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THE EFFECT OF "ZAROOR-E-QAWI" IN THE FORMATION OF THE HEALTHY GRANULATION TISSUE IN THE CASES OF THE CHRONIC WOUND: A SINGLE BLIND, NON RANDOMIZED PROSPECTIVE CLINICAL STUDY

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ABSTRACT

Back ground: Granulation tissue is the important component in the process of the wound healing. A wound can heal by the primary intention or by the secondary intention. In the chronic wound healing occurs through the secondary intention. The granulation tissue matrix fills up the gaps in the chronic wounds. **Objectives:** To evaluate the effect of the Unani formulation *Zaroor-E-Qawi* in the formation of the healthy granulation tissue in cases of the chronic wound. **Material and methods:** A single blind, non-randomised, prospective clinical study was carried out at National Institute of Unani Medicine, Bengaluru. The Patients in the age group of 18 to 70 years with chronic wound of Wagner's grade-0, I and II were included in the study. After proper cleaning of the wound with normal saline, research drugs *Zaroor-E-Qawi* was sprinkled over the wound and dressing done. The assessment was done on every 15th day of the study. The protocol of the study was followed up to 45 days. **Results:** The means granulation tissue percentage on the baseline day was 35.16±30.11 which reached to 99.64±1.50% at the end of 45th day of the study. Statistically 96.7% of improvement was seen at end. **Interpretation & Conclusion:** The formulation *Zaroor-E-Qawi* is effective in the formation of the healthy granulation tissue in the chronic wounds**,** so this can be a novel modality in the treatment of the chronic wound.

KEYWORDS: Chronic Wound; Healthy Granulation Tissue; *Zaroor-E-Qawi.*

BACK GROUND

Granulation tissues are the important component in the process of the wound healing. Wounds can heal by primary intention (where wound edges can be approximate easily) and secondary intention (when the edges of the wounds cannot be approximate). Granulation tissue matrix fills up the gap between the edges of the such wounds that heal by second intention.[1] Granulation tissue is the type of newly formed capillaries which results from the proliferation from the base of the wound. Such tissue imparts the three basic functions which includes Immune response: Protect the wound surface from the microbial invasion and it also protects the wound surface from injuries. The proliferative action: Fills up the wound from its base with a new tissue and with new vasculatures and temporary plugging: Replaces the necrotic tissue by the scar tissue formation.[2,3]

Under the normal conditions, the wound healing occur in the four stages which includes the stage of haemostasis, inflammatory stage, proliferative stage and remodelling stage.[4,5] During the proliferative stage, re-epithelialisation and the replacement of the clot by granulation tissue occurs simultaneously. This stage is highly cellular with the primary cell type which comprises the fibroblasts, keratinocytes and endothelial cells. Fibroblasts synthesize collagen and the extracellular matrix.[6,7] The granulation tissue itself is made up of extracellular matrix, proteoglycans, hyaluronic acid, collagen, and elastin. Cytokines and growth factors, interleukins, and angiogenesis factors are active during this stage.[5] In an ideal condition the Granulation tissue grows from the base of the wound and can fill any size of the wound. Any error in the formation of granulation tissue can result in the development of the chronic wound.[8,9]

METHODOLOGY

A single blind non-randomized and a prospective interventional clinical study were carried out in the Dept. of Surgery at National Institute of Unani Medicine, Bangalore, Karnataka. The Protocol of the study was approved by Institutional Ethics Committee. The patients were screened on the basis of inclusion and exclusion criteria to obtain the sample Size **(**n=30). The Protocol of the study was followed up to 45 days. An informed written consent was obtained from every patient before

the enrolment in the study. These patients were subjected to the local application of the Test drug '*Zaroor-E-Qawi'* over the wound. Cleaning of the wound was done with normal saline (NS) and the test drug in the form of '*Zaroor'* (a fine powder) was dusted over the wound and a sterile dressing done. The Debridement of the wound was done as per the need to remove the dead and devitalized tissue and the assessment of the wound done on every 15th day of the study i.e. on 0th day, 15th day, 30th day, 45th day of the study. To ensure single blinding of the treatment, the research drug was kept in plain and unlabelled sterilized and air tight container.

Inclusion criteria
Both genders
Ulcers not healing for more than 6 weeks
Wagner's grade-0, I and II ulcer
Patients in the age group of 18-70 years

Exclusion criteria: Patient with
Gangrenous ulcers
Pregnant and lactating women
Any severe systemic disease
Any ulcer with bony involvement
Carcinomatous ulcer

Test drug
The constituents of the test drugs are: *Sibr zard* (*Aloe barbadensis), Amba haldi* (*Curcuma aromatic), Gulnar (Punica granatum Linn), Mur maki (Comiphora myrrh) and Mazoo (Quercus infectoria*). Each ingredient was taken in equal quantity.[10,11,12] These drugs were purchased from local crude drug market of Bengaluru city and were authenticated by the Centre for Repository of Medicine Resources (C-RMR), Trans Disciplinary University Bengaluru. A Fine powder of all above drugs was prepared in the Pharmacy unit.

