European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: Applied
Website: https://farmclin.es/

Article

Topical Insulin in Wound Healing: A Randomized Controlled Pilot Assessment

Article History:
Received 12-11-2025
REVISED:25-11-2025
Accepted: 09-12-2025
Published: 18-12-2025

Name of Author:
Meenu Thomas[1], Prithpal Singh Matreja[2], Naveen Kumar Singh[3]

Affiliation:
[1]Department of Pharmacology, Teerthanker Mahaveer Medical College and Research Centre, Teerthanker Mahaveer University, Moradabad, (U.P.) 244001, India. https://orcid.org/0000-0002-4975-3367,
[2]Department of Pharmacology, Teerthanker Mahaveer Medical College and Research Centre, Teerthanker Mahaveer University, Moradabad, (U.P.) 244001, India. https://orcid.org/0000-0002-9552-3642,
[3]Department of General Surgery, Teerthanker Mahaveer Medical College and Research Centre, Teerthanker Mahaveer University, Moradabad, (U.P.) 244001, India. https://orcid.org/0000-0001-7156-9817,

Corresponding Author:
Meenu Thomas, Ph.D. Research Scholar

How to cite this article:
Meenu Thomas, Prithpal Singh Matreja, Naveen Kumar Singh. "Topical Insulin in Wound Healing: A Randomized Controlled Pilot Assessment" European Journal of Clinical Pharmacy, vol. 1, no. 1, 2025, pp.1–5.

Abstract: ***Background*:** Wounds continue to have significant negative implications on the socio-economic and psychological aspect of an individual as well as the whole society, globally. Cost-effective, easily accessible therapeutic options to promote wound healing are the need of the hour. The purpose of this pilot study was to analyse pre-liminary effectiveness and tolerability of topical insulin on wound healing.

***Methods*:** This open-label, single-centric randomised controlled pilot study enrolled 24 patients. Patients were divided as 2 groups A and B to receive topical insulin and normal saline respectively. For effectiveness evaluation percentage reduction in wound surface area as well as reduction in visual analog pain score was noted. For safety evaluation adverse drug reactions were noted both spontaneously reported as well as utilizing a pre-validated checklist. Statistical analysis included both descriptive and inferential statistics such as Chi-square test.

***Results*:** The insulin group displayed statistically and clinically significant percentage reduction in wound surface area., $\chi 2(1, N = 24) = 8.22$, $p = 0.004$. (OR = 15, 95% CI [2.02, 111.71]). Also, adequate pain control was observed in the insulin group $\chi 2(1, N = 24) = 17.14$, $p = $ □0.001. (OR = 6, 95% CI [1.69, 21.26]). 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, this being a pilot study, larger multi-centric studies in future can build up on this pre-liminary research.

Keywords: Healing, Insulin, Saline, Topical, Wound

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.

Authors contribution:
Conceptualisation: Meenu Thomas
Methodology: Meenu Thomas, Prithpal Singh Matreja
Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review and editing: Meenu Thomas
Resources, Visualisation, Supervision - Project administration: Meenu Thomas, Prithpal Singh Matreja, Naveen Kumar Singh
Writing, review & editing: Meenu Thomas, Prithpal Singh Matreja, Naveen Kumar Singh.

Funding:
Nil

INTRODUCTION

A wound as per definition is out-and-out destruction of the living tissue, such as the skin, mucous membranes, and organs. Alternative definitions include interruption in the skin or mucosal epithelial lining's continuity expediated by heat or physical injury.[1,2] This split can also impact the Musculo-skeletal, neuro-vascular, subcutaneous and bony structures. Skin being the largest human organ is most vulnerable to injury.[3] Since the creation of Adam wounds have been accompanying him. The knowledge of treatment of wounds have advanced over the years yet wound healing remains a conundrum.[4] Chronic wound occurrence has been rising like a "silent epidemic." A 2018 retrospective study states that wounds agonize around 8 million individuals globally.

The clinical and financial impact of wounds on the world's healthcare systems is significant, and it noticeably reduces the quality of life of the injured. Consequences of the wounds are not only limited to the discomfort from the wound itself but they extend to the afflicter's social, physical, or psychosocial well-being.[5] Insulin has been studied for topical application in wound healing. Numerous biochemical mechanisms are implicated in enhancement of wound healing in diabetics. Insulin employs both the Phosphatidylinositol 3-kinase (PI3K) /AKT and Mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK) pathways that have critical growth and development impacts.[6]

Prior research suggests that insulin advances wound healing in non-diabetics by boosting re-epithelialization and angiogenesis. Insulin receptor substrate (IRS) proteins are crucial insulin signalling injured skin insulin-regulated cellular proliferation in skin. Insulin is essential for controlling cellular proliferation. It regulates post injury inflammation in the surrounding tissues by stimulated migration and propagation. After removing the exudate and necrotic tissue it promotes surrounding cellular layer regeneration. Insulin in addition impedes bacterial colonization.[7]

Furthermore, topical insulin treatment for wound healing produced fewer adverse drug reactions (ADRs) and is less expensive as per research.[8] The World Health Organization defines ADR's as "a response to a medication that is noxious and unintended and occurs at doses normally used in man."[9]

