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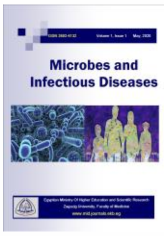

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Original article

Assessment of the effect of pulsed electromagnetic field therapy in the treatment of chronic wounds

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ABSTRACT

Background: Recent innovations, such as hydrosurgery, ultrasound therapy, and plasma-mediated bipolar radio-frequency ablation therapy could represent an alternative to conventional debridement in many cases, especially for chronic non-healing wounds. Pulsed electromagnetic field (PEMF) has been used clinically as an intervention to enhance healing of chronic infected wound. The aim is to evaluate the effect of PEMF therapy on healing of chronic wounds, as regard timing and quality of healing. **Methods:** Fifty cases with chronic wounds, according to inclusion and exclusion criteria, the patient's age ranged from 20 -70 years, from outpatient clinic of military or transferred through civilian outpatient's clinic in different hospitals and specific diabetic foot centers. They are diagnosed as infected resistant chronic wounds depending on clinical, laboratory and radiological investigations due to various reasons will be managed by PEMF therapy. **Results:** There were statistically significant associations between treatment outcomes and pain (p =0.018), edema (p =0.005), number of sessions (p <0.001), microbial eradication (p =0.008). On the other hand, we found that there were statistically significant associations between complication rates and treatment outcome (p=0.008), microbial eradication (p <0.001), and hospital stay (p =0.002). **Conclusion:** the PEMF therapy is a safe and effective treatment option for patients with chronic, resistant, wounds. The current study shows that the PEFM achieved a high success rate. In addition, our analysis showed that achieving complete closure of the wound can be associated with significant symptomatic relief and few incidences of complications. Nevertheless, further studies are still needed to confirm our findings.

Introduction

A wound can be described as a defect or a break in the skin, resulting from physical or thermal damage or as a result of the presence of an underlying medical or physiological condition [1]. Wound healing is a dynamic process consisting of three continuous, overlapping, and precisely programmed phases. [2].

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Optimal wound healing involves the following events: rapid hemostasis; appropriate inflammation; mesenchymal cell differentiation, proliferation, & migration to the wound site; suitable angiogenesis; prompt re-epithelialization (regrowth of epithelial tissue over the wound surface). In addition, proper synthesis, cross-linking, and alignment of collagen to provide strength to the healing tissue. Wounds that exhibit impaired healing, including delayed acute wounds and chronic wounds, generally have failed to progress through the normal stages of healing. Such wounds frequently enter a state of pathologic inflammation due to a postponed, incomplete, or uncoordinated healing process. [3]

Multiple factors can lead to impaired wound healing, categorized into: Local factors (as oxygenation, infection, foreign body, and necrosis) and systemic factors (as nutrition, age and gender, sex hormones, stress, ischemia), diseases (as diabetes, jaundice, uremia), obesity, medications (as glucocorticoid steroids and non-steroidal anti-inflammatory drugs), chemotherapy, alcoholism, smoking and Immunocompromised conditions (as cancer and radiation therapy) are the overall health or disease state of the individual that affect his or her ability to heal. Correctly identifying the etiology of a chronic wound as well as the local and systemic factors that may be contributing to poor wound healing is key to successful wound treatment [4]. Chronic infected wounds are treated by several ways, hydrosurgery (Versajet), ultrasound therapy (MIST therapy device), and plasma-mediated bipolar radio-frequency ablation therapy (Coblation). Novel approaches in managing this type of wounds are non-invasive PEMF to generate short bursts of electrical current in injured tissue without producing heat or interfering with nerve or muscle function. Recently, increased understanding of the mechanism of action of PEMF therapy has permitted technologic advances yielding economical and disposable PEMF devices. With these devices, PEMF therapy has been broadened to include the treatment of postoperative pain and edema in both outpatient and home settings, offering the physician a more versatile tool for patient management [5, 6].

Aim of this study to assess the effect of therapy on healing of chronic wounds, as regard timing and quality of healing.

Patients and Methods

Fifty cases with different types of chronic wounds, according to inclusion and exclusion criteria, the patient's age were ranged from 20 -70 years. Selected from outpatient clinic of military or transferred through civilian outpatient's clinic in different hospitals and specific diabetic foot centers. They are diagnosed as infected resistant chronic wounds depending on clinical, laboratory and radiological investigations due to various reasons will be managed by pulsed EMF therapy.

Inclusion criteria

All male and female admitted patients reported as chronic wounds or ulcers (Diabetic ulcers-Decubitus ulcers) Large wound defect (post-operative- post traumatic), wounds with massive exudate/ transudate. patients ≥ 20 years of age, body mass index less than 30 kg/m^2. Female patients agreed to use a medically acceptable physical contraceptive barrier method during the treatment phase.

Exclusion criteria

Pregnancy and breast feeding, patients who are unstable hemodynamically, haemodynamic support devices, cardiac and peripheral artery stents and devices, electronic implant or device, any type of metallic prosthesis, mentally or neurologically disabled patients, in addition refusal to give informed consent, any types of cancer. Patients who had participated in another research study involving an investigational product in the past 12 weeks.

Informed consent

A written informed consent was obtained from each patient before he/she got enrolled into the study.

Ethical principles

This clinical trial was conducted in accordance with the principles laid down by the 18th World Medical Association **(Helsinki, 1964)** and all applicable amendments laid down by the World Medical Association and ICH guidelines for Good Clinical Practice.

