Tualang Honey Hydrogel in the Treatment of Split-Skin Graft Donor Sites

Farrah-Hani Imran1, Aravazhi Ananda Dorai2, Ahmad Sukari Halim1 and Wan Azman Wan Sulaiman2

1 Plastic and Reconstructive Sciences Program, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia.
2 Plastic and Reconstructive Surgery, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia.

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*Corresponding author: Email: ashalim@kb.usm.my

Summary

Hydrogel is an established wound dressing. In this prospective single arm study the benefits conferred when tualang honey was added to a hydrogel dressing were investigated with regards to the healing of split skin graft donor sites. Efficacy was evaluated by examining rates of wound healing and pain during the healing of split-skin graft donor using Tualang Honey Hydrogel. Patients who underwent split skin grafting were screened and those who met the inclusion criteria were recruited from the patient population in Hospital Universiti Sains Malaysia (HUSM) over a period of 18 months. Individual informed consent was obtained from each patient. Thirty-five patients received Honey Hydrogel dressing applied to their split skin graft donor sites. All donor sites were inspected on the 10, 15 and 20th post-operative day. Complete healing between post-operative day 10 and post-operative day 15 was observed, with minimal pain, discomfort and pruritus. Honey Hydrogel may be effective in the treatment of split-skin graft donor sites, warranting further studies to compare it with existing dressing materials.

Keywords: skin graft donor site, hydrogel, honey hydrogel, dressings and wound healing

Introduction

An ideal wound dressing protects the wound from bacterial infection, controls hydration, gas permeability to the wound bed, absorbs wound exudate, and enhances wound healing. Additionally, it should be composed of materials that are non-toxic, non-immunogenic, flexible, durable, and comfortable when worn (Kelly and Li, 2002). It should also be pleasant to touch and painless during removal, able to maintain mechanical strength, and with the potential to act as a barrier against microbes (Ajji et al., 2005; Ajji and Mirjalili, 2008).

Hydrogel dressings are cross-linked polymer gels that are often shaped into sheets to provide and maintain a moist wound environment. They are water or glycerin based products, which are usually clear or translucent, enabling a wound to be monitored without removing the dressing. By increasing moisture content, hydrogels have the ability to help clean and debride necrotic tissue.

Hydrogels possess excellent tissue compatibility with their high porosity and good biocompatibility, hydrogel dressings are considered to be a promising candidate biomaterial for pharmaceutical and tissue engineering applications (Qing, 2009). However, one of their main disadvantages is that they exhibit poor mechanical properties after swelling. In order to overcome this disadvantage, hydrogels can be modified by physical blending or/and chemical modification by grafting, interpenetrating polymer networks and cross linking (Yang et al., 2004). In this study, honey hydrogel sheets were modified with the cross-linking method during the preparation process at Nuclear Malaysia (Kuala Lumpur, Malaysia).

Historically, honey has been used for the treatment of wounds for centuries, from the Egyptians to the Romans. The medicinal benefits of honey were recorded in sayings of the Prophet Muhammad and in the Holy Quran. Honey is used by the Buddhists of India to commemorate Buddha's retreat. The Jewish Rosh Hashanah is celebrated with honey-dipped apples. According to the Old Testament and the book of Exodus, Moses, Samson and John the Baptist have had encounters with honey. Honey consists of multiple components derived from plants and bees during the maturation processes. It is a mixture of sugars prepared by the bees from the natural sugar solutions called nectar obtained from flowers. By
inverting the sucrose in the nectar, the bee increases the attainable density of the final product, and thus raises the efficiency of the process in terms of caloric density. The higher osmotic pressure obtained precludes bacterial growth (Subrahmanyam, 1996, 1998, 1999).

Materials and methods

A prospective single-arm study was conducted at the Reconstructive Sciences Department, Hospital Universiti Sains Malaysia. The inclusion criteria included adults and teenagers with ages ranging from 13-65 years, who were admitted for skin grafting with donor sites restricted to either the inner arm or the thigh. The exclusion criteria applied were immuno-compromised patients, patients with major systemic illness, with an ASA score (the American Society of Anesthesiologists) of III or greater. Also excluded were patients who had previously had a skin graft taken from the intended donor sites and patients whose donor site depths were either too thin or too thick. Maximum size of the split skin graft donor wound was 25 cm².