According to the literature, available topical therapies like Growth factors are significant technological developments that have the potential to revolutionize the overlook of wound healing. Recombinant human platelet-derived growth factor-BB (PDGF), granulocyte colony-stimulating factor (CSF), and epidermal growth factor are the most important growth factors employed. The research done so far utilizing these agents has not yielded significant results. Furthermore, these growth factors are customarily highly-priced expensive.[10]

Secondly, safety profile of insulin is well known. Thirdly, new drug development is a costly affair and drug repurposing reduces time and cost effective.[11] With this prior database, we may consider that topical insulin is a less expensive and more effective supplementary active wound care, particularly in developing countries like India. Hence, we planned to conduct this pilot study to evaluate the efficacy of topical insulin in wound healing as a new hope and possibly a revolution in the field of this silent epidemic of wounds and if later on expand it further.

AIM

To assess effectiveness and safety of topical insulin on wound healing.

OBJECTIVE

- 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

This open-label, single-centric, parallel group, randomized controlled pilot study was done on patients visiting the General Surgery OPD as well as the in-patients visiting a tertiary care hospital in northern India. In accordance with the Indian Council of Medical Research (ICMR) National Ethical Guidelines, post-approval from College Research Committee and Institutional Ethical Committee, informed consent was taken individually from each patient after debriefing the subjects about the purpose of the research. Calculation of sample size for a pilot study is not usually done as it primarily does not test the hypothesis. Nonetheless, as

per research suggesting 12 subjects per group, we took 24 total patients.[12] However, to keep sample size identical with the further planned study inclusion and exclusion criteria were kept same.
The subjects were selected according to the following inclusion and exclusion criteria.

INCLUSION CRITERIA

- Age18-65 years old[13]
- Either gender
- Class II wound classifications as per Centers for Disease Control and Prevention [14]
- Wound surface area 10 (less than 20cm2)
- Patients willing to give informed consent

EXCLUSION CRITERIA

- Pregnancy
- Patients on immunosuppressive treatment
- Wounds that are complicated (e.g., Bleeding or infection)
- Medications that may impact the study's outcome
- Cardiovascular illnesses (uncontrolled hypertension, recent myocardial infarction or cardiac surgery), Peripheral artery disease or Renal and hepatic failure

Once enrolled the patients were randomized into two groups A and B using a random number table. Participant enrolment is depicted in Figure 1.

