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Topical Insulin Therapy for Enhanced Wound Healing: An Open-Label Randomized Controlled Clinical Study

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ABSTRACT

Background:
Wounds cause consequently significant negative implications on the socio-economic and psychological aspect of an individual as well as the whole society, globally. The purpose of this study was to develop, cost-effective, easily accessible therapeutic options to promote wound healing.

Methods:
This open-label, single-centric randomised controlled study enrolled 82 patients. Patients were divided as 2 groups A and B to receive topical insulin and normal saline respectively. For effectiveness evaluation change in mean surface area (SA), percentage reduction in wound SA, pace and depth of granulation tissue and reduction in visual analog pain score (VAS) was noted. For safety evaluation adverse drug reactions (ADRs) were noted. Statistical analysis included both descriptive and inferential statistics such as repeated measures one way ANOVA.

Results:
A statistically significant difference in mean Surface area, wound depth and VAS over time with large effect size; groups ($F(3.214, 130.166) = 12.478$, $p < 0.0005$, $\eta p^2 = 0.210$), ($F(2.113, 85.589) = 2.132$, $p < 0.05$, $\eta p^2 = 0.040$) and ($F(3.618, 146.52) = 14.960$, $p < 0.0005$, $\eta p^2 = 0.462$) respectively was observed. Also, Group A ($M = 4.14.90$, $SD = 1.13$) reported significantly lesser time to granulation tissue formation than Group B ($M = 9.48$, $SD = 1.62$), $t(71) = 17.244$, $p < 0.0005$, $d = 3.82$ and greater percentage reduction in wound SA ($M = 36.70$, $SD = 11.45$) than Group B ($M = 14.87$, $SD = 12.36$), $t(80) = 8.29$, $p < 0.0005$, $d = 1.83$. Additionally, no major ADRs were observed in both the groups.

Conclusion:
Topical insulin receiving group demonstrated good wound healing as compared to the saline group. Additionally, topical insulin demonstrated a good safety profile. However, large scale multi-centric studies in future can build up on this pre-liminary research.

KEYWORDS: Healing, Insulin, Saline, Topical, Wound

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INTRODUCTION

Wound by definition means an epithelial discontinuation in the skin or mucosal layer brought upon by a thermal or a physical insult.[1,2] This interruption can have implications on the muscles and related tissues, neuronal structures as well as bones, soft tissues and even the organs. However, human skin being the largest organ is most susceptible to wounds.[3] Since mankind's creation wounds have been its partner, yet even with technological advances over the years they continue to be an enigma.[4] Wounds have been on a rise and have become a "silent epidemic." A 2018 retrospective study states that worldwide approximately 8 million people are afflicted with chronic wounds. Major disease burden resultant of wounds and its economic

and effective surgical therapy have led to categorisation of wounds as an essential surgical condition necessitating worldwide surveillance.[5]

Globally the impact of wounds on a health care system's clinical and monetary aspect is noteworthy and in addition it adversely affects the quality of life of the wounded. The wounds expand beyond just physical discomfort to the wounded person's psychosocial well-being.[6] Topical application of insulin has been researched for wound healing in various studies. Key role of Mitogen-activated protein kinase (MAPK) signal-regulated kinase (ERK) pathways and Phosphatidylinositol 3-kinase (PI3K) via insulin having significant impact on growth and development of cells has been observed in diabetic patients.[7] Prior research also demonstrates that in non-diabetic patients, insulin augments re-epithelialization and neo-angiogenesis and is crucial for cell proliferation via insulin receptor substrate (IRS) proteins. In addition, it stimulates cell migration and propagation and cellular epithelial regeneration mitigating inflammation that develops post-injury alongside exhibiting anti-bacterial properties.[8]

Contemporary research suggests that considering tolerability, topical insulin therapy for wound healing demonstrates lesser adverse drug reactions (ADRs) and is cost-effective as per research.[9]According to the current literature research, available topical therapies to facilitate wound healing such as growth factors are a remarkable technological breakthrough displaying huge potential to transfigure the whole wound healing dynamics. Recombinant platelet-derived growth factor beta polypeptide (PDGFB), Colony-Stimulating Factor 3 (CSF 3), and human epidermal cell growth factor are the most important growth factors employed. In spite of that, firstly, the research done so far utilizing these agents has not yielded significant results. Furthermore, these growth factors are conventionally exorbitant.[10]

Secondly, safety profile of insulin is well researched and documented. Thirdly, new drug development is a pricey, cumbersome and time-consuming task while drug repurposing saves time and money.[11] With this prior database, considering the fact that India being a developing currently requires cost-effective wound care therapeutic strategies and insulin might be considered as an option, additionally it has no concern of anti-microbial resistance. Hence, we designed this open-label randomised control trial to gauge the effectiveness of topically applied insulin in wound management as an emerging prospect and perhaps a breakthrough to manage this silent epidemic.

