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A comparative study to assess the clinical outcomes of conventional Eusol dressing versus triple combination (metronidazole, povidone iodine and hydrogen peroxide) topical dressing in Necrotizing Fasciitis Wounds in a tertiary care hospital

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ABSTRACT

Background/ introduction:

Necrotizing fasciitis (NF) is a rapidly progressive potentially life-threatening soft tissue infection requiring prompt surgical and antimicrobial management. Both systemic antibiotics and topical therapy is essential in its management. Various materials like Edinburgh University's solution of lime (EUSOL), normal saline, povidone-iodine and honey have been used as dressing solutions for necrotizing fasciitis. This study compares the clinical efficacy of Eusol dressing versus triple combination (metronidazole, povidone iodine and hydrogen peroxide) topical dressing in Necrotizing Fasciitis Wounds in NF wound care.

Methods:

A randomized clinical trial was conducted at a tertiary care centre in Northern India between Jan 2024 to March 2026 after approval by the ethical committee of the institution. Based on the dressing solution for necrotizing fasciitis, patients were divided into two groups, The EUSOL group contains 50 patients, and TRIPLE COMBINATION GROUP OF 50 patients. Primary outcomes included final white blood cell (WBC) count, percent wound effluent

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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 conventional EUSOL group (5,125±1435 cells/µl; p=0.001). Wound effluent reduction was also greater in the triple group (81.97%±8.92) vs. EUSOL group (64.67%±10.11; p=0.001). Granulation tissue appeared earlier in the triple group (4.48±0.79 days) than in the EUSOL group (6.89±1.98 days; p=0.001). Treatment success was significantly higher with triple therapy (84.0%) versus EUSOL (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 EUSOL group, achieving faster infection resolution, enhanced wound granulation and higher treatment success rates. This approach may offer an accessible adjunct in NF care, particularly in resource-limited settings.

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

INTRODUCTION

Necrotizing fasciitis (NF) is a severe, rapidly progressing and potentially fatal infection of the soft tissue and fascia associated with significant morbidity and mortality. Reported mortality rates vary widely but a Danish nationwide cohort study including over 1500 patients found 30-day and 1-year mortality rates of up to 26% and 40%, respectively.[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]

It is rare but very lethal soft tissue infection with high mortality rates ranging from 20% to 40% depending on the population and healthcare setting and can be even higher in cases of delayed diagnosis or treatment. [3,4] Recent studies in the United States and Europe confirm that mortality remains substantial, with U.S. data showing an age-adjusted mortality rate rising

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from 0.44 to 0.71 per 100,000 between 2003 and 2020 and overall mortality rates in hospital cohorts between 20% and 37%.[5]

Key risk factors for death include advanced age, immunocompromised status, diabetes, cardiovascular disease and the presence of streptococcal toxic shock syndrome. Early surgical intervention(debridement) and prompt antibiotic administration are critical for survival. [6] NF is typically categorized into four types based on microbiological etiology. Type I (most common) is polymicrobial, 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. [7]

Current treatment for necrotizing fasciitis includes appropriate intravenous antibiotics with urgent radical surgical debridement. A *second look* operation is usually planned in 24–48 hours depending on clinical response. [8]

So, multiple, urgent and aggressive surgical debridements along with systemic antibiotic therapy and intensive supportive care may be required. Systemic antibiotics, although essential, often fall short in effectiveness within the necrotic zone due to impaired perfusion and the presence of biofilms that hinder drug penetration.[9] Therefore, local wound management, particularly topical antimicrobial agents, are of increasing interest in improving outcomes.

The conventional dressing is done with Edinburgh University's solution of lime (EUSOL). EUSOL is an antiseptic solution composed of chlorinated lime and boric acid. Removing slough and necrotic tissue from the wound is used as a surgical dressing and promotes wound healing.

