Treatment of lepromatous ulcers using citric acid as a sole antimicrobial agent

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ABSTRACT
A prospective study was carried out to assess the role of citric acid as a sole antimicrobial agent in the management of lepromatous ulcers. Thirty-four known cases of lepromatous ulcers not responding to conventional antibiotic therapies for long duration were investigated for culture and susceptibility studies. Staphylococcus aureus (25·00%) and Klebsiella spp. (23·43%) were found to be the most common isolates. Amikacin (68·75%) and ciprofloxacin (67·18%) were found to be the most effective antimicrobial agents. Topical application of citric acid ointment resulted in complete healing in 25 (73·52%) cases. In eight cases (26·48%), there was elimination of infective agent from ulcer site and formation of healthy granulation, but no complete healing of ulcer was seen. Results indicate that citric acid is the best alternative for the effective management of lepromatous ulcers when other therapies are exhausted.

Key words: Citric acid treatment • Healing of ulcer • Lepromatous ulcers

INTRODUCTION
Involvement of peripheral nerve tissue is a unique feature of leprosy. Involvement of peripheral nerve leads to sensory, motor and trophic changes in extremities predisposing and causing ulcers (1,2). These ulcers in leprosy patients are of neuropathic type; hence, healing is a problem because of repeated stress at the painless feet. Chronic ulceration is the most common problem in the feet of leprosy patients. These ulcers are usually longstanding, do not heal easily, tend to recur rapidly and carry the potential to destroy the feet progressively. Chronic ulcers remain unhealed as they are not allowed to heal because of breaking up of delicate granulation and epithelial tissue on walking. Trophic ulcers are hard to heal, and if not treated properly in time may undergo malignant transformation (3).

Citric acid, which has medicinal properties, is a natural acid that is found in many citrus fruits such as lemon, orange, leech, grapefruits, etc. Its use has been reported previously in the effective treatment of chronic wound infections caused by various bacteria. The use of citric acid has been proved highly effective and economical in the management of various types of chronic wound infections (4,5). In this study an attempt was made to treat chronic ulcers in leprosy patients using citric acid as a sole antimicrobial agent.

MATERIALS AND METHODS
This prospective study, carried out during the period January 2003 to December...
Key Points

- a total of 34 clinically and microbiologically confirmed cases of leprosy having chronic ulcers about 2–8 cm in diameter and 0.5–1 cm in depth for a prolonged period (1 month to 2 years) not responding to conventional therapy were included in this study
- the application of citric acid ointment was started after a thorough debridement of ulcer
- this treatment modality was used once daily till the ulcer healed completely or showed formation of healthy granulation tissue
- no antibiotics were given to any of the patients

2009, was approved by institutional ethical committee. A total of 34 clinically and microbiologically confirmed cases of leprosy having chronic ulcers about 2–8 cm in diameter and 0.5–1 cm in depth for a prolonged period (1 month to 2 years) not responding to conventional therapy (one antibiotic from aminoglycosides group – gentamicin or amikacin, another antibiotic from cephalosporin group – ceftazidime, ceftriaxone or fluoroquinolones group – ciprofloxacin and metronidazole) and local wound care (daily dressing of ulcers with betadine) were included in this study. These cases referred by treating dermatologists/leprologists or surgeons dealing with ulcers were either receiving the antileprosy drugs simultaneously or had already completed the prescribed course of antileprosy drugs. They were also receiving the specific supportive therapy for neuropathy. After taking a detailed history and performing a thorough clinical examination, localised infection was ascertained by signs of mild local inflammation (redness, swelling and warmth) and indirectly by raised erythrocyte sedimentation rate (ESR) and leucocytosis on peripheral blood. A swab from ulcer was collected and processed for isolation of bacteria by conventional techniques (6) to confirm the infection. The infection was confirmed by isolation of bacteria in significant numbers from ulcers (This was defined as a confluent growth on primary and secondary streaking or minimum 100 colonies).