AIM

To assess effectiveness and safety of topical insulin on wound healing

OBJECTIVES

- To study the effectiveness of topical insulin on wound healing
- To assess the safety of topical Insulin
- To compare the topical insulin with normal saline in terms of efficacy and safety

METHODOLOGY

STUDY DESIGN

This was an open-label, single-center, parallel-group, randomized controlled trial conducted to evaluate the effectiveness and safety of topical insulin on wound healing.

STUDY LOCATION

he study was conducted in the General Surgery Outpatient Department (OPD) and inpatient wards of Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India.

STUDY PERIOD

The study was carried out over approximately 24 months, following approval from the College Research Committee (CRC) and Institutional Ethics Committee (IEC).

STUDY POPULATION: Adult population of either gender with Class I and II wounds as per CDC (Centers for Disease Control and Prevention) classification [12,13]

Calculation of Sample Size [14]

$$n = (\sigma 1\ 2 + \sigma 2\ 2)\ \frac{[Z1\text{-}\alpha/2 + Z1\text{-}\beta]^2}{(\bar{x}1 - \bar{x}2)2}$$

Where;

n: sample in each group

$\bar{x}1$: mean of the variable in group 1

$\bar{x}2$: mean of the variable in group 2

σ1: standard deviation of the variable in group 1

σ2: standard deviation of the variable in group 1

Z1-α/2: value of the normal deviate at considered level of confidence (for two-sided test)

Z1-β: value of the normal deviate at considered power of the study (for two-sided test)

For getting statistically significant result, at least 82 total samples, 41 in each group were taken so we may generalize the result to the whole population.

Participants were selected according to the following decided inclusion and exclusion criteria.

Inclusion criteria:

- Age18-65 years old[12]
- Either gender
- Class I & II wound classifications as per Centers for Disease Control and Prevention [110]
- Wound surface area less than 20cm^2
- Patients willing to give written informed consent

Exclusion criteria[11]

- Pregnancy
- Patients on immunosuppressive treatment
- Complicated (bleeding or infected) Wounds
- Study outcome affecting intake of medications
- Cardiovascular illnesses, Peripheral artery disease or Renal and liver cell failure

RANDOMIZATION AND ALLOCATION

Participants were randomized into two groups A and B using a random number table.
Group A: Intervention (topical insulin)
Group B: Control (normal saline)
A CONSORT flow diagram summarizing enrollment, allocation, and analysis is presented in Figure 1.