Laws and regulations

Conducted in compliance with international laws and regulations of clinical trials, and national laws and regulations of Egypt, as well as any applicable guidelines.

Statistical analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis; the following tests were used to test differences for significance. Differences between frequencies (qualitative variables) and percentages in groups were compared by Chi-square test., multiple groups by ANOVA, ROC curve for cut off, Kappa agreement to test the agreement. *p* value was set at <0.05 for significant results & <0.001 for high significant result.

Results

The diagnosis of chronic wounds based on a combination of a compatible history – examination- and investigation.

In **table (1)** 17 cases 34.0% out of 50 cases were healthy (standard) weight, distributed with age which ranged between 21 – 68 years old.

The association analysis showed that there were no statistically significant associations between treatment outcomes and age (*p* =0.44), wound type (*p* =0.63), and organism (*p* =0.444) **(Table 2)**.

Similarly, **(Table 3)** represent no statistically significant associations between treatment outcomes and type of organism (*p* >0.5), presence of resistance (*p* =0.074), and adjuvant therapy (*p* =0.087).

In **table (4)** no statistically significant associations between treatment outcomes and hyperemia (*p* =0.72), complications rate (*p* =0.055), and hospital stay (*p* =0.232). In contrary, there were statistically significant associations between treatment outcomes and pain (*p* =0.018), edema (p =0.005), number of sessions (p <0.001), microbial eradication (*p* =0.008), and type of complications (*p* =0.014).

Table 5 showed no statistically significant associations between complications rate and coexisting illness (*p* =0.627) and type of wound (p =0.76).

Similarly, in **table (6)** no statistically significant associations between compilation rate and number of organism (*p*=0.78) and type of organism (*p* >0.05).

There were no statistically significant associations between complication rates and resistance (*p* =0.145) and need for adjuvant therapy (*p* =0.22) **(Table 7)**.

In **table (8)** no statistically significant associations between complication rates and pain (*p* =0.225), hyperemia (*p* =0.52), edema (*p* =0.163), number sessions (*p* =0.065), and duration of treatment (*p* =0.97). In contrary, there were statistically significant associations between complication rates and treatment outcome (*p* =0.008), microbial eradication (*p* <0.001), and hospital stay (*p* =0.002).

In **table (9)**, there were statistically significant associations between hospital stay and coexisting illness (*p* =0.045) and wound type (*p* =0.042).

In contrary, **Table 10** represent there were no statistically significant associations between hospital stay and number of organisms (*p* =0.177) and type of organism (*p* >0.05).

In **table (11)**, there were no statistically significant associations between hospital stay and resistance (*p*=0.219) and adjuvant therapy (*p* =0.237).

In **table (12)** showed there were no statistically significant associations between complication rates and pain (*p* =0.225), hyperemia (*p* =0.52), edema (*p* =0.163), number sessions (*p* =0.065), and duration of treatment (*p*=0.97). In contrary, there were statistically significant associations between complication rates and treatment outcome (*p* =0.008), microbial eradication (*p* <0.001), and hospital stay (*p* =0.002).

Table 1. Sex, age and BMI distribution among study groups.

Items		**No. = 50** [**No. (%)**]
Sex	Females	16 (32.0%)
	Males	34 (68.0%)
Age	Mean ± SD	50.34 ± 11.08
	Range	21 – 68
BMI	Underweight	15 (30.0%)
	Healthy weight	17 (34.0%)
	Overweight	18 (36.0%)

Table 2. Associations between treatment outcomes and pre-procedure data.

Pre-procedure data		**Treatment Outcome**		**Chi-square test**		
		Partial Closure	**Complete Closure**	**X²**	***P*-value**	**Sig.**
		No. (%)	**No. (%)**			
Co-existing illness	None	4 (40.0%)	14 (35.9%)	1.622	0.444	NS
	DM	4 (40.0%)	22 (56.4%)			
	Bedridden	2 (20.0%)	3 (7.7%)			
Wound type	D. foot ulcer	4 (40.0%)	22 (56.4%)	1.690	0.639	NS
	Traumatic ulcer	2 (20.0%)	6 (15.4%)			
	Decubitus ulcer	2 (20.0%)	3 (7.7%)			
	Post operative wound	2 (20.0%)	8 (20.5%)			
Organisms	Single	9 (90.0%)	31 (79.5%)	.639a	0.444	NS
	Mixed	1 (10.0%)	8 (20.5%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Table 3. Associations between treatment outcomes and type of organism or resistance.

		Treatment Outcome		**Chi-square test**		
		Partial Closure	**Complete Closure**	**X²**	***p*-value**	**Sig.**
		No. (%)	**No. (%)**			
Proteus	Negative	8 (80.0%)	35 (89.7%)	0.703	0.402	NS
	Positive	2 (20.0%)	4 (10.3%)			
Staph. aureus	Negative	8 (80.0%)	22 (56.4%)	1.866	0.172	NS
	Positive	2 (20.0%)	17 (43.6%)			
Psudomonus A.	Negative	9 (90.0%)	30 (76.9%)	0.838	0.360	NS
	Positive	1 (10.0%)	9 (23.1%)			
E.coli	Negative	8 (80.0%)	28 (71.8%)	0.275	0.600	NS
	Positive	2 (20.0%)	11 (28.2%)			
Streptcoccus group A	Negative	6 (60.0%)	33 (84.6%)	2.969	0.085	NS
	Positive	4 (40.0%)	6 (15.4%)			
Resistance	No resistance	3 (30.0%)	24 (61.5%)	3.200	0.074	NS
	MDR	7 (70.0%)	15 (38.5%)			
Adjuvant treatment	None	4 (40.0%)	12 (30.8%)	4.879	0.087	NS
	Antibiotics	3 (30.0%)	24 (61.5%)			
	VAC therapy	3 (30.0%)	3 (7.7%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Table 4. Associations between treatment outcomes and procedure data.