Topical agents use in necrotizing fasciitis is not widely standardized, yet clinical smaller studies suggest that adjunctive topical therapies may enhance bacterial clearance, reduce local inflammation and accelerate wound bed preparation for closure.[10] Among several topical agents, three are notable for their combined antimicrobial and wound management properties: liquid metronidazole, povidone iodine and hydrogen peroxide. Metronidazole, a nitroimidazole

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antibiotic with activity against obligate anaerobes, works by disrupting bacterial DNA synthesis, resulting in cell death under anaerobic conditions. [11,12]

Commonly administered topical formulations of metronidazole have demonstrated effectiveness in managing anaerobic skin infections, pressure ulcers and malodorous wounds. [13,14] Despite these advantages, its use in necrotizing fasciitis remains underexplored though it is effective and appropriate in anaerobic infections.

Povidone iodine is a broad-spectrum antimicrobial agent with bactericidal, virucidal and fungicidal properties. [15] It works by releasing free iodine, which penetrates microbial cell walls and disrupts protein and nucleic acid structure. [16]

Hydrogen peroxide is a classic oxidizing antiseptic that exerts its antimicrobial effect through the generation of reactive oxygen species. It disrupts microbial membranes and DNA while also offering mechanical benefits through its bubbling action, which helps remove debris and pus. [17] 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. The aim of this study is to compare the effects of dressings with conventional EUSOL and triple combination (metronidazole, povidone iodine and hydrogen peroxide) in the management of NF wounds. 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 care of necrotizing fasciitis, particularly in resource constrained settings where treatment alternatives are limited.

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METHODS:

Study design and setting

A prospective, randomized clinical study trial was conducted from Jan 2024 to March 2026 to compare the effects of dressing with EUSOL or triple combination (metronidazole, povidone iodine and hydrogen peroxide) in managing NF wounds in the Surgery department of Government Medical College, Amritsar (India) after approval from Ethics Committee. After giving their informed consent, patients were randomly assigned to one of the two groups.

Group A: conventional EUSOL group, 50 pts

Group B: triple combination group, 50 pts

Patient selection criteria

Inclusion criteria included adults (18-70 years) with a clinical or intraoperative diagnosis of NF.

After giving their informed consent, patients were randomly assigned to one of the two groups with Group A underwent conventional EUSOL dressing and Group B received topical triple combination dressing 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: EUSOL Group

Triple-combination group: Treated with topical 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.[18] UPON admission, all patients were started on empirical broad-

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spectrum parenteral antibiotics (typically ceftriaxone, metronidazole and Amikacin), fluid resuscitation and glycaemic control as appropriate. Once stabilized, surgical debridement was performed under regional anaesthesia.

Preparation of topical broth: Once patients were stabilized, they underwent surgical debridement under regional anaesthesia. Intraoperatively, all necrotic fascia and visibly nonviable tissues were excised. The necrotising fasciitis wounds were packed with 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 100ml of povidone iodine, 50ml of metronidazole and 30ml of hydrogen peroxide in 100ml 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 TLC counts returned to normal ranges, vital signs 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 TLC 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 from patient using a standardized data collection template. The variables included demographic information, clinical characteristics including cause of injury and wound

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location and outcome measures such as initial and final TLC 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 analysed using Chi-square tests or Fisher's exact test, depending on distribution. A p-value less than 0.05 was considered statistically significant.

RESULTS

The study included a total of 100 patients with a mean age of 44.4±14.2years. According to Table 1, the average body mass index (BMI) was 28 ± 10.2kg/m². Majority of the patients were male (76.0%), while females accounted for 24.0%. 34.0% had primary education, 46.0% had secondary education and 20.0% had tertiary education. Road traffic accidents (RTA) were most common cause of injury, reported in 42.0% of cases, followed by burns (28.0%), industrial accidents (24.0%) and post-surgical infections (6.0%). Leg was the most affected site (48.0%), followed by the arm (28.0%), thigh (16.0%) and abdomen (8.0%).In table 2, the initial Total leucocyte counts(TLC) 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), TLC 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 TLC reduction of 7,685.24 cells/µl(61.1%) in the triple