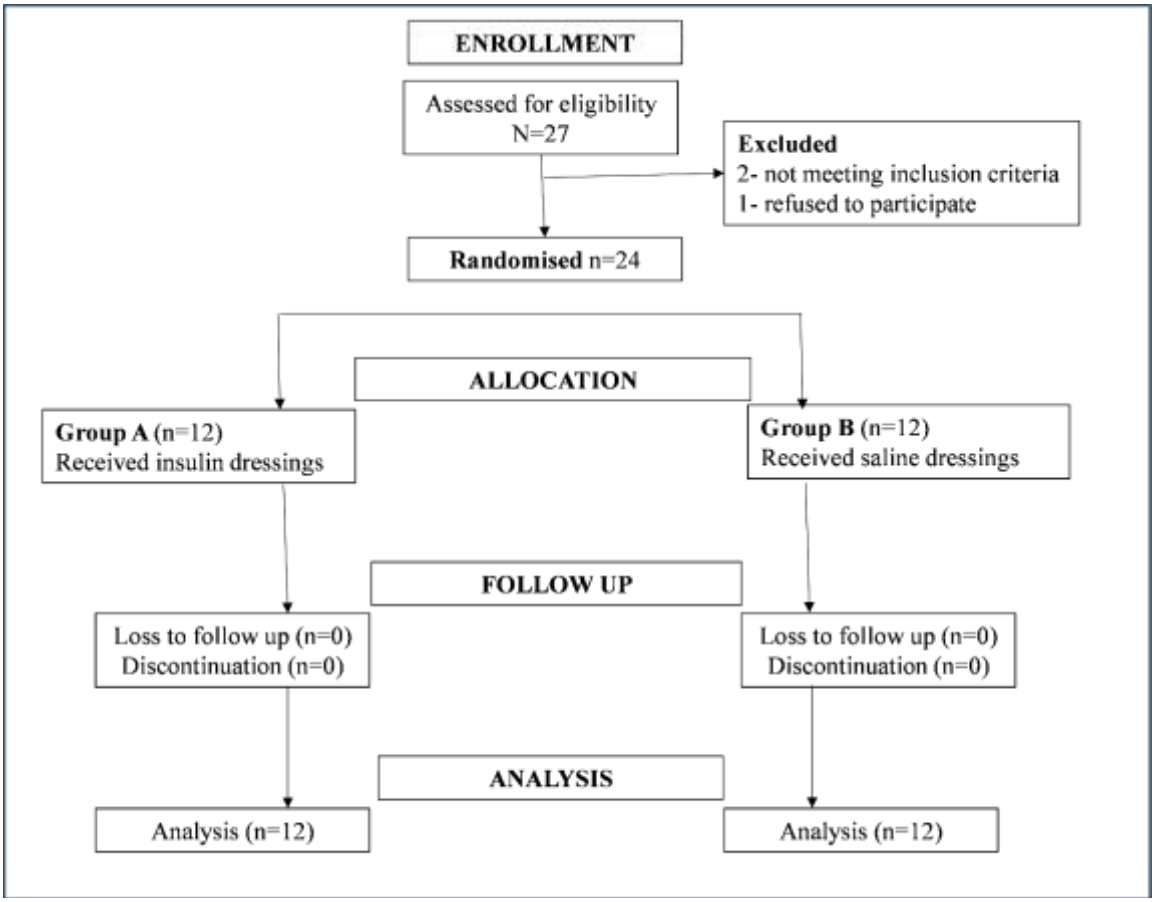


Figure 1: CONSORT diagram: Enrolment, randomization, and allocation of patients participating in the study.

TREATMENT

Group A: wound was cleaned with normal saline and then irrigated with 4 units (0.1 ml) of human soluble insulin (same brand was consistently used which was available at our institution) in 1 ml normal saline (0.9%) for each 10 cm2 of wound.[14] The solution prepared was sprayed on the wound surface with an insulin syringe and wound was left to dry and then covered with sterile cotton gauzes.

Group B: wound was cleaned with 1 ml normal saline (0.9%) for each 10 cm2 of wound without insulin, allowed to dry and covered with sterile gauzes.

Both the groups received the designated dressings every 48 hours for 14 days.

EFFECTIVENESS ASSESMENT

Wound surface area and VAS (visual analog scale) pain score at day zero,7 and 14 were noted. Wounds were measured using a sterile transparent paper placed on the wound to mark the wound borders. The two largest perpendicular diameters were measured using a ruler (in millimetres). To calculate the wound area, these two diameters were multiplied to obtain area of ulcer in mm^2. 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] More than 50% reduction in percentage of surface area in 4 weeks is considered a good indicator of healing in research.[17] Our research was for two weeks, therefore we considered 25%

reduction as cut off to determine good or inadequate healing.

Pain was assessed using VAS as an indicator of healing.[18] A 33% change in VAS score from baseline implies significant pain control as per research.[19] Hence, we considered a round off of 30% or less score to suggest adequate pain control and an indirect indicator of wound healing. For maintaining the accuracy of the test all the readings were taken by a single observer and same instruments.

SAFETY ASSESMENT

Spontaneous ADRs were noted as well as utilising a self-structured pre-validated checklist for local or systemic ADRs were monitored. The Naranjo Adverse Drug Reaction Probability Scale was used to establish causality while Hartwig and Siegel Severity Assessment Scale to determine the severity of Adverse Drug Reactions.[20] Data obtained was entered and transferred to excel sheet- master chart prepared.

STATISTICAL ANALYSIS

Twenty- four subjects were enrolled with no loss to follow up hence were used for the analysis. For statistical analysis the wound healing was categorised as good healing or inadequate healing (considering 25 % reduction in wound surface area in 2 weeks as threshold) and VAS score as adequate and inadequate pain control (change of 30% taken a scut off). To define the characteristics of subjects, descriptive statistics was used. The Chi square test was used for categorical variables. Age being a continuous variable was categorised into two groups considering median age. The association of age, gender, occupation, education qualifications, aetiology of wound, smoking status, alcoholic status, to wound healing was assessed by doing the chi square tests and estimating the odds ratio. A p-value ≤ 0.05 were considered significant. The analysis was done using SPSS version 21.

RESULTS

The baseline demographic characteristics of the 24 patients enrolled are depicted in Table 1. Majority of patients were males, employed, educated upto10th or more, non -smokers and non- alcoholics. Most wounds were due to trauma. Mean age was 37.3± 15. Median age was 33.5 years, based on that patients were divided into two categories age ≤33.5 years and > 33.5 years.

Table 1: Baseline Demographic characteristics

Characteristics	**Frequency (%)**				
Age (years)	≤33.5	> 33.5 years			
	12 (50)	12 (50)			
Gender	Female	Male			
	10 (40)	14 (56)			
Occupation	Housewife	Employed/service	Student	Self-employed	Unemployed
	5(20)	11(44)	4(16)	4(16)	0(0)
Educational qualification	Illiterate	Less than 10th class	Equal to or more than 10th class		
	3(12)	2(8)	19(76)		
Aetiology	Trauma	Burns	Others		
	20 (80)	4(16)	0(0)		
Smoker	Yes	No			
	7(28)	17(68)			
Alcoholic	Yes	No			
	1(4)	23(92)			

The concomitant medications taken by the enrolled patients is depicted in Figure 2, whereas the Figure 3 displays the various co-morbidities endured by them. Majority (62.5%) of the patients had no co-morbidities followed by hypertension (12.5%) hence the concomitant medication mostly (29%) prescribed was losartan-hydrochlorothiazide.

