Citric acid treatment of surgical site infections: a prospective open study

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Abstract

Background: Surgical site infections are one of the most common hospital-acquired infections and are an important cause of morbidity and mortality. These infections are difficult to control and, if not treated in time, increase further morbidity. In the present study, an attempt was made to develop simple and effective treatment modality by using citric acid as a sole antimicrobial agent to control surgical site infections.

Methods: A total of 70 cases of surgical site infections not responding to conventional treatment modalities were included in the present study. Pus from each case was processed for culture and susceptibility. Susceptibility of clinical isolates to citric acid was determined by broth dilution method. Three per cent citric acid ointment was applied to the wound daily once until it healed completely or showed formation of healthy granulation tissue.

Results: Culture and susceptibility results showed *P. aeruginosa* (34.37%) as the commonest isolate and amikacin (58.33%) as the most effective agent. All the isolates were found to be inhibited by citric acid (MIC – 500 to 2,500 μg/ml). Application of 3% citric acid to wounds resulted in complete healing of postoperative wounds or formation of healthy granulation tissue in 6 to 25 applications in 69 cases (98.57%). In 12 cases (17.14%) wounds were closed by suturing after formation of healthy granulation tissue.

Conclusion: Citric acid treatment was found to be safe and useful in the treatment of surgical site infections. Hence, the topical use of citric acid is recommended, especially when the treatment of surgical site infections is a matter of great concern.

Keywords: surgical site infections, citric acid treatment

Introduction

Infections of surgical wounds are one of the most common hospital-acquired infections and are an important cause of morbidity and mortality. Surgical site infections represent a substantial burden of disease for patients and health services. The delay in recovery and subsequent increased stay in hospital because of infection has economic consequences also. It has been estimated that each patient with surgical site infection will require an additional 6.5 days in hospital, which results in the doubling of hospital costs associated with that patient[1]. Wound infections following surgery have always been a problem to clinicians. In spite of standards of preoperative preparation, antibiotic prophylaxis and refinement in anaesthetic and operative techniques, postoperative wound infections continue to cause considerable morbidity, prolonged hospital stay and treatment expenditure. In recent decades, *Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, Klebsiella* spp., *Proteus* spp., *Citrobacter* spp. coagulase negative staphylococci, and so on, have emerged as the most notorious nosocomial pathogens. Their ability to survive in the hospital environment by developing resistance to antimicrobial/disinfectant agents make them the main culprit as aetiological agents in nosocomial surgical site infections. Their capabilities to colonise rapidly in a compromised host make them very difficult to deal with[2]. These infections caused by nosocomial pathogens need special attention, if uncontrolled, may become life-threatening. The important reason for this is their resistance to many currently available antibiotics.

The topical use of citric acid for the treatment of chronic wound infections caused by multiple antibiotic-resistant *P. aeruginosa*, *Escherichia coli* and other bacterial pathogens has been reported previously[3-5]. In the present study, an attempt was made to treat surgical site infections caused by nosocomial pathogens including multiple antibiotic resistant microbes by using citric acid as a sole anti-microbial agent.

Patients and methods

Study design: A prospective open study on surgical site infections was carried out during the period January 2005 to July 2010. This study was approved by the institutional ethical committee.

Patients: A total of 70 cases of surgical site infections not responding to conventional antibiotic therapy administered postoperatively for more than 15 days and local wound care with daily application of betadine for more than 15 days, were included in the present study (superficial and deep incisional wounds). These patients included were from the obstetrics and gynaecology (15), orthopaedics (15) and general surgery (40). The severity of the local infection for each patient was documented before starting treatment and the diagnosis was made on the basis of local signs of infection. These included the classical signs related to the inflammatory process[6] such as localised erythema, localised pain or tenderness, localised oedema, localised redness/heat and the presence of slough, purulent discharge from the surgical site, presence of granulation tissue and isolation of infecting bacterium from pus in significant numbers, that is, a confluent growth on primary and secondary streaking or a minimum 100 colonies.

Diagnosis of infection and measurement of antibiotic resistance: Pus from each case was processed for aerobic culture by using standard techniques[7]. Susceptibility to

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Figure 1. Postoperative infected abdominal wound – before application of citric acid ointment.

Figure 2. Postoperative infected abdominal wound – after 11 applications of citric acid ointment.

Figure 3. Postoperative infected abdominal wound – after 24 applications of citric acid ointment.