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group, exceeding the 7,529.42 cells/µl(59.5%) reduction observed in the standard group. In the standard group (Table 4), 56.0% (28 out of 50) achieved treatment success, while 44.0% (22 out of 50) experienced treatment failure. In contrast, the triple-combination group had a significantly higher success rate of 84.0% (42 out of 50), with only 16.0% (8 out of 50) 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 presentation of patients

VARIABLE	N (%)
Age (in yrs)	
Mean ± SD	44.4±14.2
BMI	
Mean ± SD	28 ± 10.2
Gender	
Male	76(76.0)
Female	24(24.0)
Educational status	
Primary	34(34)
Secondary	46(46)
Higher	20(20)
Cause of injury	
Road traffic accidents	42(42)
Industrial accidents	28(28)
Burns	24(24)
Post surgical infections	6(6)
Location of wound	
Legs	48(48)
Arms	28(28)
Thigh	16(16)
Abdomen	8(8)

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TABLE 2 : Comparison of treatment outcome between Group A(standard) and Group B(triple combination group)

Outcome	Group A(n=50)	Group B(n=50)	t	p-value
TLC(initial)	12654.6 ± 5125.2	12585.2 ± 1902.1	-0.191	0.341
TLC(final)	5125.2 ± 1435.2	4900.0 ± 1234.4	-9.123	0.001
Effluent reduction percent	64.6 ± 10.1	82.0 ± 8.9	-6.413	0.001
Granulation day	6.9 ± 2.0	4.5 ± 0.8	5.654	0.001

Table 3: TLC (WBC Count) trends in group A (standard) and group B (triple combination group)

Group	TLC initial per µl	TLC final per µl	Reduction (of TLC)	Trend	% reduction in TLC
A	12654.65	5125.23	7529.42	Decrease	59.5
B	12585.24	4900	7685.24	Decrease	61.1

Table 4: comparison of treatment success between group A (standard) and group B (triple combination group)

	Outcome	
	Failed	Success
Standard	22(44.0)	28(56.0)
Triple group	8(16.0)	42(84.0)
Total	30(30.0)	70(70.0)

χ^2=4.667, p=0.031, p-value < 0.05

DISCUSSION

The present study provides evidence that 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 (EUSOL). Previous studies have validated the use of EUSOL in managing necrotizing fasciitis wounds. EUSOL is an antiseptic solution composed of chlorinated lime and boric acid. Removing slough and necrotic tissue from the wound is used as a surgical dressing and promotes wound healing.

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While EUSOL has well documented benefits, our protocol which combines metronidazole, povidone iodine and hydrogen peroxide builds on these therapeutic effects by adding 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.[7,13,16] Together, these mechanisms likely contribute to the superior clinical outcomes observed in our study as compared to standard EUSOL treatment. The greater reduction in white blood cell count observed in the group treated with the triple combination therapy indicates superior inflammatory control which 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.[13] Hydrogen peroxide contributes a mechanical debridement effect through effervescence, facilitating the removal of necrotic debris and promoting oxygenation in the wound bed.[19] Together, this combination 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.[20] 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.[21] 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 treatment has limited antimicrobial spectrum and it may contribute to a slower resolution of infection and systemic inflammation. This is consistent with the slower decline in WBC count and delayed granulation tissue formation observed in the standard group. Importantly, elevated TLC count has been linked to poor outcomes in necrotizing fasciitis, including progression to septic shock, multiple organ dysfunction and death.[22]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

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late and is associated with high mortality. The findings of this study build upon the existing literature and highlight the potential of topical combination of metronidazole, povidone iodine and hydrogen peroxide to improve infection control and accelerate recovery in necrotizing fasciitis. Future multicentred 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 triple combination therapy consisting of metronidazole, povidone iodine and hydrogen peroxide significantly improves clinical outcomes in the management of necrotizing fasciitis when compared to conventional EUSOL therapy. The combination achieved a greater reduction in systemic inflammation, evidenced by lower final WBC 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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Ethical approval: The study was approved by the Institutional Ethics Committee

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