Objective parameters: Healthy granulation tissue (percentage)

Method of calculation of granulation
The red granulation tissues were considered as healthy one. The area of the healthy granulation tissues was first calculated by multiplying the maximum length and breadth of the area with healthy granulation tissue. The percentage of granulation tissues was calculated by dividing this area with the total area of the wound and multiplying it by 100.

Withdrawal criteria
Failure to follow the protocol.
Non-compliance with therapy.
Any adverse effect.

Assessment of safety: Any adverse event during the study was recorded. The safety outcomes were assessed on basis of clinical symptoms.

Evaluation of results: The data was compared and analysed with appropriate statistical tests and $P < 0.05$ was considered as significant difference. Descriptive and inferential statistical analysis of the data was carried out. Results on continuous measurements presented as Mean ± SD (Min-Max) and results of the categorical measurements were presented in the Number (%). The level of the significance of the results was assessed at 5%. The Student t test (two tailed, dependent) was used to find the significance of study parameters on continuous scale within each group. Paired Proportion test was used to find the significance of proportion in the paired data. The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 was used for the analysis of the data and Microsoft word and Excel was used to generate graphs and tables.[13,14,15]

RESULT

The means healthy granulation tissues percentage before the commencement of the study was 35.16±30.11 which improved with the start of the study and it reaches up to 89.74±17.08% by the end of the 15th days and 95.09±12.45% by the end of 30th days of the study and it reached to 99.64±1.50% by the end of the 45th days of the study. On the baseline day, out of the 30 patients, 2 (6.7%) patients had absolutely no healthy granulations tissue, 7(23.3%) patients had healthy granulation tissue between 1-10%, 5(16.7%) patient had 11-20% of the healthy granulation tissue, 2(6.7%) patient had healthy granulation tissue between 21-30%, 1(3.3%) patient had healthy granulation tissue between 31-40%, 3(10%) patients had healthy granulation tissue between 41-50%, 3(10%) patients had healthy granulation tissue between 51-60%, 2(6.7%) patient had healthy granulation tissue between 61-70%, 2(6.7%) patients had healthy granulation tissue between 71-80%, 2(6.7%) patient had healthy granulation tissue between 81-90%, only 1(3.3%) patients had healthy granulation tissue between 90-100%, at the end of the 45 days of the study, almost 100% granulations tissues achieved in all the 30 cases. Statistically 96.7% of improvement was seen with $P < 0.001$, which is highly Significant.

Table 1: Granulations tissue (percentage).

Granulation tissue (percentage)	Before Treatment	After Treatment	Day 0	Day 15	Day 30	Day 45	% difference
0	2(6.7%)	0(0%)	2(6.7%)	0(0%)	0(0%)	0(0%)	-6.7%
1-10	7(23.3%)	0(0%)	7(23.3%)	0(0%)	0(0%)	0(0%)	-23.3%
11-20	5(16.7%)	0(0%)	5(16.7%)	0(0%)	0(0%)	0(0%)	-16.7%
21-30	2(6.7%)	0(0%)	2(6.7%)	1(3.3%)	0(0%)	0(0%)	-6.7%
31-40	1(3.3%)	0(0%)	1(3.3%)	0(0%)	0(0%)	0(0%)	-3.3%
41-50	3(10%)	0(0%)	3(10%)	1(3.3%)	1(3.3%)	0(0%)	-10.0%
51-60	3(10%)	0(0%)	3(10%)	0(0%)	0(0%)	0(0%)	-10.0%
61-70	2(6.7%)	0(0%)	2(6.7%)	1(3.3%)	0(0%)	0(0%)	-6.7%
71-80	2(6.7%)	0(0%)	2(6.7%)	3(10%)	2(6.7%)	0(0%)	-6.7%
81-90	2(6.7%)	0(0%)	2(6.7%)	5(16.7%)	2(6.7%)	0(0%)	-6.7%
91-100	1(3.3%)	30(100%)	1(3.3%)	19(63.3%)	25(83.3%)	30(100%)	96.7%
Total	30(100%)	30(100%)	30(100%)	30(100%)	30(100%)	30(100%)	-
The value of P <0.001, paired proportion test used, 96.7% improvement seen.							

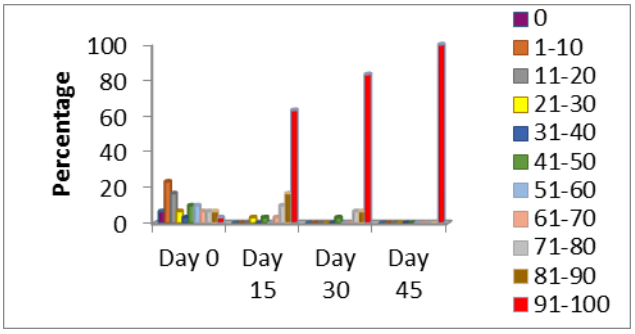

Figure 1: Granulation Tissue (%) at different point of the study.