Procedure data		Treatment Outcome		Chi-square test		
		Partial Closure	**Complete Closure**	**X²**	***p*-value**	**Sig.**
		No. (%)	**No. (%)**			
Pain	Not improved	6 (60.0%)	8 (20.5%)	8.024	0.018	S
	Improved	3 (30.0%)	30 (76.9%)			
	Increased	1 (10.0%)	1 (2.6%)			
Hyperemia	None	4 (40.0%)	18 (46.2%)	0.122	0.727	NS
	Increased	6 (60.0%)	21 (53.8%)			
Edema	None	7 (70.0%)	9 (23.1%)	7.969	0.005	HS
	Reduced	3 (30.0%)	30 (76.9%)			
Number of sessions	< 12	2 (20.0%)	18 (46.2%)	17.544	0.000	HS
	(12 - 24)	2 (20.0%)	19 (48.7%)			
	> 24	6 (60.0%)	2 (5.1%)			
Duration of treatment	< 6 weeks	1 (10.0%)	14 (35.9%)	9.760	0.008	HS
	(6 - 12)	5 (50.0%)	23 (59.0%)			
	> 12 weeks	4 (40.0%)	2 (5.1%)			
Microbial eradication	No	3 (30.0%)	0 (0.0%)	12.463	0.000	HS
	Yes	7 (70.0%)	39 (100.0%)			
Complications	Not complicated	7 (70.0%)	36 (92.3%)	3.686	0.055	NS
	Complicated	3 (30.0%)	3 (7.7%)			
Type of complications	Oozing	0 (0.0%)	3 (100.0%)	6.000	0.014	S
	Persistant infection	3 (100.0%)	0 (0.0%)			
Hospital stay	No	10 (100.0%)	34 (87.2%)	1.428	0.232	NS
	Yes	0 (0.0%)	5 (12.8%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Table 5. Associations between complications rate and pre-procedure data.

		Complications		Chi-square test		
		Not complicated	**Complicated**	**X²**	**P-value**	**Sig.**
		No. (%)	**No. (%)**			
Co-existing illness	None	15 (34.9%)	3 (42.9%)	0.935	0.627	NS
	DM	23 (53.5%)	4 (57.1%)			
	Bedridden	5 (11.6%)	0 (0.0%)			
Wound type	D. foot ulcer	23 (53.5%)	4 (57.1%)	1.143	0.767	NS
	Traumatic ulcer	7 (16.3%)	1 (14.3%)			
	Decubitus ulcer	5 (11.6%)	0 (0.0%)			
	Post-operative wound	8 (18.6%)	2 (28.6%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Table 6. Associations between complications rate and type of organism.

		Complications		Chi-square test		
		Not complicated	**Complicated**	**X²**	***p*-value**	**Sig.**
		No. (%)	**No. (%)**			
Organisms	Single	35 (81.4%)	6 (85.7%)	0.076	0.783	NS
	Mixed	8 (18.6%)	1 (14.3%)			
Proteus	Negative	38 (88.4%)	6 (85.7%)	0.040	0.841	NS
	Positive	5 (11.6%)	1 (14.3%)			
Staph aureus	Negative	26 (60.5%)	4 (57.1%)	0.028	0.868	NS
	Positive	17 (39.5%)	3 (42.9%)			
Psudomonus A.	Negative	34 (79.1%)	6 (85.7%)	0.166	0.684	NS
	Positive	9 (20.9%)	1 (14.3%)			
E.coli	Negative	31 (72.1%)	6 (85.7%)	0.581	0.446	NS
	Positive	12 (27.9%)	1 (14.3%)			
Strept group A	Negative	35 (81.4%)	5 (71.4%)	0.374	0.541	NS
	Positive	8 (18.6%)	2 (28.6%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Table 7. Associations between complications rate and resistance.

		Complications		Chi-square test		
		Not complicated	**Complicated**	**X²**	***p*-value**	**Sig.**
		No. (%)	**No. (%)**			
Resistance	No resistance	25 (58.1%)	2 (28.6%)	2.119	0.145	NS
	MDR	18 (41.9%)	5 (71.4%)			
Adjuvant treatment	None	14 (32.6%)	3 (42.9%)	3.025	0.220	NS
	Antibiotics	25 (58.1%)	2 (28.6%)			
	VAC therapy	4 (9.3%)	2 (28.6%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Table 8. Associations between complications rate and procedure data.

