

A RANDOMIZED, OPEN-LABEL, COMPARATIVE STUDY OF LYSINE CREAM WITH STANDARD TREATMENT IN PATIENTS WITH SECOND-DEGREE SUPERFICIAL BURNS

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ABSTRACT

Objective: To evaluate the efficacy and tolerability of lysine cream in patients with second-degree superficial burns.**Methods:** In this randomized, open label, comparative study patients with second degree superficial burns received either combination of lysine cream 15% and silver sulfadiazine cream 1% or sulfadiazine cream 1% alone, twice daily for period of 4 weeks. The primary outcome, pain, discharge, size and total body surface area (TBSA) were assessed in each visits.**Results:** Patients in the study group showed significant change than the control group in pain, discharge, size, and TBSA during the first 4 weeks after treatment. In addition, significantly more patients in lysine group had adequate relief of itching and increased epithelialization.**Conclusions:** Combination of lysine cream and silver sulfadiazine cream for 4 weeks provided significant relief of pain, discharge, size, TBSA, and itching. Lysine cream was well tolerated.**Keywords:** Growth factor, Angiogenesis, Lysine, Body surface area.© 2017 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2017.v10i5.16431>

INTRODUCTION

Burns are injuries to the skin or other tissues, caused by heat, radiation, chemicals, or electrical contact. Burn injuries are among the most devastating of all injuries and a major global public health crisis [1].

During the healing process, the body requires increased amount of proteins. Administration of high protein to burns patients improves nutritional status and immunological response. Dietary supplementation with pharmacological levels of specific amino acid and fatty acid, either alone or in combination, may improve the clinical course of critically ill burns patients [2].

L-lysine is an essential amino acid in that it is required for human nutrition but not produced by the body. Lysine has been shown to remarkably improve both the rate and quality of wound healing with less scarring and deformation. Wounds which are treated topically with lysine show a controlled degree of inflammation and angiogenesis process, whereby, probably, required extent of cellular and serum growth factors entry into the wound beds are ensured, thereby augmenting the healing process *in situ*. Lysine-mediated angiogenesis is postulated to be a result of the molecule acting as cell surface bridge, binding the angiogenic factors to their receptors. This augments the angiogenesis induced by lysine molecule by means of the ligand-receptor binding process. Thus, L-lysine has been shown to promote therapeutic angiogenesis in wound healing [3,4]. Hence, this study has been undertaken to find out the efficacy of topical L-lysine cream in second-degree superficial burns in terms of wound healing and also to compare the same with silver sulfadiazine cream, which is used in the hospital as part of the standard treatment schedule.

METHODS

A randomized, open-label, comparative, prospective, parallel group study was conducted on patients with second-degree superficial burns (only limbs) <10% involvement, attending the outpatient Department

of Burns, Plastic and Reconstructive Surgery, Kilpauk Medical College and Hospital and outpatient Department of Plastic Surgery, Rajiv Gandhi Government General Hospital Chennai, Tamil Nadu, between August 2010 and June 2011. The study duration for each patient was 4 weeks with four visits. The study was commenced after obtaining approval from the Institutional Ethical Committee.

Inclusion criteria

- Hemodynamically stable and age ranges between 20 and 50 years of both sex
- Second-degree superficial burns (only limbs) with <10% of the total body surface area (TBSA).

Exclusion criteria

- First-, second-degree deep, third-, and fourth-degree burns
- Head, neck, torso (anterior and posterior) burns
- Wound swab positive for pathogenic bacteria
- Patients with associated severe comorbid diseases
- Pregnant and/or lactating women
- Suspected medico-legal cases.

Groups

Patients were randomized to enter any of the two groups: Silver sulfadiazine therapy (Group A) and combination therapy comprising of both silver sulfadiazine and lysine (Group B). Each group consisted of 20 patients.

Parameters assessed

The size, degree, pain, discharge, and TBSA were assessed in each visit.

RESULTS

In this study, 125 patients were screened, of which 40 patients, who met the inclusion criteria, were recruited. All the 40 patients who

were enrolled, completed the study, and there were no dropouts. The following clinical parameters were assessed in all patients during each visit:

- The size of the burns wound was measured with a ruler, taking the longest and widest aspect of the wound into consideration
- The degree was recorded based on the depth
- The presence or absence of pain
- The presence or absence of discharge
- TBSA was estimated using the "rule of nines" in adults, where the total body was divided into sections of 9% or multiples of 9%
- The rate of healing.

