ADDICTION OF ANTIOXIDANTS AND POLYETHYLENE GLYCOL 4000
ENHANCES THE HEALING PROPERTY OF HONEY IN BURNS

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SUMMARY. A prospective study was carried out in two groups of 42 randomly allocated patients with partial-thickness burns to compare the effect of honey alone with that of honey fortified with antioxidants (vitamin C and vitamin E) and polyethylene glycol (PEG) 4000. Burns treated with honey plus antioxidants and PEG healed earlier than those treated with honey alone (mean 6.4 days versus 8.3). In this study the addition of antioxidants and PEG 4000 accelerated the healing properties of honey in burns.

Introduction

Honey has been popular as a wound dressing since ancient times. It has been found to be useful in the healing of burn wounds.1-4 The viscous barrier that honey presents to wound invasion by micro-organisms and to fluid loss is an important factor in rendering the burn wound sterile and preventing colonization. It must however be realized that honey is not and never will be a well-defined product.1' Various factors, e.g. type of bee and plant species involved, influence the effectiveness of different honeys.

The thermal injury of skin is an oxidation injury. There is always an increase in xanthine oxidase activity which is accompanied by an increase in lipid peroxidation.2 The normal strategy for diminishing lipid peroxidation is to raise the supply of antioxidants, such as vitamin C and E, to administer SOD-liposomes, or to use enzyme-inhibitors like allopurinol. After thermal injury a high cell antioxidant concentration is very important.3 Though the antioxidants needed for cell protection should be present in the daily diet, many anti-oxidants are only partly available. Adding antioxidants to honey may therefore be beneficial.

Polyethylene glycol (PEG) 4000 is a macromolecule that has been used mixed with honey and pollen extract for treating test lesions in milking cows4 and for preventing peritoneal adhesions by promoting non-adherent healing.5 In this prospective randomized study, honey with antioxidants and PEG was used in the treatment of burn wounds.

Patients and methods

Eighty-four patients with partial-thickness burns in less than 40% BSA were treated in our Unit in the period January 1993 to June 1994. After initial management, patients were assigned randomly to two groups. In group I patients (N' = 42) pure, unprocessed undiluted honey obtained from beehives was applied (15-30 ml) over the burn area, after washing with normal saline, and covered with pads and bandages. In group 2 patients, (N' = 42) the same batch of honey as used in group I was applied together with vitamin C, vitamin E and PEG over the burn area in the same quantity. For this purpose, 300 mg of vitamin C, 400 mg of vitamin E (alpha-tocopherol-acetate) and 1 nit of 25% PEG 4000 (Abbott Laboratories, Illinois, USA) was added to 100 g of honey. The quantity of PEG 4000 added to the honey was fixed on a trial-and-error basis in order to make the mixture semisolid or ointment-like. The wounds were covered with an absorbent dressing. In both groups the dressing was changed on day 2 and if there was no evidence of infection this was repeated on alternate days until the wound healed. Bacterial culture and sensitivity determinations were performed in all wounds on admission and on days 8 and 21 in all cases or until wound healing. The time taken for complete healing was noted in both groups and the data were analysed using the chi-square test.

The general management of the patients was the same in both groups.
Results

Of the 84 patients, 61 were male and 23 female. The youngest patient was 2 years old and the oldest, 78 years old. The IIASA area ranged from 10 to 35% (mean 17.6%) in group 1 and from 11 to 40% (mean 18.2%) in group 2. Table I shows possibly by protecting the tissues from the cytotoxic effects of lipid peroxidation.

<table>
<thead>
<tr>
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<th>Group 1 (Patients treated with honey only)</th>
<th>Group 2 (Patients treated with honey plus anti-oxidants and PEG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>Male</td>
<td>29</td>
<td>32</td>
</tr>
<tr>
<td>Female</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Mean age (yr)</td>
<td>26.0</td>
<td>27.2</td>
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<tr>
<td>Age range (yr)</td>
<td>2-62</td>
<td>3-63</td>
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<tr>
<td>Mean % BSA</td>
<td>17.6</td>
<td>18.2</td>
</tr>
<tr>
<td>% BSA range</td>
<td>10-35</td>
<td>11-40</td>
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</tbody>
</table>

Table I - Patient data

The addition of the macromolecule also transformed the mixture into a paste or ointment, without any adverse effects. This ointment form appears to be more acceptable to patients than honey alone. This may therefore be a further step in the increased use of honey, a naturally occurring cheap and valuable substance, in the treatment of burn wounds. The extremities and abdomen were involved in 90% of the cases.