The antibiotic susceptibility of each isolate was studied by Kirby–Bauer disc diffusion method (7). Minimum inhibitory concentration (MIC) to citric acid was determined by broth dilution method (8). Simultaneously, application of 3% citric acid ointment, prepared by mixing of 3 g of pure citric acid with 100 g of white soft paraffin (100% pure petroleum jelly), a hydrocarbon base not absorbed by skin was used as inert vehicle for citric acid. The citric acid ointment was prepared by mechanical mixing in a mortar by taking all sterile precautions. The application of citric acid ointment was started after a thorough debridement of ulcer. This treatment modality was used once daily till the ulcer healed completely or showed formation of healthy granulation tissue. No antibiotics were given in any of the patients. The patients were advised complete rest during this treatment modality. The ulcers were observed frequently for formation of healthy granulation tissue, reduction of discharge, reduction in the size of ulcer, margin of ulcer, etc. to monitor the progress of the ulcers. This treatment was given on outpatient department (OPD) basis in 28 patients, and in 6 patients with severe ulcers, this treatment was given on inpatient department (IFD) basis.

RESULTS

This study yielded Staphylococcus aureus (25-00%) as the most common isolate followed by Klebsiella spp. (23-43%), Escherichia coli (12.5%) and other bacteria in decreasing order of frequency. Amikacin (68-75%) followed by ciprofloxacin (67-18%), ceftazidime (65-62%) and pefloxacin (62-5%) were found most effective antimicrobial agents in in vitro study. Ampicillin (26-56%) was found to be the least effective antimicrobial agent (Table 1). All bacterial isolates were found to be inhibited by citric acid. The MIC of citric acid in vitro was found in the range of 500–2500 μg/ml against different clinical isolates. Pseudomonas aeruginosa was found to be most susceptible (MIC, 500–1000 μg/ml) and Klebsiella spp. was found to be least susceptible (MIC, 2000–2500 μg/ml) (Table 2). Topical application of 3% citric acid ointment once daily on lepromatous ulcers resulted in either complete healing or formation of healthy granulation tissue and successful elimination of the pathogens from infection sites in 11–33 applications in 11–33 days (Figures 1–3). Of 34 cases, the lepromatous ulcers were healed completely in 25 cases (73.52%); however, in 9 cases (26.48%), infection was controlled and a healthy granulation tissue was formed, but the complete healing did not occur. Citric acid ointment was found effective against all bacterial pathogens including notorious pathogens such as S. aureus and P. aeruginosa. No adverse effects were noted in any of the patients during the study.

DISCUSSION

Trophic ulceration of feet in the leprosy patients is responsible for much of the morbidity associated with leprosy. It is a pathetic situation in leprosy, which hampers the restoration of the social status to leprosy
Table 1 Clinical isolates from lepromatous ulcers and their antibiogram

<table>
<thead>
<tr>
<th>Serial no.</th>
<th>Name of organism</th>
<th>No. of isolates</th>
<th>A (25·00)</th>
<th>G (25·00)</th>
<th>Ak (62·5)</th>
<th>Cf (68·75)</th>
<th>Pf (62·5)</th>
<th>Ca (62·5)</th>
<th>Ce (56·25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>S. aureus</td>
<td>16</td>
<td>04</td>
<td>04</td>
<td>10</td>
<td>12</td>
<td>11</td>
<td>10</td>
<td>09</td>
</tr>
<tr>
<td>2</td>
<td>Klebsiella spp.</td>
<td>15</td>
<td>02</td>
<td>07</td>
<td>11</td>
<td>09</td>
<td>09</td>
<td>10</td>
<td>08</td>
</tr>
<tr>
<td>3</td>
<td>E. coli</td>
<td>08</td>
<td>02</td>
<td>04</td>
<td>06</td>
<td>05</td>
<td>05</td>
<td>07</td>
<td>03</td>
</tr>
<tr>
<td>4</td>
<td>Streptococci</td>
<td>07</td>
<td>05</td>
<td>09</td>
<td>06</td>
<td>05</td>
<td>07</td>
<td>03</td>
<td>04</td>
</tr>
<tr>
<td>5</td>
<td>P. aeruginosa</td>
<td>07</td>
<td>00</td>
<td>03</td>
<td>04</td>
<td>03</td>
<td>03</td>
<td>03</td>
<td>03</td>
</tr>
<tr>
<td>6</td>
<td>Staphylococcus albus</td>
<td>06</td>
<td>03</td>
<td>03</td>
<td>03</td>
<td>03</td>
<td>03</td>
<td>03</td>
<td>03</td>
</tr>
<tr>
<td>7</td>
<td>Citrobacter spp.</td>
<td>05</td>
<td>01</td>
<td>04</td>
<td>04</td>
<td>03</td>
<td>02</td>
<td>04</td>
<td>02</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>64</td>
<td>17</td>
<td>34</td>
<td>44</td>
<td>43</td>
<td>42</td>
<td>32</td>
<td></td>
</tr>
</tbody>
</table>

A, ampicillin; Ak, amikacin; Ca, ceftazidime; Ce, ceftriaxone; Cf, ciprofloxacin; G, gentamicin; Pf, pefloxacin.

