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Potassium permanganate in treatment of diabetic foot ulcer: A randomized clinical trial

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Abstract

Background and Aims: Diabetic foot ulcers (DFU) are a severe complication in diabetes patients, often resulting in significant morbidity and mortality due to non-healing. This study investigated the effectiveness of 5% topical potassium permanganate on these ulcers.

Methods: A clinical trial was conducted on 23 patients with Wagner grade I and II DFU. Patients in the control group received standard treatment, while those in the intervention group also received 5% potassium permanganate topically. Data were recorded at 0, 7, 14, and 21 days for analysis.

Results: Among 23 patients studied, 7 (30.4%) were male and 16 (43.7%) female, with an average age of 59 ± 4 years. Both groups showed a statistically significant decrease in wound size and infection over time ($p < 0.001$). The intervention group, however, had a more substantial reduction in wound size and infection rate ($p < 0.05$).

Conclusion: Potassium permanganate, when applied topically, is both well-tolerated and effective in enhancing wound healing and reducing infection in DFU, suggesting its potential as a complementary treatment.

KEYWORDS

diabetic, diabetic foot, foot, foot ulcer

1 | INTRODUCTION

Diabetic foot ulcer (DFU), a serious complication of diabetes, frequently results in amputation, represents a major cause of hospitalization for diabetic patients, and is attributed to over half of non-traumatic lower limb amputations. Over half of non-traumatic lower limb amputations are due to DFUs, highlighting the gravity of this issue.[1,2]

DFUs not only pose a threat to physical health, leading to increased frailty and reduced life expectancy but also impose a substantial financial burden on healthcare systems, particularly in low-income countries.[3–6] In Iran, where the prevalence of diabetes exceeds the global average, finding cost-effective treatments for diabetes-related complications like DFUs is crucial.[7]

Effective monitoring standards for DFUs encompass pressure redistribution, debridement of necrotic tissue, infection management, and revascularization of distal limb vessels.[8]

However, these methods do not fully address the complex nature of DFU healing. Enter potassium permanganate ($KMnO_4$), an

oxidizing agent known for its antimicrobial properties and ability to promote wound healing.[9]

$KMnO_4$ is safe for topical use, environmentally stable, and aids in the formation of granulation tissue and collagen synthesis, essential for wound repair. Despite its potential benefits, including cost-effectiveness, ease of application, and low patient risk, there is a lack of comprehensive research on $KMnO_4$'s effectiveness in treating DFUs.[10]

This study aims to fill this gap by examining the topical application of a 5% potassium permanganate solution on DFUs. It seeks to determine whether $KMnO_4$ can be a viable, affordable option in the management of DFU, especially in resource-constrained settings.

2 | METHODS

We conducted a randomized clinical trial to investigate the effects of topical $KMnO_4$ on DFU. The study centered on diabetic patients presenting with at least one-foot ulcer (either plantar or dorsal surface) and a Wagner score of one or two. Grade one is considered a full thickness involvement of the skin and grade two is when ulcer penetrates through skin, fat and ligaments and not bones.[11] Eligible participants were those with type 2 diabetes, aged 18–65 years, who sought care at Velayat Scar Clinic and displayed chronic neuropathic and nonischemic ulcers. We excluded participants with any ulcer side effects, those experiencing $KMnO_4$-related pain, individuals with progressive infections, or signs of pus, patients requiring debridement, those exhibiting ischemia in the lower limbs, and any with an ABI/TBI score below 0.7. A general surgeon executed the DFU diagnosis and patient selection.

Following the screening process, 23 qualifying patients entered the study at Velayat Scar clinic in 2022.

Ethics: Our trial adhered to the Declaration of Helsinki. The Institutional Review Board (IRB) of Guilan University of Medical Sciences sanctioned the protocol (IR.GUMS.REC.1401.292), and the Iranian Registry of Clinical Trials endorsed it on 02-11-2022 (registration reference: IR.GUMS.REC.1401.292). Every participant was briefed on the study's purpose, procedures, potential risks, and benefits. Written informed consent was mandatory for enrollment. We prioritized participants' privacy, ensuring data anonymization before analysis. The research team was versed in ethical conduct standards, and the IRB was promptly informed of any adverse or unforeseen events.