		Complications		Chi-square test		
		Not complicated	**Complicated**	**X²**	***p*-value**	**Sig.**
		No. (%)	**No. (%)**			
Pain	Not improved	11 (25.6%)	4 (57.1%)	2.985	0.225	NS
	Improved	30 (69.8%)	3 (42.9%)			
	Increased	2 (4.7%)	0 (0.0%)			
Hyperemia	None	19 (44.2%)	4 (57.1%)	0.407	0.524	NS
	Increased	24 (55.8%)	3 (42.9%)			
Edema	None	13 (30.2%)	4 (57.1%)	1.943	0.163	NS
	Reduced	30 (69.8%)	3 (42.9%)			
Number of sessions	< 12	20 (46.5%)	0 (0.0%)	5.452	0.065	NS
	(12 - 24)	17 (39.5%)	5 (71.4%)			
	> 24	6 (14.0%)	2 (28.6%)			
Duration of treatment	< 6 weeks	13 (30.2%)	2 (28.6%)	0.042	0.979	NS
	(6 - 12)	25 (58.1%)	4 (57.1%)			
	> 12 weeks	5 (11.6%)	1 (14.3%)			
Treatment Outcome	No Closure	0 (0.0%)	1 (14.3%)	9.558	0.008	HS
	Partial Closure	7 (16.3%)	3 (42.9%)			
	Complete Closure	36 (83.7%)	3 (42.9%)			
Microbial eradication	No	0 (0.0%)	4 (57.1%)	26.708	0.000	HS
	Yes	43 (100.0%)	3 (42.9%)			
Hospital stay	No	41 (95.3%)	4 (57.1%)	9.764	0.002	HS
	Yes	2 (4.7%)	3 (42.9%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Table 9. Association between hospital stay and pre-procedure data.

		Hospital stay		Chi-square test		
		No	**Yes**	**X²**	***p*-value**	**Sig.**
		No. (%)	**No. (%)**			
Co-existing illness	None	16 (35.6%)	2 (40.0%)	6.214	0.045	S
	DM	26 (57.8%)	1 (20.0%)			
	Bedridden	3 (6.7%)	2 (40.0%)			
Wound type	Diabetic foot ulcer	26 (57.8%)	1 (20.0%)	8.189	0.042	S
	Traumatic ulcer	8 (17.8%)	0 (0.0%)			
	Decubitus ulcer	3 (6.7%)	2 (40.0%)			
	Post operative wound	8 (17.8%)	2 (40.0%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Table 10. Association between hospital stay and type of organism.

		Hospital stay		Chi-square test		
		No	**Yes**	**X²**	***p*-value**	**Sig.**
		No. (%)	**No. (%)**			
Organisms	Single	38 (84.4%)	3 (60.0%)	1.822	0.177	NS
	Mixed	7 (15.6%)	2 (40.0%)			
Proteus	Negative	39 (86.7%)	5 (100.0%)	0.758	0.384	NS
	Positive	6 (13.3%)	0 (0.0%)			
Staph aureus	Negative	28 (62.2%)	2 (40.0%)	0.926	0.336	NS
	Positive	17 (37.8%)	3 (60.0%)			
Psudomonus A.	Negative	37 (82.2%)	3 (60.0%)	1.389	0.239	NS
	Positive	8 (17.8%)	2 (40.0%)			
E.coli	Negative	33 (73.3%)	4 (80.0%)	0.104	0.747	NS
	Positive	12 (26.7%)	1 (20.0%)			
Strept group A	Negative	36 (80.0%)	4 (80.0%)	0.000	1.000	NS
	Positive	9 (20.0%)	1 (20.0%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Table 11. Association between hospital stay and resistance.

		Hospital stay		Chi-square test		
		No	**Yes**	**X²**	***p*-value**	**Sig.**
		No. (%)	**No. (%)**			
Resistance	No resistance	23 (51.1%)	4 (80.0%)	1.512	0.219	NS
	MDR	22 (48.9%)	1 (20.0%)			
Adjuvant treatment	None	17 (37.8%)	0 (0.0%)	2.881	0.237	NS
	Antibiotics	23 (51.1%)	4 (80.0%)			
	VAC therapy	5 (11.1%)	1 (20.0%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Table 12. Association between hospital stay and procedure data.

		Hospital stay		Chi-square test		
		No	**Yes**	X^2	***p*-value**	**Sig.**
		No. (%)	**No. (%)**			
Pain	Not improved	13 (28.9%)	2 (40.0%)	0.438	0.803	NS
	Improved	30 (66.7%)	3 (60.0%)			
	Increased	2 (4.4%)	0 (0.0%)			
Hyperemia	None	19 (42.2%)	4 (80.0%)	2.585	0.108	NS
	Increased	26 (57.8%)	1 (20.0%)			
Edema	None	15 (33.3%)	2 (40.0%)	0.089	0.765	NS
	Reduced	30 (66.7%)	3 (60.0%)			
Number of sessions	< 12	20 (44.4%)	0 (0.0%)	7.071	0.029	S
	(12 - 24)	17 (37.8%)	5 (100.0%)			
	> 24	8 (17.8%)	0 (0.0%)			
Duration of treatment	< 6 weeks	14 (31.1%)	1 (20.0%)	1.315	0.518	NS
	(6 - 12)	25 (55.6%)	4 (80.0%)			
	> 12 weeks	6 (13.3%)	0 (0.0%)			
Treatment Outcome	No Closure	1 (2.2%)	0 (0.0%)	1.567	0.457	NS
	Partial Closure	10 (22.2%)	0 (0.0%)			
	Complete Closure	34 (75.6%)	5 (100.0%)			
Microbial eradication	No	4 (8.9%)	0 (0.0%)	0.483	0.487	NS
	Yes	41 (91.1%)	5 (100.0%)			
Complications	Not complicated	41 (91.1%)	2 (40.0%)	9.764	0.002	HS
	Complicated	4 (8.9%)	3 (60.0%)			
Type of complications	Oozing	0 (0.0%)	3 (100.0%)	7.000	0.008	HS
	Persistant infection	4 (100.0%)	0 (0.0%)			

p-value > 0.05: Non significant; *p*-value < 0.05: Significant; *p*-value < 0.01: Highly significant

Figure 1. correlation between number of session (duration of therapy) and patient's cure (closure of wound).