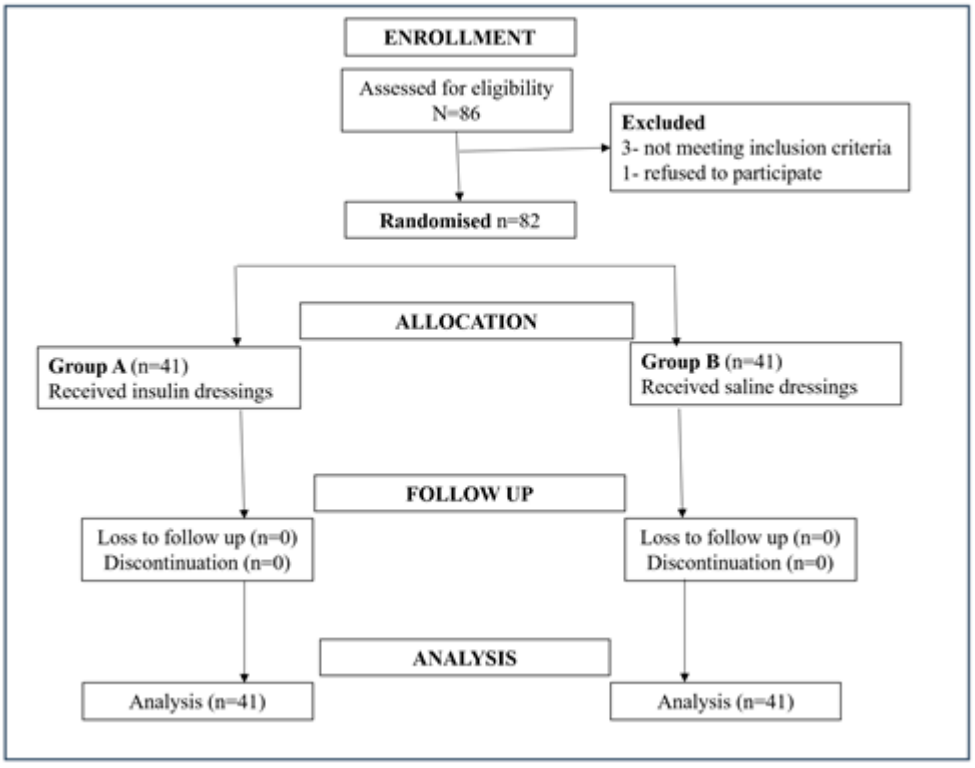


Figure 1: CONSORT diagram

Intervention

Group A – Topical Insulin

- Wound cleansing with normal salinepplication of 4 units (0.1 mL) human soluble insulin diluted in 1 mL of normal saline per 10 cm² wound area[15]
- Insulin solution sprayed using an insulin syringe
- Wound allowed to air-dry and subsequently covered with sterile gauze

Group B – Control

- Wound cleansing with normal saline (1 mL per 10 cm²)
- Air-drying followed by sterile gauze dressing

Both groups received the assigned treatment every 48 hours for 14 days, with the same insulin product used throughout for standardization.

OUTCOME MEASURING TOOLS

EFFECTIVENESS EVALUATION

- Wound Surface Area Measurement: Trace method using sterile transparent sheet; two perpendicular diameters measured with a ruler and multiplied to obtain area (mm²).
- Percentage Reduction in Wound Area:Percentage reduction in wound surface area was calculated using formula: [(A_0 −

$A_t)/A_0] \times 100$, where A_0 is the initial wound area and A_t is the wound area at each time point.[16]

- Granulation Tissue Formation: Time to onset and thickness (mm) were documented.
- Pain Assessment: Using the Visual Analog Scale (VAS).[17]

All measurements were performed by a single trained observer using the same instruments, ensuring reliability and minimizing measurement bias.

Safety assessment:

- Monitoring for local/systemic adverse drug reactions (ADRs) using a validated checklist
- Causality assessment: Naranjo ADR Probability Scale[18]
- Severity assessment: Hartwig and Siegel Scale[18]

All safety data were recorded in a pre-designed case record form.

STATISTICAL ANALYSIS

Eighty-two participants were enrolled with no loss to follow up hence were used for the analysis. Descriptive statistics were utilised to describe the population under study. Inferential statistics such as repeated measures one way ANOVA and independent t-tests were employed to assess the association of age, gender, occupation, education qualifications, aetiology of wound, smoking status, alcoholic status, to wound healing comparing two groups. The effect size was estimated and appropriate post-hoc analysis was carried out if needed. A p-value ≤ 0.05 were considered significant. The analysis was done using SPSS version 25.

RESULTS

The baseline demographic characteristics of the 82 participants enrolled are depicted in Table 1. Majority of participants were males, employed, educated upto10th or more, non -smokers and non- alcoholics. Most wounds were due to trauma. Mean age was 37.3± 15 years. Median age was 44.7± 16.2 years.

Table 1: Both groups baseline Demographic characteristics

Characteristics	Frequency (%)				
Gender	Female	Male			
	31 (37.8)	51 (62.2)			
Occupation	Housewife	Employed/service	Student	Self-employed	Unemployed
	17(20.7)	27(45.1)	10(12.2)	13(15.9)	5(6.1)
Educational qualification	Illiterate	Less than 10th class	Equal to or more than 10th class		
	16(19.5)	12(14.6)	54(65.8)		
Wound Class	Class 1	Class 2			
	0(0)	82(100)			
Aetiology	Trauma	Burns	Others		
	70 (85.4)	9(11)	3(3.7)		
Smoker	Yes	No			
	21(25.6)	61(74.4)			
Alcoholic	Yes	No			
	3(3.7)	79(96.3)			

Table 2 (a): Comparative Baseline participant characteristics

Characteristics	Group A	Group B	P value
Age	**47.14± 16.64**	**42.41± 15.59**	**0.40***
Gender			
Female	18	13	**0.26$^{\#}$**
Male	23	28	
Occupation			