Figure 2: Concomitant medications

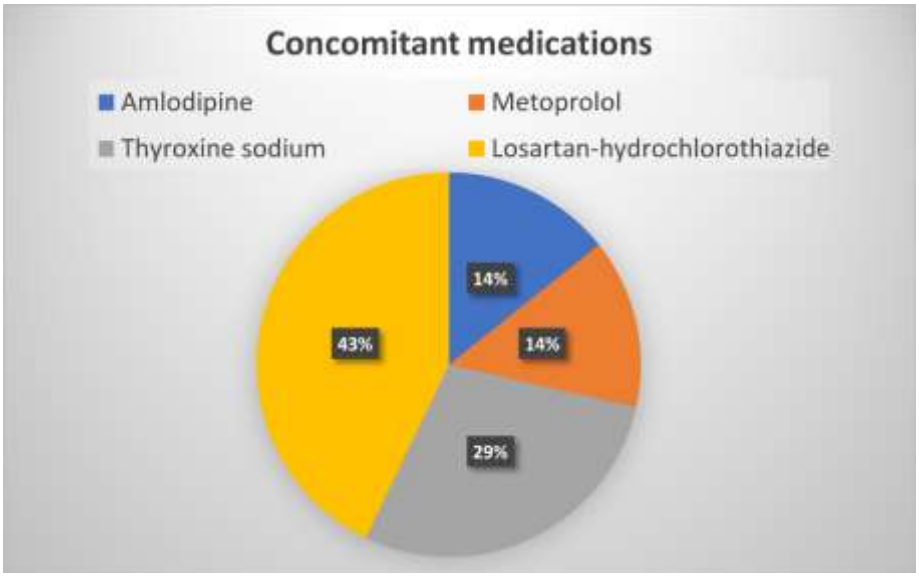
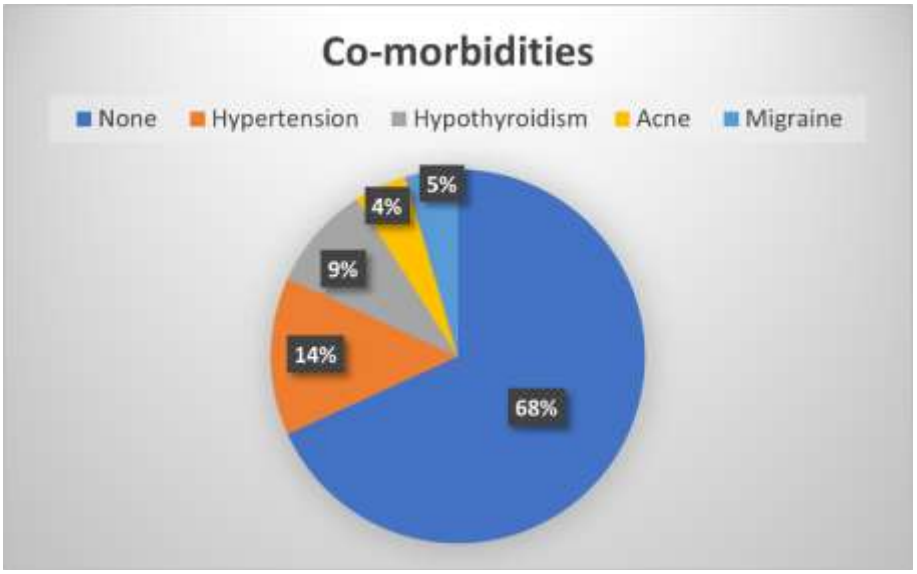


Figure 3: Co-morbidities.



EFFECTIVENESS

For statistical analysis purpose the wound healing was categorised as a Good healing or inadequate healing in accordance with recent research. Table 2 demonstrates the association of various demographic parameters with healing as reflected by percentage reduction in wound surface area. The data suggests that only the group i.e. Insulin or saline had statistically significant association with Healing, with Insulin group reflecting good healing, $\chi^2(1, N = 24) = 8.22$, $p = 0.004$. (OR = 15, 95% CI [2.02, 111.71])

Table 2: Association between demographic parameters and percentage reduction in surface area of wound

	Percentage reduction in wound surface area				
Characteristics	**Category**	**Chi Square (X^2)**	**Degree of freedom**	**P value**	**Odds Ratio/Phi or Cramer V (as applicable)**
Age group (years)	**≤33.5**	1.510	1	0.219	0.251#
	> 33.5				
Gender	**Female**	0.1201	1	0.729	0.71#
	Male				
Group	**Insulin**	8.224	1	0.004*	0.585#

					OR 15(95% CI 2.02,111.17)
	Saline				
Educational qualification	**Illiterate**	0.645	2	0.724	0.164[$]
	Less than 10th				
	Equal to or more than 10th				
Occupation	**Housewife**	2.743	3	0.433	0.338[$]
	Employed				
	Student				
	Self-employed				
	Unemployed				
Aetiology	**Trauma**	1.645	1	0.200	0.262[#]
	Burns				
Smoker	**Yes**	0.509	1	0.476	0.146[#]
	No				
Alcoholic	**Yes**	1.233	1	0.267	0.227[#]
	No				
Concomitant medications	**Yes**	4.913	5	0.662	0.304[#]
	No				
Co-morbidities	**Present**	1.145	1	0.285	0.440[#]
	Absent				