The split skin graft was harvested with a dermatome or Humby knife either under local, regional or general anaesthesia aiming to take a medium thickness graft (0.012-0.018 mm) as judged by the appearance of the donor bed (McGregor, 2000). Haemostasis of the donor site was achieved with topical adrenaline (1 mg adrenaline / 200 mL anaesthetic solution). The wound was cleaned with normal saline prior to application of each dressing. Secondary dressings included gauzes, gamgee and crepe bandages. Photodocumentation was performed using a Canon power shot A650 IS (Image Stabiliser) digital camera. An occlusive dressing technique using Hypafix® or Micropore® adhesive tape was employed for the Honey Hydrogel dressing.

The tualang honey hydrogel dressings were prepared at the Nuclear Malaysia (Kuala Lumpur, Malaysia) facility. Tualang honey (AgroMas, Malaysia) was added to a mixture of 15% polyvinyl pyrrolidone (PVP) (Kollidon 90), 1% protein free agar (Oxoid) solution and 1% polyethylene glycol (PEG). The mixture was then poured into a 10 x 10 cm plastic mold with 3-4 mm thickness and left to set at room temperature before being covered with a polyethylene sheet and individually packed. The gel was cross-linked as well as sterilized by electron beam at 25 kGy at Alutron Irradiation Facility, Nuclear Malaysia (Model EPS-3000, conveyor speed of 4.4 m/min, beam current of 10 mA and energy of 3 MeV). The end result was sterilized gel sheets of Honey Hydrogel, packaged and ready for application in this study (Norimah and Ainul, 2007).

Fig. 1. Packaged Honey Hydrogel Gel Sheets, as received by the Reconstructive Sciences Unit of Hospital Universiti Sains Malaysia, Kelantan, from Nuclear Malaysia (Kuala Lumpur, Malaysia).

Assessment

All donor sites were inspected on the 10th, 15th and 20th post operative day (POD10, POD15 and POD20 respectively). Photographs were taken from every patient during their wound assessments. These digital images were assessed by an independent observer and blinded in order to avoid inter-observer bias. The wounds were defined as healed when an intact epithelium was detected. Unhealed donor sites were traced on a sterile 1 cm-scale transparency. The unhealed area was estimated by adding squares and calculating as a percentage of the original donor area.

Pain assessment was performed throughout the first 7 postoperative days and at each dressing change using a Verbal Analogue Chart (from 1 = No pain to 5 = excruciating pain). Essentially, pain assessment was conducted twice a day for the first three days followed by daily from the forth to seventh day. The analgesics which the patients received postoperatively were standardized (IM Pethidine 1 mg/kg body weight 8 hourly) for a period of two days followed by NSAIDS (8 hourly) from the third to fifth days and thereafter paracetamol tablets (8 hourly) from the sixth to seventh days. Any additional analgesics that were required was documented. Any leakage from the dressing was managed by overlying application of additional medium sized gamgee and a 6 inch crepe bandage.

When there was clinical evidence of infection at the split skin graft donor site which was demonstrated by the presence of purulent discharge or slough during the time of wound assessment, wound swabs for culture and sensitivity were sent for microbiological assessment and recorded on the protocol forms.
Results

Thirty five patients who met the criteria were assigned to a dressing regime of Honey Hydrogel (Figure 1). All of the donor site wounds were healed by post operative day 20 (Table 1); progress in two patients is illustrated in Figure 2.

The general findings of the study revealed full epithelialisation with Honey Hydrogel dressings by post-operative day 10 and post-operative day 15, with minimal symptoms of pain, discomfort and pruritus.

The majority of patients experienced minimal pain discomfort and pruritus (Table 2).

Discussion

Combining the honey with hydrogel created a wound-healing environment that appeared to meet the criteria set forth above for an ideal wound dressing (Norimah and Ainul, 2007). Signs of bacterial infection were not apparent during gross examination of the wounds, suggesting that the materials effectively protected the wound from bacterial infection. The wounds exposed to Honey Hydrogel were found to be moist and hydrated, thus demonstrating that evaporative water loss and wound dehydration had been prevented. The honey component provided a pleasant odour to the wounds.