Housewife	10	7	**0.12$**
Employed/service	15	22	
Student	5	5	
Self-employed	10	3	
Unemployed	1	4	
Education qualification			
Illiterate	11	5	**0.25#**
Less than 10th class	6	6	
Equal to or more than 10th class	24	30	
Aetiology of wound			
Trauma	34	36	**0.80@**
Burns	5	4	
Others	2	1	
Smoker			
Yes	14	7	**0.08#**
No	27	34	
Alcoholic			
Yes	1	2	**0.55@**
No	40	39	

*- independent t-test, #-Chi-square, $-Fisher's exact, @-Likelihood ratio

The comparative baseline participant characteristics are depicted in Table 2(a) and Table 2(b). From these tables we can observe that the baseline characteristics of the patients in both the groups i.e. Group A and Group B were comparable (p>0.05).

Table 2 (b): Comparative Baseline participant characteristics

Characteristics	Group A	Group B	P value
Other medications			
Amlodipine	3	2	**0.23@**
Metoprolol	0	3	
Losartan - hydrochlorothiazide	17	10	
Escitalopram	1	0	
Formoterol	0	1	
Budesonide	0	1	
Metformin	3	4	
Sitagliptin	1	1	
Glimepiride	1	1	
Thyroxine sodium	2	1	
No medications	30	33	
Co-morbidities			

No co-morbidities	24	31	**0.19@**
Hypertension	8	5	
Diabetes	4	3	
Hypothyroidism	2	1	
COPD	1	1	
Bronchial Asthma	0	1	
Acne	0	1	
Migraine	1	0	
Anxio-depressive illness	1	0	
BPH	1	0	
Surface Area	1223.39±420.45	1351.21±341.34	**0.14***
Wound depth	6.87± 1.53	7.46±1.35	**0.06***
VAS	6.36 ± 0.91	6.71 ± 0.75	**0.07***

*- independent t-test, @-Likelihood ratio

The concomitant medications taken by the participants is depicted in Figure 2, whereas the Figure 3 displays the various co-morbidities endured by them. Most (76.8%) of the participants were not on any concomitant medication, while commonest concomitant medication was losartan-hydrochlorothiazide. Majority (67.0%) of the participants had no co-morbidities. In the co-morbidities reported hypertension was the commonest as depicted in Figure 3.