Patients were randomized into either the intervention or control group. While the control group received the standard DFU treatment (pressure reduction, daily cleaning of the DFU with soap and water, and daily ulcer assessment),[9,10] the intervention group also received topical $KMnO_4$ solution, strictly applied to the ulcer and avoiding healthy skin. Patients were instructed to self-administer the treatment daily. Apart from the standard DFU treatment, the control group received topical and systemic antibiotics in terms of infection, but no dressings were utilized.

The primary metric was ulcer length, gauged using an electronic caliper. Secondary measures encompassed local infection, scar healing (evaluated by a plastic surgeon), healing duration, demographics, fasting blood glucose, and HbA1C levels as a glycemic control indicator. A plastic surgeon performed weekly patient assessments, involving interviews, physical check-ups, and ulcer digital photography. The treatment spanned 21 days, with tri-weekly patient consultations.

We used restricted randomization (random allocation rule) for randomizing patients into treatment groups. In the process of random assignment, the analyst creates a random sequence, and one of the nurses assigns the patients to the intervention and control groups based on the entry and exit criteria in the study, and the project manager assigns the participants to the intervention and control groups based on a certain randomization method. To concealment, the concealment method of random allocation has been used. In this method, using identical sealed envelopes with a random sequence in such a way that each of the generated random sequences is recorded on a card, and the cards are placed inside the envelopes in order. To maintain the random sequence, the outer surface of the envelopes is numbered in the same order. At the time of starting the registration of eligible patients for the study, one of the envelopes will be opened in order, and the candidate patient will receive one of two types of treatment.

Patients were grouped using restricted randomization. Descriptive and inferential statistics analyzed the data. Tests for data normality included Kolmogorov–Smirnov and Shapiro–Wilk. Lune's test verified variance homogeneity. Depending on the assumptions met, we employed independent *t*-tests, repeated measures tests, Mann–Whitney tests, Friedman tests, and Bonferroni corrections, among others. Qualitative data analyses used the χ^2 or Fisher's exact test. All analyses were conducted on SPSS version 28, with a significance threshold set at 0.05.

To monitor patient adherence to the trial, a trained nurse called the participants every day to check for the daily treatment and ask for any specific side effects.

3 | RESULTS

From October 2022 to January 2023, we evaluated 41 patients, of whom 23 completed the trial (Figure 1). The patients' ages ranged from 48 to 65 years, with a mean age of 59.3 ± 4.5 years. Table 1 demonstrates that aside from HbA1c and scar duration, our results couldn't show significant differences in baseline characteristics between the groups. The main parameters were examined each week by the plastic surgeon, and the results are shown in Table 2.

In the intervention group, six patients had ulcers near the fingers and another six on the plantar foot surface. Conversely, the control group comprised four patients with finger ulcers and seven with plantar foot ulcers.

Both groups exhibited significant reductions in ulcer length. By the third session, the intervention group's mean ulcer length was notably less than that of the control group ($p = 0.05$). Furthermore,

FIGURE 1 Patient selection.