Data analysis

The data was tabulated in Microsoft Excel and analyzed using SPSS version 16. The comparison between test and control group in each category (prevalence of pain, wound discharge, size of burns, TBSA of burns) at each visit was done using an independent t-test. The level of significance was set to $p < 0.05$ (where p is the probability value).

OBSERVATION

The following parameters are tabulated (Table 1-7).

Table 1: Mean age

Study groups	n	Age in years (mean±SD)	Student independent t-test
Group A	20	31.400±6.660	p=0.173NS
Group B	20	28.550±6.328	

SD: Standard deviation, NS: Non-significant

Table 2: Distribution of sex

Gender	n (%)		Chi-square value	Student independent t-test
	Group A	Group B		
Male	12 (60.0)	13 (65.0)	0.107	p=0.744 (NS)
Female	8 (40.0)	7 (35.0)		
Total	20 (100)	20 (100)		

Table 3: Prevalence of pain

Visits	Group A		Group B		Chi-square value	Student independent t-test
	Present	Absent	Present	Absent		
1	20	0	20	0	0.000	p=1.000 (NS)
2	20	0	19	1	1.026	p=0.311 (NS)
3	15	5	8	12	5.013	p=0.025 (S)
4	1	19	0	20	1.026	p=0.311 (NS)
5	0	20	0	20	0.000	p=1.000 (NS)
Friedman test	p<0.001 (S)		p<0.001 (S)			

S: Significant, NS: Non-significant

Table 4: Wound discharge

Visits	Group A		Group B		Chi-square value	Student independent t-test
	Present	Absent	Present	Absent		
1	20	0	20	0	0.000	p=1.000 (NS)
2	20	0	10	10	13.333	p<0.000 (S)
3	3	17	0	20	3.243	p=0.072 (NS)
4	0	20	0	20	0.000	p=1.000 (NS)
5	0	20	0	20	0.000	p=1.000 (NS)
Friedman test	p<0.001 (S)		p<0.001 (S)			

S: Significant, NS: Non-significant

DISCUSSION

Second-degree superficial burns heal by themselves even though infection is the most frequent and life-threatening complication in patients with burns. The three efficacious and most extensively used topical antimicrobial agents available for the treatment of second-degree superficial burns are silver sulfadiazine cream, mafenide acetate cream, and 0.5% silver nitrate soaks [5]. However, no single agent is totally effective and has its own advantages and disadvantages.

Among the three topical agents, silver sulfadiazine is most favored agent because of its high patient compliance, excellent spectrum of activity, low toxicity, easy application, and also it does not impede epithelialization.

A large number of molecules are being tested for the promotion of therapeutic angiogenesis including vascular endothelial growth factor. L-lysine monohydrochloride (L-lysine) has been shown to promote therapeutic angiogenesis in wound healing [3,4]. Pre-clinical studies done by Siméon *et al.* and Fromes *et al.* in the wound healing showed that lysine when given with other amino acids (naturally occurring copper complex of a glycyl-L-histidyl-L-lysine peptide and acetyl-serine-aspartyl-lysine-proline) as a topical agent hastened wound healing process. The topical application of L-lysine monohydrochloride 15% with silver sulfadiazine 1% increases the healing rate by promoting rapid epithelialization of second-degree superficial burns. Lysine has been shown to improve both the rate and the quality of wound healing with less scarring. This study was undertaken to evaluate the efficacy of lysine cream in second-degree superficial burns. Our study is the first of its kind using lysine cream in the treatment of second-degree superficial burns. In this study, 40 patients were enrolled and divided into two groups. One group received silver sulfadiazine cream, and other group received lysine in addition to silver sulfadiazine cream for 4 weeks. The following parameters were evaluated - size, pain, discharge, and TBSA of burns.

There was no statistically significant difference between the groups in mean age. This shows that both groups belong to the same population ($p=0.173$). The distribution of sex in both groups did not show any statistically significant difference ($p=0.744$). Our study showed that in Group B, there was a significant reduction in the size of the burn wound and also TBSA of the burns.