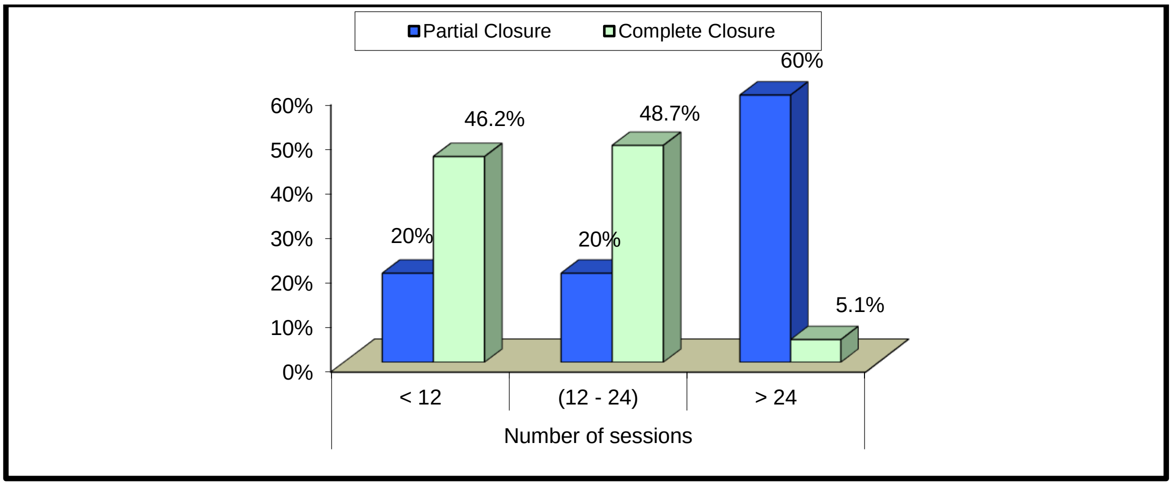

Figure 2. Correlation between microbial eradication and patient's cure**.**

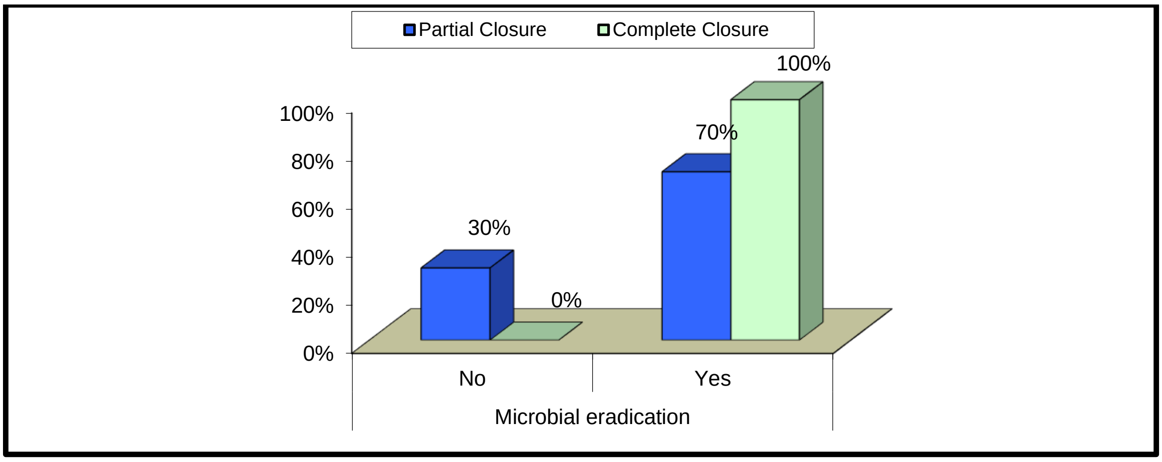

Figure 3. Decubitus ulcer in breast after PEMF 25 sessions.

Figure 4. Association between Hb, TLC and C-RP pre and post sessions.

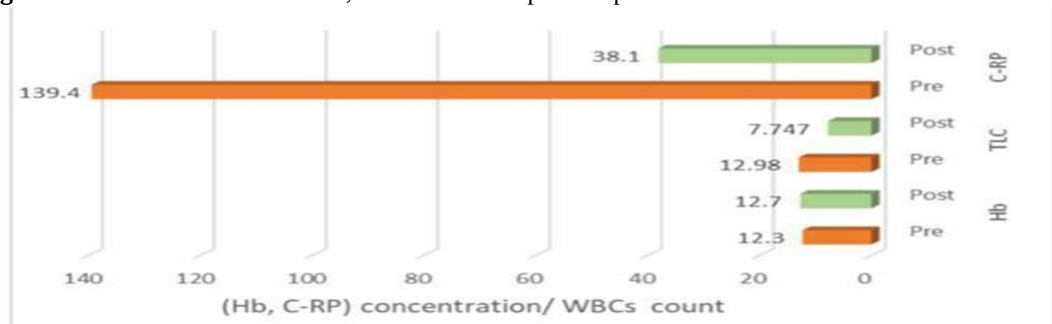

Figure 5. Complete wound closure and microbial eradication after 10weeks.