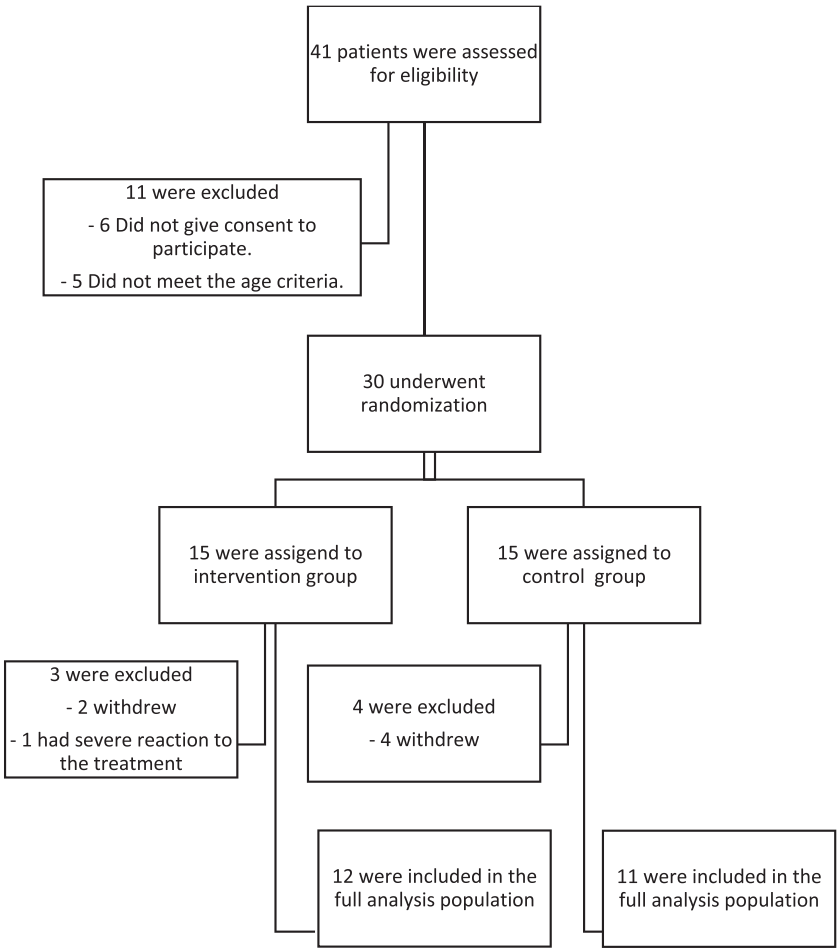

TABLE 1 Baseline characteristics.

		All	Intervention group	Control group	*p* Value
Age	Mean (SD)	59.3 (4.5)	59.7 (1.2)	58.5 (1.4)	0.60
Sex	Female	16	8	8	0.80
	Male	7	4	3	
Hypertension	Positive	13	6	7	0.43
	Negative	10	6	4	
Dyslipidemia	Positive	13	6	7	0.43
	Negative	10	6	4	
Smoking	Positive	10	6	4	0.43
	Negative	13	6	7	
Duration of the disease (years)	Mean (SD)	14 (6.3)	12.8 (1.7)	15.6 (1.1)	0.29
FBS	Mean (SD)	198 (46.6)	196 (12.3)	200.1 (15.8)	0.93
HbA1c	Mean (SD)	8.7 (1.2)	8.1 (0.2)	9.3 (0.3)	0.05
Scar duration (days)	Mean (SD)	9.3 (3.3)	10.7 (1)	7.8 (0.7)	0.05
ESR	Mean (SD)	21.5 (11.5)	19.8 (2.8)	23.1 (4.1)	0.07
WBC	Mean (SD)	11,095.6 (2750.2)	10,633.3 (494.2)	11,600 (1082)	0.85

TABLE 2 Scar features during the trial.

		Day 0	Day 7	Day 14	Day 21	*p* Value[a]
Ulcer length (mm)	Intervention group	239.9 (75.1)	179.8 (25)	115.8 (33.1)	53.5 (33.8)	<0.001
	Control group	372.1 (6)	281.1 (18)	204.9 (91.6)	117.6 (45.1)	<0.001
	p Value[b]	0.012	0.020	0.024	0.006	
Wound infection	Intervention group	66.7%	8.3%	0%	0%	<0.001
	Control group	72.7%	63.6%	36.4%	0%	<0.001
	p Value[b]	0.07	0.005	0.022	-	

[a]Related-samples Cochran's Q test.

[b]Independent-sample proportions test (Wald test).

the intervention group consistently reported lower local infection rates than the control group ($p = 0.03$).

Relative wound healing improvements were evident in both groups on Days 7 and 14. By Day 21, 4 of 12 patients in the intervention group achieved complete wound healing, whereas none in the control group reported full recovery.

4 | DISCUSSION

Potassium permanganate, a recognized oxidizing agent, has the ability to disrupt bacterial activity, particularly for anaerobes like clostridia.[12]

Although it's been employed in wound management for years, its application for DFU remains under-researched. However, a few recent studies, such as those by Chen et al.[10] and Rai,[13] have hinted at its potential, emphasizing the need for more conclusive research.