*Figures in parentheses indicate percentage.

Table 2 Minimum inhibitory concentration (MIC) of citric acid against clinical isolates

<table>
<thead>
<tr>
<th>Serial no.</th>
<th>Name of microbe</th>
<th>MIC value (μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>P. aeruginosa</td>
<td>500–1000</td>
</tr>
<tr>
<td>2</td>
<td>Klebsiella spp.</td>
<td>2000–2500</td>
</tr>
<tr>
<td>3</td>
<td>S. aureus</td>
<td>900–1000</td>
</tr>
<tr>
<td>4</td>
<td>E. coli</td>
<td>1500–2000</td>
</tr>
<tr>
<td>5</td>
<td>S. albus</td>
<td>1200–1500</td>
</tr>
<tr>
<td>6</td>
<td>Streptococci</td>
<td>1000–1500</td>
</tr>
<tr>
<td>7</td>
<td>Citrobacter spp.</td>
<td>1000–1500</td>
</tr>
</tbody>
</table>

The citric acid has been used in the treatment of a variety of chronic wounds (4,5,10,11) and even in lepromatous ulcers caused by E. coli (12,13). Based on earlier experience of citric acid in a variety of chronic wounds and also in lepromatous ulcers caused by E. coli, an attempt was made to use citric in the treatment of lepromatous ulcers caused by a variety of bacteria including E. coli. By using citric acid locally, it was possible to control infection in all cases of lepromatous ulcers and complete healing of chronic ulcers was seen in 73·52%, but complete healing did not occur in 26·48% cases, although infection was controlled and healthy granulation was formed. This non healing of ulcers in 26·48% cases may be because of underlying neuropathy and vasculopathy.

The microbiological studies and rapid clearing up of infected sites suggest that citric acid is antibacterial in nature and has antiseptic.

Figure 1. Lepromatous ulcer – before application of citric acid ointment.

Figure 2. Lepromatous ulcer – after 12 applications of citric acid ointment.

Figure 3. Healed lepromatous ulcer – after 20 applications of citric acid ointment.
The results of this study indicate that citric acid treatment could be a reliable and effective option in the management of lepromatous ulcers; hence, one can think of using citric acid as one of the alternative therapeutic options. This antiseptic property may be attributed to lowering of pH that makes an environment unfavourable for growth and multiplication of bacterial pathogens at infection sites. Citric acid also enhances epithelization, which is a major factor in successful wound healing. Hydration, oxygenation and removal of dead tissue ensure good epithelization. Citric acid helps to keep wound surface moist and to prevent wound desiccation, which retards wound healing. Thus, it reduces dehydration necrosis. Histological studies showed that citric acid enhances the healing process by boosting fibroblastic growth and neovascularization, which in turn increases microcirculation that enables the formation of healthy granulation tissue thereby leading to faster healing. Vascularity also helps to remove the dead tissue and makes the wound healthy (14). As a result of these actions, there is an increased migration of epithelial cells from surrounding skin, which enhances epithelization acting as a stimulus for laying of ground substances.

The interesting clinical observations of complete healing of ulcers in 73·52% cases and formation of healthy granulation tissue in 26·48% cases using citric acid as a sole antimicrobial agent show that citric acid effectively controls infection, reduces discharge and smell, and increases patient comfort.

CONCLUSION
The results of this study indicate that citric acid treatment could be reliable and effective option in the management of lepromatous ulcers; hence, one can think of using citric acid as one of the alternative therapeutic options. Especially, when healing of ulcer in leprosy patients is a matter of great concern by using conventional methods, the value of topical agent such as citric acid should not be forgotten.

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REFERENCES