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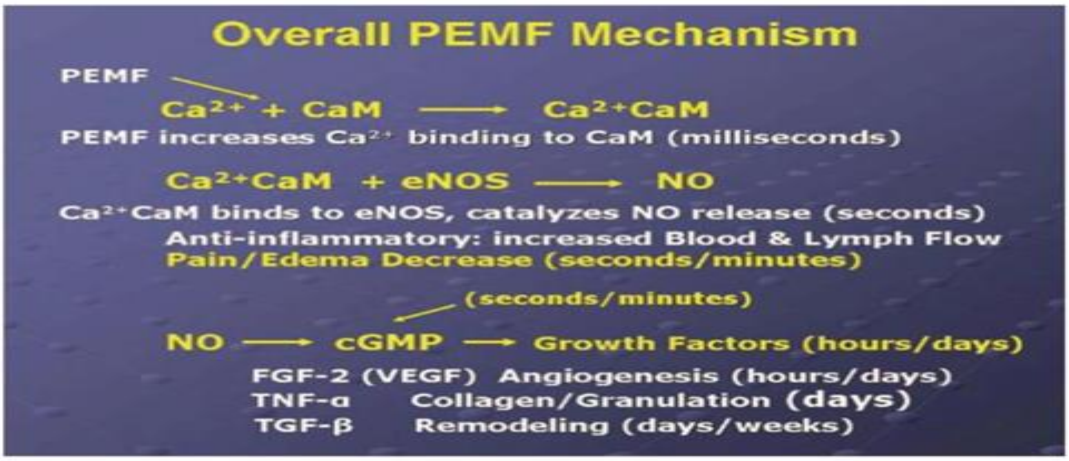
Figure 6. Complete wound closure and microbial eradication after 10 weeks

Figure 7. Partial closure after 18 weeks.

Figure 8. Overall PEMF mechanism of wound healing.



Discussion

When wound healing does not progress normally, a chronic wound may result, and this is a significant burden to both the patient and the medical system. A patient with a single diabetic ulcer or chronic wound carries a high cost in both medical management and follow up, with the number of patients affected growing yearly from 6.5 million, given the increasing prevalence of diabetes and other chronic diseases that may affect wound healing [7].

Wound debridement consists of removing necrotic or devitalized tissue and reducing bacterial load, it is an essential step to bring about wound healing. Numerous debridement methods exist, such as autolytic, enzymatic, biodebridement, and surgical/ sharp and mechanical methods. Although sharp debridement using a scalpel or curette remains the gold standard, these techniques have several disadvantages. They are not appropriate for large surfaces, are not optimal for saving tissue, and they often lead to an uneven wound bed [8].

Recent innovations, such as hydrosurgery (Versajet), ultrasound therapy (the MIST therapy device), and plasma-mediated bipolar radio-frequency ablation therapy (Coblation) could represent an alternative to conventional debridement in many cases, especially for chronic non-healing wounds [9].

Pulsed electromagnetic field (PEMF) has been used clinically as an intervention to enhance healing of chronic ulcers. Previous studies have shown that PEMF accelerated wound closure, reduced wound pain, enhanced healthy granulation and promoted circulation. A systematic review concluded that PEMF could significantly accelerate the healing of chronic ulcers (decubitus, venous and plantar) in patients [9] **(Figures 3, 7).**

Nevertheless, there is a scarcity in the published literature regarding the effect of PEMF on chronic wound healing. Therefore, we performed the present study to evaluate the effect of PEMF therapy on healing of chronic wounds, as regard timing and quality of healing.

In the present prospective non-randomized clinical trial, we included 50 patients with different types of chronic wounds. The most common cause of the chronic wound was diabetes (54%), followed by traumatic ulcer (16%) and decubitus ulcer (10%), while the most commonly causative organism was *staphylococcus aureus* (40%), and followed by *E. coli* (26%) and *Pseudomonas* (20%).

In line with our findings, [10] recruited a total of 241 patients with chronic wounds of more than 2 weeks' duration from wound healing department in Shanghai, China. Among those patients, the most common cause of chronic wound was diabetes, followed by pressure ulcers.

In addition, [11] performed a cross sectional study on a sample of patients with chronic infected vascular wounds, the species most frequently isolated were *Staphylococcus aureus, E.coli*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*.

In the present study, 46% of the patients exhibited multidrug-resistant organisms (MDR). The most common MDR species was *Staphylococcus aureus* (26%) followed by *Proteus* and Strept group A (21.7% for each) then *Pseudomonas* and *E.coli* (17.3% for each). Multidrug-resistant organisms (MDRO) are increasingly implicated in both acute and chronic wound infections. The limited therapeutic options are further compromised by the fact that wound bacteria often co-exist within a biofilm community which enhances bacterial tolerance to antibiotics [12]**.** In the present study co-existing bacteria within one biofilm were isolated from 9 patients (18%) which is considered as a very significant and alarming sign for the increasing prevalence of the mixed infected wounds. Similarly, [13] performed a retrospective study comparing the wound infections of 41 DM patients to those of 74 non-diabetic patients to test the hypothesis that infections with MDRO were more prevalent in the diabetes population. Overall, the rate of MDRO was almost 50%.