***** - statistically significant p value (>0.05), [#] - Phi value, [$] -Cramer's V value

For statistical analysis purpose the difference in VAS was categorised as adequate pain control or inadequate pain control based on the difference in VAS score in alignment with current research. Table 3 demonstrates the association of various demographic parameters with VAS score as indirect measure of healing or effectiveness of therapy in terms of pain control. It was observed that only the group i.e. Insulin or saline had statistically significant association with pain control, with Insulin group displaying adequate pain control and therefore reflecting better healing., $\chi^2(1, N = 24) = 17.14$, p = >0.001. (OR = 6, 95% CI [1.69, 21.26])

Table 3: Association between demographic parameters and change in Visual analog scale score

	Difference in VAS				
Characteristics	Category	Chi Square (X^2)	Degree of freedom	P value	Odds Ratio/Phi/Cramer V (as applicable)
Age group (years)	≤33.5	0.686	1	0.408	0.169[#]
	> 33.5				
Gender	Female	0.490	1	0.484	0.143[#]
	Male				
Group	Insulin	17.143	1	>0.001	0.845[#]
	Saline				
Educational qualification	Illiterate	0.144	2	0.930	0.78[$]
	Less than 10th				
	Equal to or more than 10th				
Occupation	Housewife	4.064	3	0.255	0.412[$]

	Employed				
	Student				
	Self-employed				
	Unemployed				
Aetiology	Trauma	0.549	1	0.459	0.151[#]
	Burns				
Smoker	Yes	3.408	1	0.81	0.356[#]
	No				
Alcoholic	Yes	0.745	1	0.388	0.176[#]
	No				
Concomitant medications	Yes	3.913	5	0.562	0.404[#]
	No				
Co-morbidities	Present	1.143	1	0.285	0.218[#]
	Absent				

* - statistically significant p value (>0.05), [#] - Phi value, [$] -Cramer's V value

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. where one patient developed transient itching at site of insulin application in insulin group (Group A) with no systemic adverse effects reported. However, in Saline group i.e. Group B, one patient complained of increased pain, while one complaint of headache. The adverse drug reactions observed had possible causality and severity of mild level 1. Overall safety profile for both groups was good.

DISCUSSION

Research suggests that wounds especially non-healing chronic ones are implicated to be causative in significant burden not only on a person, but the entire society and health-care infrastructure. The thrust of the wounds encompasses socio- economic as well as psychological aspects and is a major emerging concern.[21]

Wound healing is a complex process and currently continues to be challenging as the available therapeutic options are not very effective and are not cost-effective and not affordable by all.[22] The supportive management includes protection of the exposed healthy tissue, reducing risk of infection, preventing pigmentation and promoting skin regeneration.[23]

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 insulin-like growth factor (IGF), epidermal growth factors (EFG), fibroblast growth factors (FGF), platelet-derived growth factor (PDGF), transforming growth factor-beta 1 (TGF-β1), tumour necrosis factor-alpha (TNF-α), and vascular endothelial growth factor (VEGF). A number of proteins like insulin, collagen, keratin, gelatin are also vital for assisting in effective wound healing.[24]

Numerous pre-clinical and clinical studies suggest that insulin being a peptide when topically applied hastens wound healing, stimulates early neutrophil recruitment and displays anti-inflammatory properties.[25] Wound studies meta- analysis report that granulation tissue growth is enhanced and new blood vessels are formed in the insulin treated group as compared to controls in various animals. Also, in various clinical studies the time to healing is also significantly cut short.[26]

Topically applied insulin augments wound healing due to its antioxidant and anti-inflammatory characteristics. Topical insulin has been found to mitigate reactive oxygen species in thermal injury wounds in rodents. Another research implicates this property due to enhancement in the levels of IL-10 levels and therefore removing necrotic tissue. Additionally, by stimulating the PI3K-AktRac1 pathway it facilitates migration of keratinocyte and kick starts fibroblasts.[27]

In our research we used regular insulin keeping in consideration the available current research which predominantly uses the same preparation. We also kept the brand (no funding received) same to avoid any inconsistencies.[28] In our research the median age of patients was 33.7. This goes parallel with another research which reported young patients with average age of 33.4 years.[29] However, another research suggests otherwise where the overall median age of patients with traumatic injuries was 63.6 years.[30] The possible reason for our study having more young individuals could be attributed to the fact that they are more outgoing in terms of job and employment and are more exposed to occupational as well as traumatic injuries and in our study most of the subjects were working and had trauma as their aetiology of wounds.