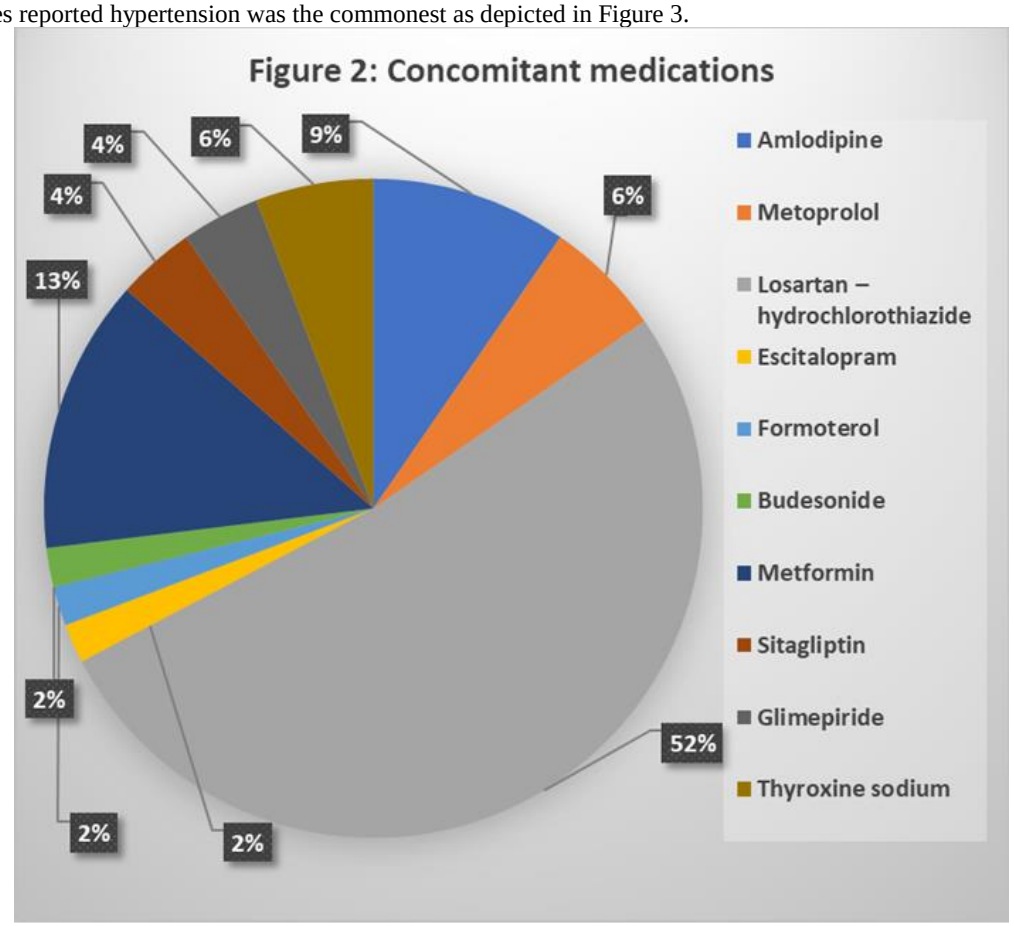


Figure 2: Concomitant medications

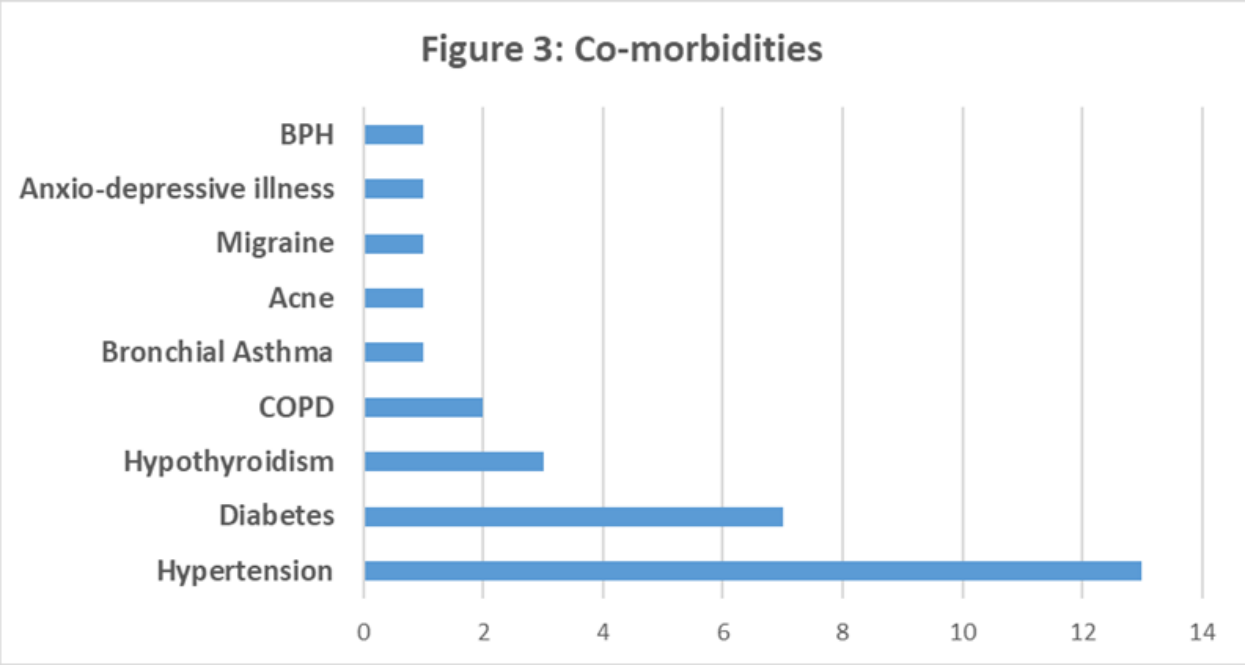


Figure 3: Co-morbidities

A one-way repeated measures ANOVA was conducted to determine if there were significant differences in wound surface area, depth of the wound and VAS across the three time points i.e. day 0,7 and 14 in the two groups A and B. Mauchly's test of sphericity was employed to determine in the variances of the differences between all combinations of related groups were equal. P value was <0.05 hence it indicated violation of sphericity. Greenhouse-Geisser correction applied when epsilon value was <0.75, and Huyn-Feldt correction when otherwise.