As [14] advised, treatment begins to treat pain and edema, is generally administered every 4 hours for 30 minutes for 3 days, and then every 8 hours for the next several days until pain and edema are not significant. For the treatment of chronic wounds, the regimen is 30 minutes twice a day until healed, by rate of 3 sessions per week.

In terms of the primary outcomes of the present study, 40% of the patients required less than less than 12 sessions of PEMF therapy and 44% of them required 12-24 sessions, while 16% needed more than 24 sessions of therapy by rate of 3 sessions per week to achieve the aimed progress in healing process.

In concordance with our findings, [15] conducted a randomized trial to assess the effectiveness of PEMF in healing of pressure ulcers in patients with neurological disorders Six patients with 13 ulcers received PEMF therapy and the remaining 6 patients with 11 ulcers received sham treatment, for 30 sessions (45 minutes each). At the end of follow-up, significant healing of ulcers was noted with almost all patients had completed or partial closure of the wound.

Similarly, [16] performed a randomized, double-blind study to determine if non-thermal PMEF treatment significantly increases the healing rate of pressure ulcers in patients with spinal cord injuries. Subjects included volunteers admitted to a Veteran's Administration Hospital in New York over a 2-year period and consisted of 30 male spinal cord-injured patients, 20 with Stage II and 10 with Stage III pressure ulcers. The 20 patients with Stage II pressure ulcers, the active group had a significantly increased rate of healing with a greater percentage of the ulcer healed at one week than the control group.

Many pathogenic bacteria synthesize and secrete siderophores; small, high-affinity iron-chelating compounds [17]. Siderophore has the ability to bind ferric iron (Fe^{3+}) with an affinity that can exceed that of human Fe^{3+}-binding proteins like transferrin or lactoferrin, enabling siderophores to "steal" iron from these host proteins resulting in iron deficiency anemia [18].

Therefore, in the present study we used hemoglobin concentration as a marker for monitoring the prognosis of chronic wounds microbial eradication, which approved obvious relation by 38 improved patients out of 50 (76%) with higher concentration of hemoglobin post microbial eradication.

Similarly, C-reactive protein (C-RP) and white blood cells (WBCs) count were used as markers for monitoring infection and microbial eradication, that's because they both increase rapidly in concentration following infection. C-reactive protein acts as an opsonin enhancing phagocytosis of microbes and activates complement [19].

Hence, decreased levels of C-RP concentration and (WBCs) count after exposure to ELF-EM field denotes inhibition of the phagocytosis and opsonization resulting from successful microbial eradication and resolved infection [20].

That's why in the present study almost all the patients revealed a dramatic decrease in C-RP level (98%) and obvious WBCs count improvement in 45 patients (90%) proving the golden role of EMF therapy in microbial eradication **(Figure 4).**

To sum up, [6] performed a systematic review to review the major scientific breakthroughs and current understanding of the mechanism of action of PEMF therapy. A total of 7 studies were included which assessed the efficacy of PEMF in the setting of chronic wound healing. The authors concluded that the rate of wound closure after PEMF therapy ranged between 60-84 %. The included studies also showed decrease in edema and pain after therapy.

In the present study, almost 78% of the patients had complete closure **(Figures 5,6)** and 20% had partial closure **(Figure 8)**. Microbial eradication was achieved in 92% of the patients. In addition, pain and edema were improved in 66% of the patients and about 54% of chronic wounds healing were aided by the increased hyperemia**.**

In the present study, we assessed the association between the response to PEMF and clinical characteristics of the patients; the analysis showed that there were statistically significant associations between treatment outcomes and pain (p =0.018), edema (p =0.005), number of sessions (p <0.001), microbial eradication (p =0.008). Such findings are expected as appropriate closure of the wound was reported to be associated with greater reduction in symptoms severity and microbial eradication **[**23].

Although there are no published studies that correlate between the response to PEMF therapy and symptomatic reliefs, previous reports have shown that electrical stimulation therapy improves the severity of symptoms in patients with chronic wounds [21] performed a systematic and comprehensive search of four electronic databases to evaluate the effect of electrical stimulation therapy (EST) on wound healing outcomes in adults with various types of chronic wounds. Sixty-two clinical research studies involving 2082 patients with pressure ulcers, venous leg ulcers, diabetic foot wounds, and arterial/ ischemic wounds, and ulcers of mixed etiology were located. Results from 22 well-designed randomized clinical trials and 10 high-quality systematic reviews consistently support that EST can improve the symptoms of complete wound closure compared to patients with partial wound closure.

On the other hand, we found that there were statistically significant associations between complication rates and treatment outcome (p =0.008), microbial eradication (p <0.001), and hospital stay (p =0.002). Such findings can be attributed to the fact that patients with complications are more likely to have poorer outcomes and longer hospital stay [22].

Conclusion

It may be concluded from the present study that the use of EMF therapy waves at specific resonance and frequency proved to be efficient in microbial eradication especially with MDRO, aiding the healing of chronic wounds with several causes and types, besides being noninvasive, safe, fast, least side effects and at low cost.

Authors' contributions

All authors in this manuscript have participated in the research and/or article preparation, concept, design, analysis and interpretation of data, drafting or revising of this manuscript, and that they all have approved the manuscript as submitted. In addition, all authors have approved the final article and included in the disclosure.

