Comparative Effect of Betadine Ointment and Sodium Fusidate Cream on Experimentally Induced Burn Wound in Wistar Rats.

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ABSTRACT

Antibacterial agents like sodium fusidate, framycetin, calcium mupirocin are used topically to treat burn wounds. But their effect on healing as such is not known. The main objective of the present study is to compare the effect of sodium fusidate cream and betadine ointment on experimentally created burn wound healing in Wistar rats. The rats were anesthetized with ketamine 50mg/kg/ip before wounding. Burn wounds were created by pouring hot molten wax into a metal cylinder of 300 mm² circular opening placed on shaven back of the rat. Animals were divided in to three groups of six rats each. Group I did not receive any drug and served as control group. Group II and III received 25-30 mg of betadine ointment and 25-30 mg of sodium fusidate cream respectively once daily for 21 days or till complete epithelization whichever was earlier. Wound contraction and period of epithelization was noted in all the three groups by observing the animals daily. A significant decrease in epithelization and increase in % of wound contraction was observed with sodium fusidate cream compared to control and betadine group.

Keywords: Epithelization, wound contraction, wound healing

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INTRODUCTION

Burns remain a huge public health issue, at least in terms of morbidity and long term disability, throughout the world, especially in the developing countries. Burn wound healing is a complex process and does not require much help but still cause discomfort and are prone to infection and other complications. Infection is a major complication of burn injury and is responsible for 50-75% of hospital deaths [1, 2, 3]. Many of the synthetic drugs pose problems such as allergy, drug resistance, etc, forcing scientists to seek alternative drugs. Wound healing, or wound repair, is the body’s natural process of regenerating dermal and epidermal tissue [4]. When an individual is wounded, a set of events takes place in a predictable fashion to repair the damage. These events overlap in time. The wound healing process has three phases. They are the inflammatory phase, the proliferative phase, and the maturational or remodeling phase. Some authors consider healing to take place in four stages, by splitting inflammation or proliferation into separate steps [5]. The phases of wound healing normally progress in a predictable, timely manner; if they do not, healing may progress inappropriately to either a chronic wound such as a venous ulcer or pathological scarring such as a keloid scar.

One of the complications of burn injuries is life threatening infection, nearly 15% of which are caused by anaerobic bacteria [1]. Various topical agents such as sodium fusidate, framycetin, calcium mupirocin etc. are topically used in burn wound patients. Apex Laboratories, Chennai has prepared few antibacterial agents with biopolymer. One such product is sodium fusidate which is used in the management of burn wounds. Betadine ointment is also used in the management of burn wound healing.

Hence the present study was planned to compare the efficacy of betadine ointment and sodium fusidate cream on experimentally induced burn wound healing in Wistar rats.

MATERIALS AND METHODS

Eighteen adult male Wistar rats weighing 150–200 g were housed in polypropylene cages, maintained under standard conditions with temperature (22–240 C), 12-h light/12-h dark cycle and relative air humidity 40–60%. Rats had continuous access to norm caloric standard rat pellet diet and to tap water. The animals were acclimatized to the laboratory conditions for one week before the start of the experiment. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC/KMC/02/2014) and experiments were conducted according to the ethical norms approved by Ministry of Social Justices and Empowerment (Government of India), Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA) guidelines.

The rats were fasted overnight. Under ketamine and xylazine anaesthesia (80 mg/kg and 10 mg/kg respectively; i.p), burn wounds were created by pouring hot molten wax at 80°C into a metal cylinder of 300 mm² circular opening placed on shaven back of the rat [6]. This results in partial thickness burn wounds. Soon after wounding and on subsequent days Ringer lactate (1 ml/kg) was administered intraperitoneally for resuscitation. Apart from the drugs under investigation no local/systemic chemotherapeutic cover were provided to animals. Infected animals during the study were excluded and replaced with fresh animals.

In the experiment a total of 18 Wistar rats (male, pathogen free, 6-8 weeks old) were used. All the burn wound induced rats were grouped into 3 groups with 6 animals each. The treatments were carried for a period of 16 days with one time per day application of the drugs. Animals were grouped as follows-

Group I: Control rats- No drug application.
Group II: 25-30 mg of Betadine ointment was applied on the wound affected area.
Group III: 25-30 mg of Sodium Fusidate cream was applied at the wound affected area.

Parameters studied: Animals were observed daily and the healing was assessed by noting the period of epithelization and wound contraction.

