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EFFICACY OF TOPICAL HONEY THERAPY AGAINST SILVER SULPHADIAZINE TREATMENT IN BURNS: A BIOCHEMICAL STUDY.

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ABSTRACT

Thermal injury is associated with biochemical changes. The present study was undertaken to investigate relation of oxidative free radical generation and related biochemical parameters in burn trauma. The specific aim was to compare the levels of serum lipid peroxide, Ceruloplasmin and Uric Acid in burn patients during treatment with Silver Sulfadiazine Cream and honey therapy. It is a single blind prospective controlled study involving comparison of biochemical changes after treatment with silver sulfadiazine and honey treatment in burn injury. In burn trauma, there is excessive activity of free radicals at the site of injury. This is reflected in elevated blood levels of Lipid peroxide, Ceruloplasmin & Uric Acid. Honey therapy was was shown to decline the levels of serum Lipid peroxide, while there was mild increments in serum Ceruloplasmin levels whereas there was no significant effect on serum Uric Acid levels as compared to silver sulfadiazine treatment. Honey therapy seems to accelerate the process of healing. It has positive effect in reducing oxidative stressful state in burn trauma than the silver sulfadiazine treatment that results in rapid wound healing.

KEY WORD

Honey therapy (HT), Silver sulfadiazene (SSD), Total body surface area (TBSA), Lipid peroxidation product (LPP), Uric acid (UA), Ceruloplasmin (CLP), Free radical (FR).

INTRODUCTION

Thermal injury is the term most often given to supraphysiological temperature effects on the tissue. It is related to alterations in proteins structure and grossly visible change in the skin (1). Thermal injury initiates systemic inflammatory response, generation of oxygen radicals leading to peroxidation of biomolecules. Various biological and metabolic alterations follow burn injury including degradation of adenosine triphosphate and significant reduction in polyunsaturated fatty acids in red cell membrane (1, 2).

Healing of Burn wound has still remained challenge to modern medicine though many antiseptics are discovered. Many systemic and topical regimes are in use, but none is completely satisfactory. It has been shown that wound epithelialis more rapidly in moist environment (3). The maintenance of the moist environment depends on the quality of dressing such as adherence, occlusiveness and limitations of water vapour transport.

In spite of discovery of many new antiseptics choice of an ideal antiseptic for applying to the affected skin has always remained a problem. Recently honey therapy (HT) has been tried for the treatment of burn wounds in a few clinical trials (2, 4) and their results are promising. The medicinal properties of honey have been known since ages and recent studies have also shown that honey helps in acceleration of wound healing than conventional therapy (4). It appears to have several important properties that make it ideal as a dressing agent for burn wound. We therefore, decided to compare the effectiveness of topical HT against silver sulfadiazene (SSD) cream therapy in terms of the biochemical changes that occurs during recovery period .

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MATERIALS AND METHODS

In the present study, 120 patients with burn injuries and 25 healthy individuals, age and gender matched with the patients, were included as the controls. The study group included patients who were admitted in burn wards with various degree of burn injury. 60 patients were under treatment with SSD cream Remaining 60 patients were under treatment with topical HT. The evaluation for degree of burn injury was based on Wallace's *rule of nine*. The degree of burn injury varied between 10%-60% of total body surface area (TBSA).

Whole blood samples were collected at the time of admission and at a regular interval of 7 days for 3 weeks. The blood samples were processed for assay of the biochemical analytes. Lipid Peroxides (LPP) was measured in serum as thiobarbituric acid reactive substances (5), Uric acid (UA) (6) and Ceruloplasmin (CLP) (7) were estimated in serum by colorimetric methods. The statistical analysis included student "t" test as test of significance.

RESULTS

The present study involved patients with different grades of thermal injury. The biochemical analyses done were serum levels of LPP, CLP and UA. Table I shows the results of biochemical analysis done on blood samples obtained from the burn patients and the controls. It can be seen that the initial levels of mean serum LPP in all the groups of burn patients were significantly high ($P<0.001$) as compared to controls. Similarly the initial levels of mean serum CLP and UA were also significantly higher in patients ($P<0.001$) as compared to controls.

During both the therapies all the biochemical parameters showed gradual change of small increment when the data was compared after weekly intervals. Response to thermal injury can be different in individual patients. This response may depend on degree of burns, initial health status, genetic and other factors. Probably wide range of response given by the patients result in large standard deviation (S D) values.

During HT and SSD treatment a gradual decline shows the efficacy of the treatment.

Table 1 and Fig. 1 shows a gradual decrease was observed in serum LPP levels during follow up period in all the groups of burn patients treated with SSD cream as well as HT. The rate of decrease in serum LPP levels was faster during HT as compared to that observed in SSD cream treatment.

Table 1 and Fig. 2 shows that the mean levels of serum UA decline during follow up period. No significant difference was observed in mean levels of serum UA in between HT and SSD groups.

