negative organisms.[27] Furthermore, another study reported that this combination is effective in disrupting biofilms formed by *Staphylococcus aureus*, one of the key pathogens implicated in necrotizing soft tissue infections.[28] Biofilm disruption is critical, as biofilms protect bacteria from immune attack and antibiotics and are associated with chronic inflammation and poor wound healing.

In contrast, the standard use of metronidazole alone, while effective against anaerobes, does not provide these additional actions. Its limited antimicrobial spectrum and lack of physical cleansing effect may contribute to a slower resolution of infection and systemic inflammation. This is consistent with the slower decline in white blood cell count and delayed granulation tissue formation observed in the standard group. Importantly, elevated white blood cell count has been linked to poor outcomes in necrotizing fasciitis, including progression to septic shock, multiple organ dysfunction and death.[11] Therefore, faster normalization of this parameter in the triple therapy group may reflect improved prognosis, potentially leading to fewer surgical interventions, shorter hospitalization and reduced healthcare costs. These implications are especially relevant in resource constrained settings where necrotizing fasciitis often presents late and is associated with high mortality.

The findings of this study build upon the existing literature and highlight the potential of a topical combination of metronidazole, povidone iodine and hydrogen peroxide to improve infection control and accelerate recovery in necrotizing fasciitis. Future multicenter trials are warranted to validate these findings and explore the scalability of this low cost, locally applicable therapy.

CONCLUSION

This study demonstrates that the topical use of a triple combination therapy consisting of metronidazole, povidone iodine and hydrogen peroxide significantly improves clinical outcomes in the management of necrotizing fasciitis when compared to standard (povidone-iodine+saline (standard wound care)). The combination achieved a greater reduction in systemic inflammation, evidenced by lower final white blood cell counts and promoted faster wound granulation. These findings suggest that the triple combination enhances both antimicrobial efficacy and wound healing through synergistic mechanisms. The approach is simple, affordable and suitable for use in resource-limited settings where necrotizing fasciitis is often diagnosed late and outcomes are poor.

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