The results as showed in Table 3, depicted a statistically significant difference in mean Surface area, wound depth and VAS over time with large effect size as follows; groups (F (3.214, 130.166) = 12.478, $p < 0.0005$, $\eta p^2 = 0.210$), (F (2.113, 85.589) = 2.132, $p < 0.05$, $\eta p^2 = 0.040$) and (F (3.618, 146.52) = 14.960, $p < 0.0005$, $\eta p^2 = 0.462$) respectively. All the three associations established revealed large effect size, considering their partial eta squared values suggesting a strong practical significance of the analysed variable's impact.

Post hoc analysis with a Bonferroni adjustment between groups revealed a significant progressive decrease in surface area over time from zero day to day 7 (119.9mm^2, 95% CI, 55.14 to 184.67, p < 0.0005), from day 7 to day 14 (135.26mm^2, 95% CI, 25.02 to 245.50, p = 0.011) and from day 0 to day 14 (255.17mm^2, 95% CI, 151.08 to 359.26, p< 0.0005).

Bonferroni correction applied between groups revealed a significant decrease in wound depth from day 0 to day 14 (2.54mm, 95% CI, 1.89 to 3.19, p< 0.0005), however zero day to day 7 (0.02mm, 95% CI, - 3.30 to 3.35, p = 1.00), and from day 7 to day 14 (2.51mm, 95% CI, -0.84 to 5.87, p = 0.213) did not reveal statistical significance.

Post hoc analysis with a Bonferroni adjustment between groups revealed a significant progressive decrease in VAS over time from zero day to day 7 (1.02, 95% CI, 0.64 to 1.41, p < 0.0005), from day 7 to day 14 (1.13, 95% CI, 0.68 to 1.57, p < 0.0005) and from day 0 to day 14 (2.15, 95% CI, 1.65 to 2.65, p< 0.0005).

Table 3: Summary table for the one-way repeated measures ANOVA

Parameter	Mean ± SD		F statistics	dF	p value	Partial η²
	Group A	Group B				
Surface area (mm²)						
Day 0	1223.39±420.45	1351.21±341.34	12.478	(3.214, 130.166)	<0.0005*#	0.210
Day 7	1037.07±428.83	1236.34±391.38				
Day 14	796.87 ± 339.72	1159.51±377.86				

Wound depth (mm)						
Day 0	6.87± 1.53	7.56±1.35	2.132	2.133, 85.589)	<0.05*$	0.040
Day 7	6.32 ± 7.92	6.39 ± 1.37				
Day 14	2.73 ± 0.71	5.50 ± 1.31				
VAS						
Day 0	6.36 ± 0.91	6.78 ± 0.75	14.960	(3.618, 146.52)	<0.0005*#	0.462
Day 7	4.82 ± 0.89	5.80 ± 0.84				
Day 14	3.12 ± 0.92	4.70 ± 1.00				

*Statistically significant p value<0.05, #Huyn-Feldt correction, $Greenhouse-Geisser correction

Table 4: Comparative means of time to granulation tissue and percentage reduction in surface area

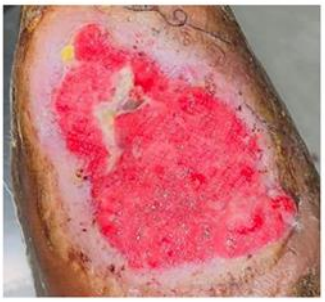
Parameter	Mean ± SD	P value	Effect Size
Time to granulation tissue (days)			
Group A	4.14 ± 1.13	< 0.005*	3.82#
Group B	9.48 ± 1.6	—	—
Percentage reduction in wound surface area			
Group A	36.70 ± 11.45	< 0.005*	1.83#
Group B	14.87 ± 12.36	—	—

*Statistically significant p value <0.05, # Cohen's d value

An independent samples t-test was conducted to compare the time to granulation tissue and percentage reduction in wound surface area between Group A and Group B. The results as depicted in Table 4, showed that Group A (M = 4.14.90, SD = 1.13) reported significantly lesser time to granulation tissue formation than Group B (M = 9.48, SD = 1.62), t (71) = 17.244, p <0.0005, d = 3.82, indicating a statistically significant difference. Also. Group A had statistically significant percentage reduction in wound surface area (M = 36.70, SD = 11.45) than Group B (M = 14.87, SD = 12.36), t (80) = 8.29 p<0.0005, d = 1.83.

Figure 4, shows pictorial representation of reduction in wound surface area. While Figure 5, shows appearance of granulation tissue.