Our study, which primarily focused on a patient demographic of women with an average age of 59 years, confirms the therapeutic advantage of potassium permanganate in conjunction with standard treatment. Significant observations were the high prevalence of smoking among the participants and the increased incidence of hyperlipidemia (HLP) and hypertension (HTN)—both aligning with previously established findings, indicating the destructive effects of smoking on diabetic patients.[14–17] Given the metabolic syndrome's nature, where diabetes, HTN, and HLP often coexist, this observation is unsurprising. However, due to our study's limited sample size, this conclusion is specific to our study participants and cannot be broadly applied to the entire statistical population. Numerous independent studies have examined the prevalence of these diseases and their interrelationships, which was not a focus of our study.

$KMnO_4$ offers several advantages, including its cost-effectiveness, low sensitization at standard concentrations, high patient tolerance, and proven efficacy.[9,10,13] These implications matter as the study was conducted in a low-income country, highlighting the importance of the cost-effectiveness of treatments. Hence, the effectiveness and affordability of $KMnO_4$ could be considered as a protocol for diabetic foot care in Iran's healthcare system. Compared to monotherapy, combination therapy of complex chronic DFUs with standard care and $KMnO_4$ is well tolerated, enhances wound healing, and reduces infection.

The control and intervention groups exhibited similarities in various metrics, such as average age, gender ratio, and duration of diabetes, validating the effectiveness of our randomization process. However, there were noteworthy differences like the HbA1c level and the onset time of treatment post-ulcer detection. HbA1c was significantly higher in the control group, indicating poor glycemic control, and patients in the control group started treatment on average 2 days later than the intervention group, which could introduce potential biases.

The average diabetes duration among patients was approximately 14 years, with no significant differences between the case and control groups. This duration is expected in patients with DFUs, as they often result from diabetic neuropathy and ischemia, which are chronic processes that take years to develop. Although not statistically significant, a longer disease duration may have influenced the control group's results, introducing a potential bias.

A notable outcome was the observed rapid wound healing among potassium permanganate users, with some even achieving full recovery within 21 days—results that mirror the findings of Delgado et al.'s study.[9]

Yet, while our study aligns with current literature, it's paramount to consider external factors like smoking, HTN, and the duration of diabetes, which play crucial roles in ulcer progression and healing. Future research should aim to isolate and understand these variables better, ensuring a more comprehensive understanding of the treatment's potential.[18] Also, we believe that patient compliance in this treatment could be measured in future studies.

One of the participants in this trial showed skin irritation around the ulcer when applying $KMnO_4$ for the first time. She was a 61-year-old woman, with a DFU of 26 mm length on the plantar surface of her foot. According to previous studies, 5% topical $KMnO_4$ is highly tolerated for topical use. Adverse effects like irritation or hypersensitivity do not seem to be permanent and disappear when the application stops.[19,20]

4.1 | Limitations and strengths

In our study, we only evaluated DFUs with a Wagner score of 1 and 2 and did not assess other ulcer types. Additionally, we did not follow-up with patients after the final visit on Day 21. The study

sample size is small (23 patients), limiting the results' generalizability. A more significant number of cases is required to make a precise evaluation of the protocol's advantage. Higher HbA1c levels in the control group indicate poor glycemic control, which can be a source of bias in terms of response rate to the treatment. We recommend that future studies focus on more severe ulcers and extend the follow-up period.

This study represents the first trial among DFUs in the Iranian population, and it raises evidence toward the effectiveness of $KMnO_4$ in treating DFUs.

5 | CONCLUSION

In conclusion, potassium permanganate, when paired with standard DFU treatment, shows promise in accelerating wound recovery. However, more expansive studies are needed to ascertain its full potential and applications.

AUTHOR CONTRIBUTIONS

Afrooz Haghdoost: Data curation; project administration; resources; supervision; writing—review and editing. **Mohammadreza Mobayen**: Conceptualization; methodology; project administration; supervision; validation. **Iraj Baghi**: Methodology; supervision; writing—review and editing. **Zahra Haghani-Dogahe**: Data curation; formal analysis; investigation; methodology; project administration; writing—original draft; writing—review and editing. **Reza Zarei**: Data curation; software; visualization; writing—original draft. **Amir Pirooz**: Project administration; resources; supervision; validation. **Heydar Ali Balou**: Investigation; methodology; visualization. **Alireza Feizkhah**: Software; writing—original draft. All authors have read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions. The corresponding author had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT

The lead author, Zahra Haghani-Dogahe, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and if relevant, registered) have been explained.

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