Number of days taken for complete epithelization was measured by recording the days required for fall of scab leaving no raw wound behind. Wound contraction was monitored by measuring wound area, planimetrically, on the alternate days till the wounds were completely healed [6]. Measurement of the wound
size was carried out by tracing the wound with a marker on a sterile transparent paper. The transparent paper was placed on a graph paper, and the number of square blocks of the graph paper within the surface area of the wound was counted, and finally multiplied by 0.04 cm$^2$, this gives the mathematical representation of the dimension of each square blocks which is equivalent to the wound area. After wound size measurement, wound dressing was done once every three days. The percent of wound contraction on day 4, 8, 12, and 16 was calculated by using the following formula:

\[
\text{Percentage edema} = \frac{\text{Initial wound size} - \text{Specific day wound size} \times 100}{\text{Initial wound size}}
\]

**Data analysis:** Using SPSS 20.0, data were expressed as mean ±standard error of mean and analyzed by one way analysis of variance (ANOVA) followed by post hoc Tukey test. P value less than 0.05 was considered as statistically significant.

**RESULTS**

There was significant increase of percentage wound contraction in sodium fusidate treated animals on 4rd, 8th, 12th and 16th day interval in comparison with control group (Table 1) whereas betadine was found to increase the percentage wound contraction significantly on day 4 and 12 only when compared with control. Sodium fusidate cream has shown an increase in percentage of wound contraction on day 4, 8, 12 and 16 when compared to betadine ointment. The period of epithelization in control group was 21.75±0.25 days. Sodium fusidate significantly reduced the period of epithelization when compared to control. Though betadine ointment reduced the period of epithelization, it was not statistically significant when compared to control group. (Table 2).

**Table 1: Effect of Betadine ointment and sodium fusidate cream on % wound contraction**

<table>
<thead>
<tr>
<th>Treatment groups</th>
<th>Percentage wound contraction (Mean ±SEM)</th>
<th>Day 4</th>
<th>Day 8</th>
<th>Day 12</th>
<th>Day 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.028±3.76</td>
<td>15.63±4.24</td>
<td>23.4±3.44</td>
<td>58.1±8.4</td>
<td></td>
</tr>
<tr>
<td>Betadine</td>
<td>6.84±1.06***a</td>
<td>14.97±2.68</td>
<td>17.44±2.20*a</td>
<td>61.13±4.38</td>
<td></td>
</tr>
<tr>
<td>Sodium fusidate Cream</td>
<td>34.03±5.66***a, b</td>
<td>53.4±3.9***a, b</td>
<td>71.6±7.67***a, b</td>
<td>92.4±7.5***a, b</td>
<td></td>
</tr>
</tbody>
</table>

a; Compared to control, b; compared to betadine, ***indicates p<0.001, * indicates p<0.05

**Table 2: Effect of Betadine and sodium fusidate on period of epithelization**

<table>
<thead>
<tr>
<th>Treatment groups</th>
<th>Days taken for complete epithelization (Mean ±SEM)</th>
<th>P value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>21.75±0.25</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Betadine</td>
<td>19.66±1.66</td>
<td>&gt; 0.05</td>
<td>NS</td>
</tr>
<tr>
<td>Sodium fusidate cream</td>
<td>17.25±1.50*a</td>
<td>&lt;0.05</td>
<td>S</td>
</tr>
</tbody>
</table>

a; Compared to control, * indicates p<0.05, NS- Not significant, S- Significant

**DISCUSSION**

The present study revealed that the sodium fusidate cream has comparatively better burn wound healing potential than the Betadine ointment (10%) in Wistar rats. Sodium susidate is known to have been used to make dermaceutical medicaments for topical application. However, these are in the form of ointment rather than cream. Drawbacks of ointments over creams are well known and it’s generally preferable to use creams rather than ointments for topical application. This may be one of the reason for better wound healing profile of sodium fusidate when compared to betadine ointment. Further, as mentioned earlier in introduction, the addition of biologically active polymers (the so-called biopolymers) is a complex process in
which the stability of the formulations could be compromised if the right biopolymer or naturally interacting formulation excipients or process parameters are not well thought through and optimized to enhance and complement therapy outcomes at the drug design stage itself. Incorporation of a functionally bio-active excipient polymer in cream matrix while retaining the functional stability of the API in a single dose format of dermaceutical cream involves resolution of problems specific to the physical stability of cream matrix [7]. The present sodium fusidate cream is prepared by using a standard biopolymer. This may be another reason for better wound healing potential of sodium fusidate compared to betadine cream.

In conclusion, the sodium fusidate cream has better burn wound healing profile when compared to betadine ointment. However, further, clinical evaluation has to be performed to precisely define the role of the role of sodium fusidate in burn wound healing in human subjects.

REFERENCES