Figure 4: Reduction in wound surface area



Safety profile: Upon using the pre-validated checklist for noting the local and systemic ADRs, both Insulin and Saline displayed a good tolerability profile. None of the groups reported spontaneous ADRs. However, in terms of local ADRs observed Insulin group had one patient with transient itching while saline group one patient reported increased pain at wound site. As far as systemic ADRs are concerned one patient each in both the groups reported headache. The adverse drug reactions observed had possible causality and severity of mild level 1. Overall safety profile for both groups was good.

DISCUSSION

Contemporary research evidence demonstrates that non- healing chronic wounds are contributory to lowering the quality of life not only of the one who is afflicted but their family, society and health care system as a whole. The impact of these wounds is not just on the physical well-being of a person but also his state of mind which makes wound management a major matter requiring global attention.[19]

The current therapeutic agents are pricey and not highly effective and are not accessible by all, hence wound healing phenomenon continues to be a conundrum.[20] The supportive threapy includes protecting the exposed healthy tissue, reducing the risk of infection, preventing pigmentation changes and scarring, and promoting faster skin regeneration.[21]

The process of wound healing is a complex process incorporating re- epithelialisation and formation of new blood vessels to facilitate healing. This process is interposed by release of numerous cytokines such as wound healing involves re-epithelialisation and research suggests that induction of neo-angiogenesis as well as re-epithelialisation is an intricate process which is mediated by release of various cytokines such as fibroblast growth factors (FGF), insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), epidermal growth factors (EFG), tumour necrosis factor-alpha (TNF-α), transforming growth factor-beta 1 (TGF-β1), and vascular endothelial growth factor (VEGF). Other crucial proteins implicated in effective healing of the wound are collagen, keratin and gelatin.[22]

Topically applied insulin also demonstrates anti-oxidant characteristics by scavenging reactive oxygen radicals in a murine species research and therefore aids wound healing. Another research suggests this anti-oxidant behaviour is a result of IL-10 level build up, stimulation of the PI3K-AktRac1 pathway and keratinocyte migration and clearance of dead necrotic tissue.[23]

Various animal and in-human research suggest that topical application of insulin with its inherent peptide nature Numerous pre-clinical and clinical studies suggest that insulin being a peptide when topically applied depicts anti-inflammatory attributes with early neutrophilic recruitment and consequently healing wound.[24] Systematic review and meta- analysis of numerous wound studies affirm that topically applied insulin hastens granulation tissue formation as compared to controls. Additionally, various clinical trials support the evidence that topical insulin curtails time to healing.[25]

Keeping in mind the data from majority of the studies, we utilised regular (soluble) insulin formulation for topical application. Moreover, attempting to maintain consistency throughout the research, we kept the brand (non-funded) same. Median age of the patients enrolled in our study came out to be 44.7± 16.2 years while reported mean age was 37.3± 15 years. This is in congruence with findings observed in a study where the median age observed was 40 years.[26] Alternatively, another research documented otherwise with the overall median age of patients enrolled with traumatic injuries was 63.6 years.[27] The reason behind this observation of more young individuals could be possibly supported by the fact that they need to go out more often for work and related tasks and therefore are more predisposed to work-related injuries and this is further corroborated by another fact observed in our research where most of the wounds were of traumatic origin.

Published data on numerous studies on wounds has displayed that majority of the patients enrolled were of male gender. This goes in alignment with our research findings which had vast majority of men.[28] In a country like India, it seems this is bound to happen for most of the studies because as per Indian socio-culture and behavioural environment it's usually the males who are or are expected to be the family head and wage holder and hence are more vulnerable to work related injuries. Moreover, most of the patients enrolled in our study were holding a job and were well educated. Now this is a common occurrence as well as the more educated a person shall be they are expected to be more self-aware and have better understanding of safety perception and willingness to reach out for medical assistance for any health concern, be it an injury.[29]

Traumatic injuries were the commonest observance in our research. This is in alignment with another research which revealed most of the wounds to be associated with trauma presented in the form of stabs or cuts (32.8%), falls (22.4%) or motor vehicle accidents (16.4%).[5] Another research carried out in Southern Tunisia also corroborates this observation.[30] Globally, burn related injuries seem to be declining, however in developing country like India it still continues to be a major concern.

As per our research findings people refraining from alcohol were the ones who reported most of the injuries. This observation is in non- congruence with some research that clearly depicted that alcoholics are more susceptible to motor vehicle accidents related injuries.[31] This contradictory observation could be a result of under-reporting and false-reporting of alcoholism due to its societal stigmatisation and also due to the factuality that it is heavy alcoholism and not occasionally a drink or two that is connected with injuries.