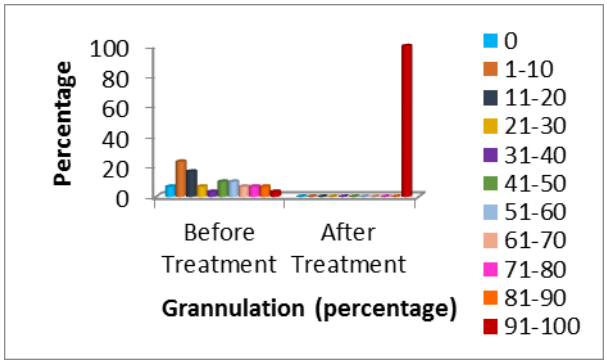

Figure 2: Granulation Tissue (%) before and after the treatment.

Table 2: Mean of healthy Granulations tissue (%).

	Min-Max	Mean ± SD
Before Treatment	0.00-91.25	35.16±30.11
After treatment	92.30-100.00	99.64±1.50
Day 0	0.00-91.25	35.16±30.11
Day 15	25.53-100.00	89.74±17.08
Day 30	42.00-100.00	95.09±12.45
Day 45	92.30-100.00	99.64±1.50

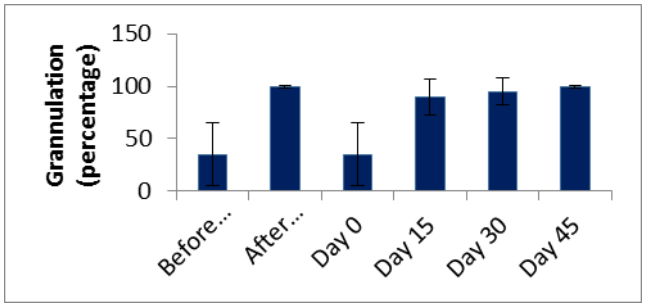

Figure 31: Mean Granulations tissue (%) at different point of time.

DISCUSSION

The mean healthy granulation tissue percentage before the commencement of the study was 35.16±30.11% which improved to 99.64±1.50% at the end of the study. This outcome is analogous to the study conducted by Peter A *et al*[16] who reported 0-10% granulation at baseline and 76-100% granulation at the end of the study. The results of our study is also analogous to the study conducted by Ahmad W. *et al*[17] who has reported the mean healthy granulations before the treatment in 30 patients as 32.71 ± 38.61% and after treatment it increased up to 99.74 ± 1.34%, In our study all the patients showed a promising response with 100% healthy granulation tissue. This outcome of our study is comparatively better than the study conducted by Sohail S.*et al*[18] who has reported that on the baseline day out of 34 patients, Only 2(8.8%) patients had no healthy granulation tissue and by the end of the study almost 100% healthy granulation tissues achieved in the 33 (97.1%) patients while 1 (2.9%) patient still did not possess any healthy granulation tissues. The stimulating effect of the test drugs in the formation of the healthy granulation tissue is attributed to the *Munmbit-E-Leham* (flesh forming), *Muhallil* (anti-inflammatory), *Mujaffif* (desiccant), *Daf-E-Ta'ffun* (antimicrobial) and *Mundamil-E-Qurooh* (wound healing) actions of its constituent drugs.[19,20,21] This effect can also be explained on the basis of the favourable actions of its phytoconstituents ike curcumin (Anti-inflammatory), curcuminoids (antioxidant actions, antimicrobial and scavenging), monoterpenoids furanosequiterpenes heerabolene, sesquiterpenoids, Tannins, eugenol, monoterpenes, flavonoids and sterols (cytoprotective healing effects, antioxidant and anti-inflammatory actions).[11,12]

CONCLUSION

The Unani formulation *"Zaroor-E-Qawi*" appears to be effective in the formation of the healthy granulation tissue so this treatment modality can emerge as affordable and a reliable alternative to the conventional methods of the antiseptic dressing in the cases of the chronic wounds.

LIMITATIONS

Apart from being a non randomized uncontrolled study, this study was also conducted on a limited sample size comprising of only Wagner grade-0, I and grade-II wound, thus the results so obtained cannot be generalized to the patients having Wagner grade-III and IV wound. A multicentre, randomized control study is suggested to derive a reliable inference in the term of the safety and efficacy. A more vigorous and extensive studies comprising of the patients with Wagner grade-III and IV wound is also suggested.

CONFLICT OF INTEREST

All the authors declare that there exists no competing interest in any part of this study.

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