All of the donor site wounds healed over the study period and full epithelialisation was achieved in majority of the wounds by post-operative day 10. Symptoms and signs such as pruritis, discomfort which included stinging pain were minimal or non-existent with Honey Hydrogel. A variety of dressings are used in different institutions, the expected healing time for full epithelialisation is by POD20.

The clinical implication of the findings of this pilot study are limited. Patients reported the cool soothing effects of honey as a calming factor during the post-operative period. The added honey component provided a lasting, pleasant odour, which patients appreciated, especially as the dressing was in place for ten days continuously post operatively. The pain level was generally minimal.

### Table 1. The number of patients with fully epithelialized wounds on Honey Hydrogel at post operative day 10, post operative day 15 and post operative day 20.

<table>
<thead>
<tr>
<th>Post-operative day (POD)</th>
<th>Mean healing rate (% of patients / no. of days)</th>
<th>% of patients with healed wounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>POD 10</td>
<td>9.41</td>
<td>94.05</td>
</tr>
<tr>
<td>POD 15</td>
<td>6.61</td>
<td>99.10</td>
</tr>
<tr>
<td>POD 20</td>
<td>5</td>
<td>100</td>
</tr>
</tbody>
</table>

### Table 2. Pain scores given by the patients between post-operative day 1 and post-operative day 7.

<table>
<thead>
<tr>
<th>Post Operative Day (POD)</th>
<th>Pain Score</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>POD 1</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0</td>
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<tr>
<td></td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>POD 2</td>
<td>1</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>POD 3</td>
<td>1</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>POD 4</td>
<td>1</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>POD 5</td>
<td>1</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>POD 6</td>
<td>1</td>
<td>35</td>
</tr>
<tr>
<td>POD 7</td>
<td>1</td>
<td>35</td>
</tr>
</tbody>
</table>

Fig. 2. Series of patients 1 and 2 on Honey Hydrogel. The rate of epithelialization is clinically obvious by post operative day 10 (POD10) with complete healing by post operative day 15 (POD15) and post operative day 20 (POD20). (a) 10 days; (b) 15 days; (c) 20 days
The medical staff performing the wound inspections found the non-adherence of the dressing helpful, as dressing changes caused minimal discomfort to the patients. The fast healing time also meant that most split skin graft donor sites treated with honey hydrogel could be exposed by post operative day 10.

Honey has been reported to promote wound healing through several mechanisms (Tonks et al., 2003). It promotes a moist wound environment by drawing lymph into the wound through osmosis and preventing the dressing from adhering to the wound bed. In addition, the glucose contained in honey may improve local nutrition and promote epithelialisation. The acidic nature of honey provides an optimal environment for fibroblast activity (Pieper, 2009; Gunes, 2007). Honey stimulates angiogenesis, thus increasing oxygen and nutrients to the wound and promoting healthy granulation tissue, hastens epithelialisation, possibly decreasing the need of skin grafting and stimulates collagen synthesis and improves tensile strength (Molan, 2006).

Honey has been reported to reduce scarring. There are three potential mechanisms resulting in this outcome, saccharides at the wound surface may encourage the production of hyaluronic acid from glucose, which simultaneously suppresses the formation of fiber-forming collagens, glucose at the wound bed creates an environment that enables wound healing proteoglycans to exert their effects without producing excessive quantities of collagens and the mechanism by which sugar attaches to collagen may change its structure (Langemo, 2009).

In this study, Tualang Honey (AgroMas, Malaysia) was used. Malaysian Tualang Honey was collected from the combs of wild Asian rock honey bees (Apis dorsata), which build their hives high up in the Tualang trees (Koompassia excelsa) found in the Malaysian rain forest. It is commonly used as traditional medicine and as a food product in Malaysian society (Hern et al., 2009).

Antimicrobial activity of honey has partially been attributed to hydrogen peroxide, which is produced by naturally occurring glucose oxidase, (White et al., 1963).

A further study is required with a control arm, with an established conventional dressing, to categorically establish the effectiveness of honey hydrogel in the treatment of split-skin donor sites and its cost-effectiveness. The power of the study must be increased by recruiting more patients. Studies which include other types of honey will allow the efficacy of tualang honey to be compared to other types of honey available worldwide. Lastly, this study was conducted in one centre. A multi-centre comparison with varying demographics will be of wider interest.

Acknowledgements

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