Table I. Levels of some Biochemical Parameters in Burn Patients during treatment of SSD cream and honey

Post burn preiod (days)	LPP (nmol/L)		UA (mg%)		CLP (mg%)	
	SSD(n=60) Mean ± SD	HT(n=60) Mean ± SD	SSD (n=60) Mean ± SD	HT(n=60) Mean ± SD	SSD (n=60) Mean ± SD	HT(n=60) Mean ± SSD
Initial (Before application of drug)	6.36±1.52	6.24±1.12	8.28±0.88	7.46±0.76	185.01±38.52	173.44±31.00
7th Day	5.43±1.57	4.88±1.02	6.98±1.24	6.07±0.89	205.31±20.48	187.13±49.73
14th Day	5.09±1.37	3.66±0.68	5.97±1.30	5.32±0.63	231.55±37.56	217.63±35.31
21th Day	4.62±1.13	3.33±0.40	5.23±.081	4.86±0.68	268.29±55.74	251.83±32.94
Control (n=25)		2.17±0.34		4.06±1.32		105.60±19.49

The Stastical Method used to compare data was student "t" (unpaired)
$P < 0.001$ Highly Significant as compared to normal controls.
The values are mean ± SD.

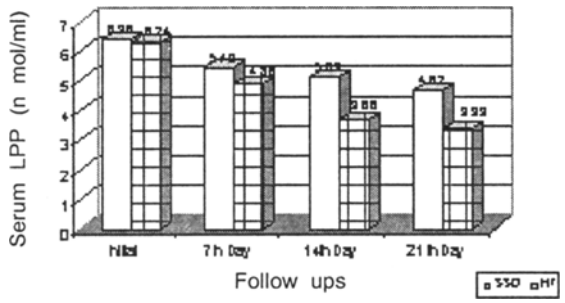

Fig. 1. Changes in LPP

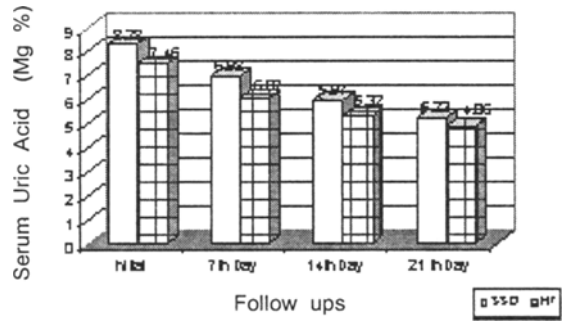

Fig. 2. Changes in uric acid

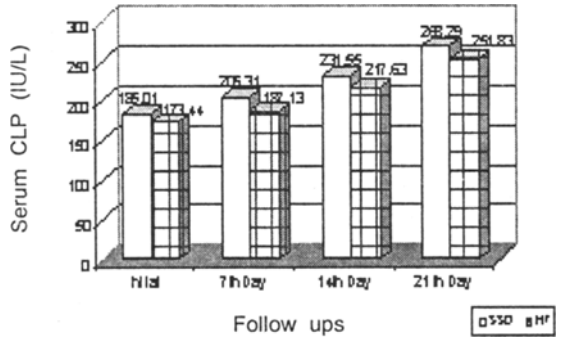

Fig. 3. Changes in ceruloplasmin

In Table 1 and Fig. 3, the levels of serum CLP are elevated in follow-up period in all burn patients treated with SSD Cream as well as HT. Rate of increase in serum CLP levels is slightly slow during HT treatment. If the mean values of the biochemical parameters are observed carefully, it is seen that there is increasing trend in the values with the degree of severity of burn injury.

DISCUSSION

Burn injury is accompanied by complex patho-physiological alterations that exert deleterious effects on various organ systems.

Although the exact mechanism is not known, elevated level of LPP in the serum in early post burn period reflects increased activity of FR. Earlier it was believed that burn toxin is a lipid protein polymer which is formed from a component of cell membranes in the skin. Now it is known that LPP are linked with lipoproteins in serum. This is further supported by the reports that levels of polyunsaturated fatty acids including arachidonic acid in red blood cell membranes of thermally injured patients are reduced . Therefore, elevated serum LPP is related to peroxidation of membrane lipids (8, 16). The changes in catalase activity are the direct consequence of thermal injury. The response to thermal injury almost correlates with the elevation in catalase activity. It is reported that growth hormone (GH) prevent lipid peroxidation and increase tissue glutathione and catalase activity in rats. It is also been shown that GH given after burn injury decreases oxidant stress by producing significant increase in the endogenous antioxidants such as glutathione and catalase (15). From the results it appears that the degree of lowering of LPP by HT is much more than with the SSD. This probably could be due to some positive effect of HT on the control of FR activity. It is quite likely that certain components of honey may be acting as antioxidants and limiting the activity of FR at the burn injury (9, 10).

It is known that copper-containing protein CLP has enzymatic activity and it has dual role to play. On one hand, it is sensitive acute phase protein that is expressed in inflammatory stressful state. On the other hand, it acts as antioxidant indirectly by limiting the Fe^{++} catalysed FR generation (11).

