"FREE RADICAL CONTROL - THE MAIN MECHANISM OF THE ACTION OF HONEY IN BURNS" volromano = "XVI" data_pubblicazione = "September 2003"

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SUMMARY. Background and objectives. Thermal injury of the skin is an oxidation injury and it is associated with biological and metabolic alterations. The use of honey in burn treatment results in biochemical alterations and may provide an insight into the mechanism of the action of honey in burns. The levels of serum lipid peroxide, serum ceruloplasmin, and uric acid in burn patients during treatment with silver sulphadiazine and honey therapy were studied. Methods. This was a single-blind prospective randomized control study involving a comparison of biochemical alterations during silver sulphadiazine treatment and honey treatment in burns. Results. 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, and uric acid. Honey treatment led to a decline in the levels of serum lipid peroxide, while there was a mild increment in serum ceruloplasmin levels; there was no significant effect on serum uric acid levels in comparison with patients treated with silver sulphadiazine. Conclusion. Honey treatment exerted a positive effect on the oxidative stressful state in burn trauma by effectively mopping up free radicals, compared with silver sulphadiazine, and resulted in rapid healing.

Introduction

Thermal injury initiates a systemic inflammatory response, the generation of oxygen radicals, and the peroxidation of biomolecules. Various biological and metabolic alterations follow burn injury, including degradation of adenosine triphosphate and a significant reduction in polyunsaturated fatty acids in red cell membrane.1

The healing of the burn wound remains a challenge to modern medicine, even if many antiseptics have been discovered. It has been shown that a wound epithelializes more rapidly in a moist environment. The maintenance of a moist environment depends on the quality of the dressing, which affects adherence, occlusiveness, and water vapour transport.2

Topically applied honey has been tried in the treatment of burn wounds in some recent clinical trials,3-6 and the results are promising. The medicinal properties of honey have long been known and recent studies have shown that honey accelerates wound healing more than conventional therapy. Honey's anti-inflammatory action is thought to reduce the damage caused by the free radicals arising from inflammation, thus preventing further necrosis.7 It has been observed that honey prevents partial-thickness burns from converting to full-thickness burns that require skin grafts.6 Topical applications of antioxidants have been found to reduce the level of reactive oxygen species, the prolonged production of which is responsible for the occurrence of fibrosis.8 The high viscosity, acidic pH, and hydrogen peroxide present in honey, as well as its high osmolarity and nutrient contents, contribute to the inhibition of bacterial growth and promote wound healing.5

The biochemical alterations that occur during treatment with topical applications may indicate other effects of honey. This study was designed to study the biochemical alterations induced by honey treatment and silver sulphadiazine (SSD) treatment in burns, from the period of treatment until recovery.

Materials and methods

A total number of 60 patients with burns in 5-30% total body surface area (TBSA) were treated in our burns unit within 4 h post-burn in the period January 2000/January 2001, and these formed the material for our study. The prospective single-blind randomized

protocol was previously approved by the Hospital Ethics Committee. Informed consent was obtained from the patient or from the patient's parents in the case of children. The patients were randomly allotted to groups by the distribution of numbered chits (the investigator was not informed of the numbering). Thirty patients were treated with honey by local application as previously described and another thirty patients were treated with SSD ointment.3

Honey was selected for the study on the basis of its antibacterial activity.9 The honey with the highest antibacterial activity was chosen. This honey was unifloral and obtained from Syzygium cumini, family Skeels, Myrtacae, of five varieties tested. The rest of the treatment was the same in both groups. Thirty healthy individuals age- and gender-matched with the patients were included as controls.

Whole blood samples were collected at the time of admission and at regular 7-day intervals for three weeks. The blood samples were processed for assay of biochemical analytes. Lipid peroxide (LP) was measured in serum as thiobarbituric acid reactive substances; uric acid and ceruloplasmin were estimated in serum by calorimetric methods. The statistical analysis was performed by Student's t test as a test of significance.

Results

"Table I ","Biochemical parameters in burn patients (values, mean ± SD) ",";Serum lipid peroxide (nmol/ml) ;Control (n = 30);Honey-treated (n = 30);SSD-treated (n = 30)@;Day 1 Day 7 Day 14 Day 21 ;2.20 ± 1.32;6.25 ± 0.51 4.54 ± 0.42 3.34 ± 0.41 2.21 ± 0.10;6.42 ± 0.71 4.90 ± 0.41 4.40 ± 0.08 3.90 ± 1.05@;Serum CLP Day 1 Day 7 Day 14 Day 21 ;100.45 ± 5.39;187.90 ± 4.27 192.71 ± 1.55 193.50 ± 69.89 200.70 ± 3.74;196.13 ± 64.96 201.43 ± 15.15 211.86 ± 9.45 22.55 ± 8.45@;Serum UA (mg/%) Day 1 Day 7 Day 14 Day 21;3.50 ± 0.22;8.12 ± 0.20 6.17 ± 0.61 5.40 ± 0.39 4.30 ± 0.42;8.15 ± 0.15 6.11

± 0.30 5.56 ± 0.68 5.00 ± 0.40","SSD = silver sulphadiazine; CLP = ceruloplasmin; UA = uric acid; p = 0.001 (highly significant)",4,300,true %>

The present study involved patients with partial-thickness burns ranging from 5 to 30% TBSA. Table I shows the results of biochemical analysis. Initial levels of mean serum LP in all the groups of burn patients were significantly high ($p > 0.001$) compared with controls. The initial levels of mean serum ceruloplasmin and uric acid were also significantly higher in all burn patients than in controls ($p > 0.001$).