On careful observation of published materials, it has been observed that studies done on wounds and wound healing incorporate a higher proportion of males. This goes in alignment with our study where male patients constituted majority.[31] This fact can be attributed to a number of social, cultural and behavioural factors which mainly include men in India who are the main bread winners and are prone to occupational injuries. Our study had most patients who were employed and

were well educated, it is often observed that people who are educated more have better safety perceptions and also those who are employed and have source of income will readily seek medical help for the same.[32]

Our research documents most wounds to be of traumatic origin which goes along with another research reporting most wounds due to trauma which included Most wounds were as a consequence of stabs or cuts (32.8 %), falls (22.4 %), or road traffic accidents (16.4 %).[33] Another research conducted in Sothern Tunisia also affirms to the fact that traumatic wounds are the commonest type.[34] Research does suggest global reduction in thermal injuries, yet the incidence continues to be still high in country like India.

Observations made from our research suggests that most injuries were reported by non-alcoholics. This is in non- alignment with some research that suggests that injuries especially road traffic accidents are more common among alcoholics.[35,36] This mismatch can be attributed to false reporting of alcoholism due to social stigma associated with it and also due to the fact that the injuries reported in research are linked with heavy alcohol use and not occasional light drinking.

Most people enrolled in our study reported themselves to be non-smokers. Even though not smoking does not offer any additional benefit in prevention or safety from injuries that are unintentional, and their reported incidents of injuries due to road traffic injuries and falls is same as the general population, such as road traffic incidents and falls. Nonetheless, the available research does reflect that non-smokers face a significantly lower risk of injury compared to smokers.[37] Most patients had hypertension as their co-morbidity which is comparable with another study done on wound healing which had the same co-morbidity in most (78%) of the patients enrolled in the study.[38]

The wound healing in terms of percentage reduction in surface area of wound as well as clinically meaningful difference in VAS score were all demonstratable in the patients receiving topical insulin for wound healing in this pre-liminary study. Another research also suggests that topical insulin application augments wound healing.[39] In another study topical insulin significantly enhanced wound healing outcomes, demonstrating a greater percentage reduction in wound surface area ($p < 0.001$) at day 7 in the insulin group compared to the saline group.[40]

As per the observed changes in VAS score from baseline to follow up at 14 days our research suggested meaningful pain reduction post application of topical insulin on wounds. Another research utilising novel organo-gel preparation of Insulin had reduction in pain in diabetic foot ulcers.[41] Another research suggested topical insulin application aided in pain relief in a case study of hidradenitis suppurativa.[42] Research done with a topical application of a combination of polymyxin B ointment, insulin and recombinant human basic fibroblast growth factor in second -degree thermal wounds in diabetic patients reported positive results suggesting reduction in pain at wound site along with reduced infection rates.[43]

Moreover, this pilot study also suggested a good tolerability of topical insulin on wound healing as no major local or systemic adverse effects were observed during the study which reflects a good safety profile of topical insulin in this context.[15] Another research conducted in Poland suggested that basic and preclinical studies affirm the fact that bio-engineered insulin matrix demonstrates promising effectiveness and good safety profile as a topical agent for promotion of wound healing.[44]

Various modified preparations of insulin such as insulin–cobalt core–shell nanoparticles also have demonstrated to be highly efficient as a therapeutic option in wound healing as well as monitoring its binding to insulin receptors through bio-imaging.[45] Even combination therapies have been shown to be synergistic and beneficial. Combining Insulin with traditional and European medicine in a study in China reported promising results in a study done on management of diabetic foot ulcers.[46] Topical insulin with micro needling has found to be beneficial in healing as well. Post- micro needling there occurs release of growth factors of Platelet rich plasma and deposition of collagen in a lattice fashion which augments post- acne scars healing. There is augmentation of vascular endothelial growth factor (VEGF)which promotes angiogenesis and maturation of type III collagen fibres in a weaved basket like pattern simulating normal skin structure.[47] These numerous studies demonstrate a promising future of topical insulin in the arena of wound healing.

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 a pilot study, 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

Topically applied Insulin may be beneficial as a safe and feasible wound healing treatment in patients with wounds as per our research findings. Nonetheless, larger sample-sized, multi-centre clinical trials are a necessity to affirm and further build up on the data obtained from our research.