Tissue ischemia is known to activate purine nucleotide catabolism and nucleotide depletion has been demonstrated in heart and lungs . This results in increased ADP degradation into UA. During reperfusion, conversion of hypoxanthine to xanthine and to UA is known to generate oxygen FR (8). In thermally injured rats, the levels of plasma histamine and xanthine oxidase activity is reported to be elevated and was parallel with the increase in UA. It is most likely that in burns these biochemical/metabolic reactions are taking place locally. The cumulative effect of these changes could be seen as elevated serum UA levels. Thus elevation of serum UA levels is expected in post burn period. Further, the extent of elevation in serum UA levels corresponds to the degree of the burn injury. Thus the increased oxidative stress appears to increase with the severity of burn trauma (13). It is again HT which resulted in lower serum UA level along with the SSD.

Number of investigations has shown that the hepatic activation of acute phase protein synthesis like CLP can be mediated by factors liberated during macrophage activation. In sepsis and Trauma, proteolysis induced by interlukin-1 stimulates the synthesis of hepatic acute phase proteins (12). Thus increased FR activity in burn trauma could trigger macrophage activation via this mechanism. Honey is reported to inhibit the growth of both gram-positive and gram-negative organisms (4). In this context quick healing due to HT may explain a slow rise in CLP level.

Honey is described in Indian system of medicine as nectar of life. In ayurveda, it is recommended as a therapy for burn wound. The healing of burn wound is not only faster but it results insignificant scar formation. Thus preserving the cosmetic value of the skin (14).

Thus, it can be seen that in burn injury, topical application of honey results not only faster healing but also better healing because the nutrient contents of honey like levulose and fructose improve the local nutrition and promote rapid epithelialisation (4). Honey seems to have better control over FR generation.(10). Presence of granulation tissue at wound site determine the healing process, but here in this study we have studied the healing process only by clinical examination of wound not by histological findings. Thus limiting the damage by FR than conventional SSD treatment. This action of honey explains the prevention of scar formation and preservation of cosmetic value of skin. In addition to the advantages of being a non-irritating, non-toxic easily available and inexpensive, HT seems to be most ideal treatment for burn injury.

REFERENCES

1. Hertford, C. and Cream, A.E. (1980) Thermal injuries. In: *Synopsis of surgery*, Liehty, R.D. ed. 4th edn, C.V. Mosby Co, P. 407.
2. Thomson, P.D., Till, G.O, and Woolhscrot, J.O. (1990) Superoxide presents lipid preoxidation in burned patient. Burns 16, 406-413.
3. Davis, J.W.L. (1984) Synthetic Material For covering burn wounds progress towards perfection I. Short term materials. Burns 10, 94-103.
4. Subrahmanyam, M. (1993) Honey as a surgical dressing for burns and ulcers. Ind. J. Surg. 55 (9), 468-473.
5. Satoh, K. (1978) Estimation of lipid peroxides by thiobarbituric acid reactive substances (TBARS). Clin. Chem. Acta. 90, 37-43.
6. Carway, W.T. (1963) Uric acid. In : *Standard method of clinical chemistry*, Seligon, D., ed. Academic press (New York), 4, 239-247.
7. Varley, H., Gowenlock, A.H. and Bell, N. (1983) *Practical Clinical Biochemistry*, 5th edition, Willan Heinemann Medical Book Limited, London, Vol. I, 946-947.
8. Nishigoki, I., Hagihora, M. and Hiramastu, (1980) Effect of thermal injury on lipid peroxide levels of rats. Biochem. Med. 24, 185-189.
9. Subrahmanyam, M. (1996) Honey dressing verus boiled potato peel in the treatment of burn : A Prospective randomized study. Burns, 2 (6), 491-493.
10. Molan, P.C. (2001) Potential of honey in the treatment of wounds and burns. Am. J. Dermatol. 2 (1), 13-19.
11. Dinurello, C.A. (1984) Inetrleukin -1 Rev. Infect. Dis., 6, 51-95.
12. White, J.W. (1963). The identification of inhibine. The antibacterial factor in honey as hydrogen peroxidase and its origin in honey glucose-oxidase system. Biochem. Biophys. Acta. 73, 57-70.
13. Hans, P.F. and Geed, O.T. (1989) Xanthine oxidase and histamine. A.J.P. Am. J. Pathol. 135 (1), 203-215.
14. Gover, S.K. (1985) Use of madhu in Ayurveda. J. of Nima. 10, 7-10.
15. Youn, Y.K., Suh, G.J. and Jung, S.E. (1998) Recombinant human growth hormone decreases lung and liver tissue lipid peroxidation and increases antioxidant activity after thermal injury in rats. J. Burn. Care Rehabil., 19, 542-548.
16. Saez, I.C., Ward, P.H. and Gunter, B. (1984) Superoxide radical involvement in the pathogenesis of burn shock. Cir. Shock. 12, 229-239.