Majority of the patients included in our study self-reported to be non- smoking people. Although not smoking has not proved to offer any undue advantage in terms of protection from unintended injuries, and the incidence of reported motor vehicle accidents and trauma among non- smokers is parallel to the general community. Yet, the available research does imply that people who do not smoke have lesser susceptibility to injuries than smokers.[32] Most widespread co-morbidity as per our research was hypertension which is in parallel with another research carried out on wound healing which had majority (78%)

of the subjects which were hypertensives.[33]

The healing of the wounds in relation to reduction in wound surface area and clinically meaningful change in VAS score was evident in insulin treated group as per our study. Research done in Maharashtra, India suggested that the insulin treated group had significantly reduced mean surface wound area (mm^2) at day 6 than saline treated group ($p<0.05$, df=58,t=3.98).[34] One more randomised study done on wound healing demonstrated that topically applied insulin facilitates wound healing.[35] Healing outcomes when analysed in another study revealed significant ($p < 0.001$) percentage decrease in wound surface area in the insulin treated group in comparison to saline treated one.[36]

Our research depicted statistically significant decrease in wound depth in insulin treated group. Research conducted by Thakur PB and his co-workers in Maharashtra, India, also revealed that mean depth of the wounds (mm) at day 6th day was significantly less in insulin treated group in comparison to saline treated group ($p<0.001$, df=58, t=4.92).[34]

Our research demonstrated change in VAS score to be more in the group which received topical insulin as compared to saline receiving group. Another study conducted in wound healing suggested that using insulin as an advance organo-gel preparation reduced had reduction in pain in diabetic foot ulcers.[37] Another research suggested topical insulin application aided in pain relief in a case of hidradenitis suppurativa.[38] A randomised clinical trial done on wound healing revealed greater reduction in pain at wound site along with reduced infection rate in a combination treatment of insulin, polymyxin-B ointment recombinant human basic fibroblast growth factor in second- degree burns in patients of diabetes milletus.[39]

An observation of reduced time to appearance of granulation tissue in insulin treated group in contrast to saline treated one was made in our research. This is alignment with a research conducted on healing of diabetic ulcers where the analysed mean time required for granulation tissue to appear was significantly less in insulin treated group in comparison to saline group ($p<0.001$, df=58, t=5.87).[34] Moreover, a recently done clinical trial where topically applied insulin significantly augmented wound healing outcomes, displayed a larger percentage decrease in wound surface area ($p < 0.001$) and a shorter time to healing at day 7 in the insulin group (4450.00 [3000.00–5460.00]) compared to the saline group (2594.00 [2090.00–7560.00]), $p = 0.001$).[40] The tolerability profile of the topical insulin for wound healing as per our research was good considering absence of any major or serious local or systemic adverse effects. As per a study that conducted extensive review of literature on the topic, that included analysis of numerous basic and preclinical studies it was affirmed that engineered polymeric matrices/scaffolds with insulin demonstrated high efficacy and good tolerability in topical wound treatment.[41]

LIMITATIONS OF THE STUDY

We acknowledge that the research was open -label, it could have been even better if the study was blinded, even single-blinded where the researcher would have been blinded could suffice. However, since it's preliminary research in this arena, in subsequent further larger study the design can be modified. It's a small sampled single- centric study so it has limited generalizability in terms of large population. The expected impact of co-morbidities and concomitant medications on wound healing outcomes also could not be ascertained probably due to limited sample size. Many such confounding factors could be tackled by planning larger multi-centric trails will help affirm and build up on the data observed from this pre-liminary research.

CONCLUSION

Topical insulin demonstrated a significant improvement in wound healing outcomes compared to normal saline, as evidenced by greater reduction in wound size, earlier granulation tissue formation, and better pain control. The treatment was well-tolerated with no major adverse effects observed. These findings suggest that topical insulin is a safe, cost-effective, and promising therapeutic option for enhancing wound healing. Larger, blinded multicentric studies are recommended to further validate these results and support wider clinical adoption.

ACKNOWLEDGEMENTS -Nil

ETHICAL ISSUES- Ethical approval taken from Teerthanker Moradabad Institutional Ethics Committee (TMU-IEC) bearing reference number TMU/IEC Nov. 23/61. Patient informed consent was also obtained from the subjects.

COMPETING INTERESTS – None

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