REFERENCES

1. Kujath P, Michelsen A. Wounds - from physiology to wound dressing. Dtsch Arztebl

Int. 2008;105(13):239-48.
2. Palackic A, Jay JW, Duggan RP, Branski LK, Wolf SE, Ansari N, El Ayadi A. Therapeutic Strategies to Reduce Burn Wound Conversion. Medicina (Kaunas). 2022;58(7):922.
3. Tottoli EM, Dorati R, Genta I, Chiesa E, Pisani S, Conti B. Skin Wound Healing Process and New Emerging Technologies for Skin Wound Care and Regeneration. Pharmaceutics. 2020;12(8):735.
4. Monika P, Chandraprabha MN, Rangarajan A, Waiker PV, Chidambara Murthy KN. Challenges in Healing Wound: Role of Complementary and Alternative Medicine. Front Nutr. 2022;8:791899.
5. Olsson M, Järbrink K, Divakar U, Bajpai R, Upton Z, Schmidtchen A, Car J. The humanistic and economic burden of chronic wounds: A systematic review. Wound Repair Regen. 2019;27(1):114-25.
6. Kolimi P, Narala S, Nyavanandi D, Youssef AAA, Dudhipala N. Innovative Treatment Strategies to Accelerate Wound Healing: Trajectory and Recent Advancements. Cells. 2022;11(15):2439.
7. Martínez-Jiménez MA, Valadez-Castillo FJ, Aguilar-García J, Ramírez-GarciaLuna JL, Gaitán-Gaona FI, Pierdant-Perez M, et.al. Effects of Local Use of Insulin on Wound Healing in Non-diabetic Patients. Plast Surg (Oakv). 2018;26(2):75-9.
8. Lima MH, Caricilli AM, de Abreu LL, Araújo EP, Pelegrinelli FF, Thirone AC, et.al. Topical insulin accelerates wound healing in diabetes by enhancing the AKT and ERK pathways: a double-blind placebo-controlled clinical trial. PLoS One. 2012;7(5):e36974.
9. Kaur M, Mongia AK, Joseph G, Bhatti N, Badyal DK. Ondansetron-induced dystonia: An uncommon case report. Natl J Pharmacol Ther. 2025;3(2):150-2.
10. Ren X, Zhao M, Lash B, Martino MM, Julier Z. Growth Factor Engineering Strategies for Regenerative Medicine Applications. Front Bioeng Biotechnol. 2020;7:469.
11. Xia Y, Sun M, Huang H, Jin WL. Drug repurposing for cancer therapy. Signal Transduct Target Ther. 2024;9(1):92.
12. In J. Introduction of a pilot study. Korean J Anesthesiol. 2017;70(6):601-5.
13. Radwa M. Ali, Al-Shaimaa F. Ahmed, Heba F. Mansour, Ahmad Kamal Abdel-Mawla. Effectiveness of Topical Insulin for Management of Diabetic Wounds: a Comparison between Short and Long Acting Insulin. J. Adv. Biomed. & Pharm. Sci .2021;4: 253- 9.
14. Onyekwelu I, Yakkanti R, Protzer L, Pinkston CM, Tucker C, Seligson D. Surgical Wound Classification and Surgical Site Infections in the Orthopaedic Patient. J Am Acad Orthop Surg Glob Res Rev. 2017;1(3):e022.
15. Sun S, Zhang L, Liu J, Li H. Insulin Topical Application for Wound Healing in Nondiabetic Patients. Comput Math Methods Med. 2021;2021:9785466.
16. Torrecillas-Baena B, Camacho-Cardenosa M, Carmona-Luque MD, Dorado G, Berenguer-Pérez M, Quesada-Gómez JM, et.al. Comparative Study of the Efficacy of EHO-85, a Hydrogel Containing Olive Tree (Olea europaea) Leaf Extract, in Skin Wound Healing. Int J Mol Sci. 2023;24(17):13328.
17. Serena T, Yaakov S, Yaakov R, King E, Driver VR. Percentage area reduction at week 4 as a prognostic indicator of complete healing in patients treated with standard of care: a post hoc analysis. J Wound Care. 2024;33(Sup9):S36-S42.
18. Li PS, Peng XM, Niu XX, Xu L, Hung Yu Ng E, Wang CC et.al. Efficacy of acupuncture for endometriosis-associated pain: a multicenter randomized single-blind placebo-controlled trial. Fertil Steril. 2023;119(5):815-23.
19. Myles PS, Myles DB, Galagher W, Boyd D, Chew C, MacDonald N, et.al. Measuring acute postoperative pain using the visual analog scale: the minimal clinically important difference and patient acceptable symptom state. Br J Anaesth. 2017;118(3):424-9.
20. Manjhi PK, Singh MP, Kumar M. Causality, Severity, Preventability and Predictability Assessments Scales for Adverse Drug Reactions: A Review. Cureus. 2024;16(5):e59975.
21. Pathak D, Mazumder A. A critical overview of challenging roles of medicinal plants in improvement of wound healing technology. DARU J Pharm Sci. 2024;32(1):379-419.
22. Zhou Z, Deng T, Tao M, Lin L, Sun L, Song X, et.al M. Snail-inspired AFG/GelMA hydrogel accelerates diabetic wound healing via inflammatory cytokines suppression and macrophage polarization. Biomater. 2023;299:122141.
23. Joseph G, Bhatti N, Badyal DK, Kaur P (2025) Stevens–Johnson syndrome: An adverse drug reaction with various drugs. Indian J. Physiol. Pharmacol. 1-4.
24. Kaur P, Choudhury D. Insulin Promotes Wound Healing by Inactivating NFkβP50/P65 and Activating Protein and Lipid Biosynthesis and alternating Pro/Anti-inflammatory Cytokines Dynamics. Biomol Concepts. 2019;10(1):11-24.
25. da Silveira VF Jr, Gomes Silva JL, Lima MHM, Saad MJA. Effects of topical insulin on second-degree burn wound healing: brief report. Wound Manag Prev. 2024;70(2).
26. Oryan A, Alemzadeh E. Effects of insulin on wound healing: A review of animal and human evidences. Life Sci. 2017;174:59-67.
27. Hermeto LC, DeRossi R, Oliveira RJ, Gomes FG, Ferreira WR, Galhardo JA, et.al. The efficacy of topical insulin application on rat model with burn wounds treated with adipose-derived stem cells. Int J Burns Trauma. 2020;10(6):296-306.
28. Wang J, Xu J. Effects of Topical Insulin on