In patients treated with honey alone, healthy granulation appeared in the majority of cases after about one week: wounds healed by day 10 days in 20 patients and by day 15 in another 12 patients. Thus 32 patients (76.1%) achieved wound healing by day 15 (mean 8.3 days). In patients treated with honey plus, granulation appeared by day 4 in the majority of cases, with wounds healing by day 6 in 34 patients and by day 9 in another 8 patients (mean 6.4 days) (Table II). The time taken for wound healing differed significantly between the two groups (p < 0.001). The results of culture swab study are shown in Table III. The organisms isolated in 26 infected patients in both groups on day 8 were: Staphylococcus aureus coagulase-positive (8 patients), Pseudomonas aeruginosa (4), Klebsiella (5), Escherichia coli (5) and Proteus (4).

There was no bleeding during dressing changes, and no difficulty in removing dressings in either group. Overgranulation was found in group 1, with minor contracture in two cases; in group 2 there was no overgranulation and only one contracture. Allergy or other side-effects such as renal failure were not observed in any patient in either group.

Discussion

Honey is a mixture of sugars prepared by bees from natural sugar solutions (nectar) obtained from flowers. The nectar collected by bees is deposited in honeycombs. By inverting the sucrose in the nectar, bees increase the density of honey, making it a thick, sweet energy food. Pure unboiled honey is composed of 40% fructose, 20% water and 40% glucose. It contains various minerals (magnesium and calcium), acids acetic acid), vitamins, and enzymes (diastase, invertase, glucose oxidase and catalase).
Honey has been used as in a(Ijuvant lot- the acceleration of wound healino since ancient tinies. Suslirma Sarnhita mentions applications of honey with some indigenous leaf juices to clean and fistulous tracts,.12 In Chinese medicine also, honey and an extract of various plants dissolved in sesame oil were found to give good healing in burns.

Topical application of honey has been observed to be effective in ulcers, infected wounds, and burns. Herbal extracts added to honey may contain antioxidants and polyunsaturated fatty acids.' These antioxidants are needed for cell protection against reactive oxygen species, as described by Friedel et if." in lbeir experinewal shidics on thermal trauma. A high cell ~ktitioxi(Ltiit conceniration after thermal injury theoretically should help the cell protection. Vitamin C, an antioxidant willi sligil pro-oxidant activity, and vitamin E are good for fftis purposc. Polyethylene glycol (PEG) 4000 is a macromolecule which has been added to honey and pollen extract for the treatment of test lesions in the cow.' It has also been used to reduce peritoneal adhesions ill experimental animals. The proposed mode of action of the macromolecule is by promotion of non-adherent healing through polymer coating or siliconization of the injured surface." On the basis of this proposed mode of action, PEG 4000 was added to honey and antioxidants. PEG 4000 is known to have toxic effects. Toxicity due to absorption of PEG in burn patients treated with PEG-based cream, resulting in renal failure, has been reported.’ However, in the present study, no toxic effects were observed in any patient, possibly owing to the reduced concentration and quantify used.

In this prospective study, burn wounds treated with honey fortified with vitamin C, vitaniin E and PEG 4000 healed more rapidly than wounds treated with honey alone. As already said, this may be due to lie non-adliercin healing property of PEG and llic action of (lie antioxidants,

**RESUME.** L’auteur a effectué une étude prospective dans deux groupes de 42 patients atteints de brûlures d'épaisseur partielle, distribués au hasard, pour comparer l'effet du miel seul à celui du miel fortifié avec des antioxydants (vitamine C et vitamine E) et le glycol polyéthylène (PEG) 4000. Les brûlures traitées avec le miel intégré avec antioxydants et PEG ont guéri plus rapidement (lue celles traitées avec le seul miel (valeur moyenne 6,4 jours contre 8,3). Selon les résultats de cette étude, l'addition des antioxydants et de PEG a accéléré les propriétés curatives du miel dans les brûlures.

**BIBLIOGRAPHY**


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