A gradual decrease in serum LP levels was observed during the follow-up period in all the groups of burn patients treated with SSD and honey. The rate of decrease in serum LP levels was faster during honey therapy than in SSD treatment. Table I also shows that the serum ceruloplasmin levels were elevated in the follow-up period in all the groups. The rate of increase in serum ceruloplasmin levels was relatively slow during honey treatment. In more severe burns the values were higher. The mean levels of serum uric acid declined during the follow-up period ($p > 0.001$, not significant).

Discussion

Burn injury is accompanied by complex pathophysiological alterations that exert deleterious effects on various organ systems. Honey treatment is reported to have better and faster wound healing effects than conventional SSD therapy.3 Although the exact mechanism is not known, an elevated level of LP in the serum in the early post-burn period reflects increased activity of free radicals. It used to be believed that burn toxin was a lipid protein polymer formed from a component of cell membranes in the skin. Now it is known that LP is linked with lipoproteins in serum. This is further supported by reports that levels of polyunsaturated fatty acids, including arachidonic acid in the red blood cell membranes of thermally injured patients, are reduced. Elevated serum LP is

therefore related to peroxidation of membrane lipids. Our results suggest that the degree of lowering of LP by honey therapy is more significant than with SSD treatment.

This could be due to the positive effect of honey therapy on the control of free-radical activity, since honey contains antioxidants. The copper-containing protein ceruloplasmin has an enzymatic activity and plays a dual role. First, it is a sensitive acute-phase protein that is expressed in an inflammatory stressful state and, second, it acts indirectly by limiting Fe++ catalysed free-radical generation. The hepatic activation of a phase protein synthesis like ceruloplasmin can be mediated by factors liberated during macrophage activation. In sepsis and trauma, proteolysis induced by interleukin-1 stimulates the synthesis of hepatic acute-phase proteins. Increased free-radical activity in burn trauma could thus trigger macrophage activation via this mechanism.1 In this context, the rapid healing following honey therapy may explain the slow rise in the ceruloplasmin level.

Tissue ischaemia is known to activate purine nucleotide catabolism, and nucleotide depletion has been demonstrated in the heart and lungs. This results in increased ASP degradation into uric acid. During reperfusion, conversion of hypoxanthine to xanthine and uric acid generates oxygen free radicals. In thermally injured rats, the levels of plasma histamine and xanthine oxidase activity are reported to be elevated, parallel to the increase in uric acid. It is very likely that in burns these metabolic reactions take place locally. The cumulative effect of the changes could be seen as elevated serum uric acid levels. The elevation of serum uric acids levels is thus to be expected in the post-burn period. Also, the extent of the elevation of serum uric acid levels corresponds to the degree of the burn injury. In our honey-treated group, the lowering of serum uric acid was greater than in the SSD-treated group.

Conclusions

Ayurveda, the Indian system of medicine, describes honey as a nectar of life and recommends it as a therapy for wounds. The healing of burn wounds is faster and presents less scar formation.4 In addition to these beneficial effects, honey appears to have better control of the generation of free radicals. If honey is applied immediately after a burn injury, it will therefore prove beneficial. It is also cost-effective and free of toxicity and allergy.

RESUME. *Antécédents et buts.* La lésion thermique de la peau constitue une lésion oxydative associée à des altérations biologiques et métaboliques. L'emploi du miel dans le traitement des brûlures produit des altérations biochimiques et peut éclairer le mécanisme de l'action du miel dans les brûlures. Les Auteurs ont étudié les niveaux de peroxyde lipidique sérique, de céruléoplasmine sérique et de l'acide urique dans les patients brûlés pendant le traitement avec la sulphadiazine argentée et la thérapie avec l'emploi du miel. *Méthodes.* Cette étude prospective randomisée de contrôle en simple insu voulait effectuer une comparaison des altérations biochimiques pendant le traitement avec la sulphadiazine argentée et le traitement avec le miel. *Résultats.* Dans les traumatismes causés par les brûlures il se vérifie une activité excessive des radicaux libres au site de la lésion qui se manifeste dans les niveaux hématiques élevés de peroxyde lipidique, de céruléoplasmine et d'acide urique.Le traitement avec le miel portait à une réduction des niveaux de peroxyde lipidique sérique et à un léger incrément des niveaux de céruléoplasmine sérique; aucun effet significatif n'a été observé dans les niveaux de l'acide sérique urique par rapport aux patients traités avec la sulphadiazine argentée. Conclusion. Le traitement avec le miel semble avoir un effet positif sur la condition oxydative stressée qui se vérifie après la brûlure moyennant une opération efficace de nettoyage des radicaux libres, par rapport à la sulphadiazine argentée, qui a porté à une guérison rapide.

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