The mean size of the wound at the end of the study was 108.00 cm² in Group B, while in Group A, it was 176.45 cm². Similarly, mean TBSA of

Table 5: Size of burns

Visits	Mean±SD		Student independent t-test
	Group A	Group B	
1	303.30±233.240	343.50±191.565	p=0.555 (NS)
2	297.65±230.932	303.50±169.393	p=0.928 (NS)
3	242.25±201.002	228.10±143.990	p=0.799 (NS)
4	215.25±187.466	161.85±110.978	p=0.280 (NS)
5	176.45±163.448	108.00±89.022	p=0.108 (NS)
Friedman test	p<0.001 (S)	p<0.001 (S)	

S: Significant, NS: Non-significant, SD: Standard deviation

Table 6: TBSA of burns

Visits	Mean±SD		Student independent t-test
	Group A	Group B	
1	2.950±1.3659	3.050±1.5720	p=0.831 (NS)
2	2.925±1.3599	2.295±1.4892	p=1.000 (NS)
3	2.475±1.3026	2.350±1.3774	p=0.770 (NS)
4	2.250±1.1754	1.775±1.1639	p=0.207 (NS)
5	1.800±1.1286	1.225±0.8955	p=0.082 (NS)
Friedman test	p<0.001 (S)	p<0.001 (S)	

TBSA: Total body surface area, S: Significant, NS: Non-significant, SD: Standard deviation

Table 7: Rate of healing (%)

Groups	Size of the ulcer, mean (%)		Rate of healing (%)
	Baseline visit	Last visit	
Group A	303.30 (100)	176.45 (58)	42
Group B	343.50 (100)	108.00 (31)	69

the burns in Group B was 1.23%, whereas in Group A was 1.80%. The reduction in size and TBSA of burns in the lysine-treated group were noticed from the 2nd week onward when compared to the standard silver sulfadiazine-treated group. This shows that the study drug lysine which was used along with silver sulfadiazine is probably responsible for this reduction in both the size and TBSA of burns.

Similarly, there was a reduction in the discharge in Group B from the 2nd week onward, and no discharge was observed from the 3rd week. This again points out that the lysine in the combination group (Group B) probably contributes to the faster healing seen in this group.

Pain reduction was statistically significant in both the groups. In the lysine combination group, the pain reduction was observed from the 2nd week itself, whereas in the other group, it was observed only from the 3rd week. This also suggests that lysine has contributed to the pain reduction and has hastened the healing process.

The rate of healing of wound in the lysine combination group (Group B) was 69% when compared to the silver sulfadiazine-treated group (Group A) which was only 42%. This probably can be attributed to the angiogenic property of lysine.

The angiogenic property of lysine was demonstrated in a study, where the effects of L-lysine monohydrochloride on ischemia reversibility were studied. L-lysine was administered intravenously at a dose of

60 mg/kg in patients with symptoms of acute hemispheric stroke. All 11 patients treated with lysine showed marked recovery in terms of significant changes in relative cerebral blood flow, relative cerebral blood volume, and mean transit time ratios. This observation suggests that functional recovery in these 11 patients was probably due to lysine-induced angiogenesis in the ischemic tissue [6].

Another study conducted by Faculty of Medicine at France with glycyl-L-histidyl-L-lysine showed that L-lysine significantly promoted wound healing [7] which is in accordance with this study. A small study conducted in our department in Grade 1 and 2 diabetic ulcers also showed that lysine promoted ulcer healing which also supports the wound healing property of L-lysine.

No adverse events were reported during the study period, which suggests that topical lysine was well tolerated. The biochemical parameters such as blood sugar, urea, serum creatinine, and electrolytes did not show any statistically significant difference between the groups, suggesting that lysine does not have any systemic effects.

As there was a definite reduction in size, discharge, pain, and TBSA of burns in second-degree superficial burns, our study conducted in the tertiary care hospital proves that L-lysine in combination with silver sulfadiazine has promoted faster healing of burn wound than silver sulfadiazine alone.

CONCLUSION

From this study, we can conclude that lysine cream is effective in promoting the healing of second-degree superficial burns and also well tolerated. Among patients who had second-degree superficial burns, treatment with lysine cream for 4 weeks provided significant improvement in pain, discharge, size, TBSA, and itching.

The rate of healing of wound in the lysine combination group was better because of the angiogenic property of lysine. In addition, significantly more patients in lysine group had adequate relief of itching and increased epithelialization.

Limitations of this study are as follows:

- The study was done in small number of patients
- Prevalence of pain, wound discharge, size of burns, and TBSA of burns were statistically not significant.

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