Wound Healing: A Review of Animal and Human Evidences. Diabetes Metab Syndr Obes. 2020;13:719-27.
29. Harna B, Arya S, Bahl A. Epidemiology of Trauma Patients Admitted to a Trauma Center in New Delhi, India. Indian J Crit Care Med. 2020;24(12):1193-7.
30. Dixon JR, Lecky F, Bouamra O, Dixon P, Wilson F, Edwards A, et.al. Age and the distribution of major injury across a national trauma system. Age Ageing. 2020;49(2):218-26.
31. Sharma A, Srivastava V, Shankar R, Yadav AK, Ansari MA, Gupta SK. Epidemiological Profile of Chronic Wounds in an Indian Population: A Community-Based Cross-Sectional Observational Study. Cureus. 2024;16(9):e68684.
32. Breslin FC. Educational status and work injury among young people: refining the targeting of prevention resources. Can J Public Health. 2008;99(2):121-4.
33. Vas Nunes JH, van Duinen AJ, Boateng D, Tommy AJ, Sankoh O, Grobusch MP, et.al; PRESSCO 2020 study group. Incidence and prevalence of traumatic and non-traumatic wounds and burns and access to wound care in Sierra Leone; data from a nationwide household survey (PRESSCO) 2020. Heliyon. 2024;11(1):e38693.
34. Ben Abid A, Rekik M, Kammoun S, Kaibi I, Ben Amor S, Trigui A. Work-related open globe injuries: demographic characteristics and prognostic factors in southern Tunisia. Tunis Med. 2025;103(1):80-5. French.
35. Yi L, Xie Z, Wang Z, Guo G, Liu D, Du Y, et.al. Time trends in thermal burns incidence among Brazil, Russia, India, China, and South Africa (BRICS), an age-period-cohort analysis from the GBD 2019. Sci Rep. 2025;15(1):6877.
36. Kudła J, Podsiadło A, Woźniak R. The effectiveness of regulations preventing alcohol-related road traffic crashes and fatalities in the European Union countries. J Safety Res. 2024;88:161-73.
37. Brooks RD, Grier T, Dada EO, Jones BH. The Combined Effect of Cigarette Smoking and Fitness on Injury Risk in Men and Women. Nicotine Tob Res. 2019;21(12):1621-8.
38. Lázaro-Martínez JL, García-Madrid M, Bohbot S, López-Moral M, Molines-Barroso RJ, et.al. Recurrence rates after healing in patients with neuroischemic diabetic foot ulcers healed with and without sucrose octasulfate-impregnated dressings: A 1-year comparative prospective study. Int Wound J. 2024;21(10):e70028.
39. Rageh MA, Elrewiny EM, Kadah AS, Zakaria HB, Abdelshakour M, Mohy SM, et.al. Fractional CO2 laser with topical insulin versus PRP for atrophic acne scars: a randomized split-face study. Arch Dermatol Res. 2025;317(1):663.
40. Khattab MA, Nabeh OA, Adel S, Abdelazeem M, Naser MM, Matter LM. Topical insulin improves postoperative wound healing in controlled diabetic patients through regulating the expression of E-Cadherin and Ki67: an open-label randomized controlled-trial. Futur J Pharm Sci. 2025;11(1):80.
41. Chauhan S, Jhawat V, Singh RP, Yadav A. Topical delivery of insulin using novel organogel formulations: An approach for the management of diabetic wounds. Burns. 2024;50(5):1068-82.
42. Edek YC, Adışen E. Use of Topical Insulin in the Wound Healing Process After Ultrasonography-Guided Modified Deroofing Surgery in a Hidradenitis Suppurativa Patient: A Case Report. Cureus. 2023;15(10):e47836.
43. Zhang JB, Li H, Zhang L, Wang JL. Observation of curative effect of recombinant human basic fibroblast growth factor combined with compound polymyxin B ointment and local application of insulin on wound healing of deep second-degree burn in diabetes mellitus: a randomized study. Eur Rev Med Pharmacol Sci. 2019;23(13):5987-93.
44. Przybyła M, Dolińska B, Ostróżka-Cieślik A. Research Progress on Insulin Dressings to Promote Wound Healing. Eng Proc. 2023; 56(1):21.
45. Sharda D, Choudhury D. Insulin-cobalt core-shell nanoparticles for receptor-targeted bioimaging and diabetic wound healing. RSC Adv. 2023;13(29):20321-35.
46. Liang X, Xu Y, Zhang Y, Feng X, Wang Y, Zhao C, et.al. An effective treatment for diabetic foot necrosis with traditional Chinese and Western medicine: a case report. J Wound Care. 2024;33(1):22-7.

Bikash C, Sarkar R. Topical management of acne scars: The uncharted terrain. J Cosmet Dermatol. 2023;22(4):1191-6.