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Conflict of interest

No conflicts of interest and the material described is not under publication or consideration for publication elsewhere.

References

1- **Childs DR, Murthy AS.** Overview of Wound Healing and Management. Surg Clin N Am 2017;97(1):189-207.

2- **Mathieu D, Linke JC, Wattel F.** Non-healing wounds. In: Handbook on hyperbaric medicine, Mathieu DE, editor., editor. Netherlands: Springer, 2010. 401-427

3- **Menke NB, Ward KR, Witten TM, Bonchev DG, Diegelmann RF** Impaired wound healing. Clin Dermatol 2011; 25:19-25.

4- **Raeder K, Jachan DE, Müller-Werdan U, Lahmann NA.** Prevalence and risk factors of chronic wounds in nursing homes in Germany: a cross-sectional study. International Wound Journal 2020;17(5):1128-34.

5- **Badr AH, Sherif M, Sayed AA, Elnakib MM.** Effects of extremely low-frequency electromagnetic fields on the susceptibility and resistance mechanisms of multi-drug resistant Pseudomonas aeruginosa. GSC Advanced Research and Reviews. 2022;12(1):091-100.

6- **Strauch B, Herman C, Dabb R, Ignarro LJ, Pilla AA.** Evidence-Based Use of Pulsed Electromagnetic Field Therapy in Clinical Plastic Surgery. Aesthetic Surgery Journal 2009; 29(2): 135–143.

7- **Han G, Ceilley R.** Chronic Wound Healing: A Review of Current Management and Treatments. Advances in Therapy 2017; 34(3): 599–610.

8- **Bekara F, Vitse J, Fluieraru S, Masson R, De Runz A, Georgescu V, et al** New techniques for wound management: A systematic review of their role in the management of chronic wounds. Archives of plastic surgery 2018;45(02):102-10.

9- **Choi HMC, Cheing AKK, Ng GYF, Cheing, GLY.** Effects of pulsed electromagnetic field (PEMF) on the tensile biomechanical properties of diabetic wounds at different phases of healing. PLoS ONE 2018; 13(1).

10- **Sun X, Ni P, Wu M, Huang Y, Ye J, Xie T.** A clinicoepidemiological profile of chronic wounds in wound healing department in Shanghai. The International Journal of Lower Extremity Wounds 2017;16(1):36-44.

11- **Tzaneva V, Mladenova I, Todorova G, Petkov, D.** Antibiotic treatment and resistance in chronic wounds of vascular origin. Medicine and Pharmacy Reports 2016; 89(3): 365–370.

12- **Bowler PG, Welsby S, Towers V, Booth R, Hogarth A, Rowlands V, et al.** Multidrug-resistant organisms, wounds and topical antimicrobial protection. International wound journal 2012;9(4):387-96.

13- **Trivedi U, Parameswaran S, Armstrong A, Burgueno-Vega D, Griswold J, Dissanaike S, et al.** Prevalence of multiple antibiotic resistant infections in diabetic versus nondiabetic wounds. Journal of pathogens. 2014;2014.

14- **Johnson MT, Ramanathan M, Owegi R, Pilla AA.** Modulation of carrageenan- induced paw edema and hyperalgesia in the rat with pulsed magnetic field therapy. Proceedings of the BEMS 30th Annual Meeting, Bioelectromagnetics Society, Frederick, MD, June 2008:156.

15-**Gupta A, Taly A, Srivastava A, Kumar S, Thyloth M**. Efficacy of pulsed electromagnetic field therapy in healing of pressure ulcers: A randomized control trial. Neurology India 2009;57(5):622.

16-**Salzberg A, Cooper SA, Perez F, Viehbeck MG, Byrne DW.** The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: A randomized, double-blind study. Ostomy/Wound Management 1995; 41(3): 42–51.

17-**Neilands JB.** Siderophores: structure and function of microbial iron transport compounds. J Biol Chem 1995 ;270(45):26723-6.

18-**Griffiths E.** "Iron in biological systems," in Iron and Infection: Molecular, Physiological and Clinical Aspects, eds J. J. Bullen and E. Griffiths (Chichester: Wiley-Interscience), 1999: 1–25.

19-**Vianale G, Reale M, Amerio P, Stefanachi M, Di Luzio S, Muraro R.** Extremely low frequency electromagnetic field enhances human keratinocyte cell growth and decreases proinflammatory chemokine production. British Journal of Dermatology 2008; 158(6): 1189-1196.

20-**Athanasiou A, Karkambounas S, Batistatou A, Lykoudis E, Katsaraki A, Kartsiouni T, et al.** The effect of pulsed electromagnetic fields on secondary skin wound healing: An experimental study. Bioelectromagnetics 2007; 28(5): 362–368.

21-**Houghton PE**. Electrical stimulation therapy to promote healing of chronic wounds: a review of reviews. Chronic Wound Care Management and Research 2017; 4: 25–44.

22-**Lagoe RJ, Johnson PE, Murphy MP.** Inpatient hospital complications and lengths of stay: A short report. BMC Research Notes 2011; 4.

Hussain MS, Anwar HW, Elnakib MM, Mosaad AE. Assessment of the effect of pulsed electromagnetic field therapy in the treatment of chronic wounds. Microbes Infect Dis 2023; 4(3): 928-942.