Table 1. Clinical isolates from postoperative wound infections and their antibiogram.

Sr. no.	Name of organism	No. of isolates	Antibiotic susceptibility							MIC to citric acid
			A	G	Ak	Cf	Pf	Ca	Ce	µg/ml
1.	*P. aeruginosa*	33 (34.37)	00	10 (30.30)	20 (60.60)	22 (66.66)	15 (45.45)	20 (60.60)	16 (48.48)	500–1000
2.	*Staph. aureus*	27 (28.12)	2 (7.40)	7 (25.92)	15 (55.55)	7 (25.92)	10 (37.03)	7 (25.92)	9 (33.33)	900–1000
3.	*E. coli*	16 (16.66)	00	4 (25.00)	9 (56.25)	9 (56.25)	5 (31.25)	7 (43.75)	3 (18.75)	1500–2000
4.	*Klebsiella* spp.	7 (7.29)	00	3 (42.85)	4 (57.14)	4 (57.14)	3 (42.85)	3 (42.85)	1 (14.28)	2000–2500
5.	*Staph. albus*	7 (7.29)	4 (57.14)	4 (57.14)	4 (57.14)	6 (85.71)	3 (42.85)	3 (42.85)	3 (42.85)	1200–1500
6.	*Citrobacter* spp.	4 (4.16)	00	2 (50.00)	2 (50.00)	3 (75.00)	2 (50.00)	2 (50.00)	1 (25.00)	1500–1600
7.	*Proteus mirabilis*	2 (2.08)	00	1 (50.00)	2 (100.00)	1 (50.00)	2 (100.00)	2 (100.00)	1 (50.00)	1500–1600
Total		96	6 (6.25)	31 (32.29)	56 (58.33)	52 (54.16)	40 (41.66)	44 (45.83)	34 (35.41)	

Note: Figures in parentheses indicate percentage

A – Ampicillin G – Gentamicin AK – Amikacin Cf – Ciprofloxacin
Pf – Pefloxacin Ca – Ceftazidime Ce – Ceftriaxone

antimicrobial agents was studied by Kirbey-Bauer disc diffusion method using ampicillin (10 µg), amikacin (30 µg), gentamicin (10 µg), ciprofloxacin (5 µg), ceftazidime (30 µg), ceftriaxone (30 µg) and pefloxacin (5 µg)[8]. A standardised inoculum was inoculated on the surface of Mueller-Hinton agar and discs of antimicrobial agents were placed firmly and then incubated at 37°C for 16–18 hours. Based on the zone of inhibition the isolate was reported as a resistant/susceptible.

Susceptibility to citric acid: Susceptibility of clinical isolates to citric acid was determined by broth dilution method[9]. For this, increasing amounts of citric acid were incorporated into Mueller-Hinton broth in test tubes and were then inoculated with test bacterium and incubated at 37°C for 16–18 hours. The end point was taken as minimum inhibitory concentration (MIC).

Method of application: For topical application 3% citric acid ointment was used. The citric acid ointment was prepared by mechanical mixing (trituration) of 3 gm citric acid in a mortar with 100 gm white soft paraffin (100% pure petroleum jelly – a hydrocarbon base not absorbed by the skin) by taking all sterile precautions. The wound was first debrided, irrigated and cleaned with normal saline. After cleaning, citric acid ointment was applied to the wound and dressed with a sterile pad. This treatment was used daily once until the wound healed completely or showed formation of healthy granulation tissue. The wound was observed daily for various adverse effects such as allergic reactions, itching and irritation. No antibiotics were given during this course of treatment. Deep and long incisional wounds were closed by approximation suturing after formation of healthy granulation tissue.

Results

A total of 96 aerobic bacteria were isolated from 70 patients. *P. aeruginosa* (34.37%) was found to be the commonest isolate. Most isolates were found to have multiple antibiotic resistance. Amikacin (58.33%) was the most effective agent, followed by ciprofloxacin (54.16%), ceftazidime (45.83%) and pefloxacin (41.66%). Ampicillin (6.25%) was found to be the least effective agent (Table 1).

All the isolates were found to be inhibited by citric acid. The minimum inhibitory concentration (MIC) of citric acid *in vitro* was found in the range of 500–2500 µg/ml against different clinical isolates. *P. 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 1). Application of 3% citric acid **once daily** successfully cleared the organisms from wounds in 6 to 25 applications in 6 to 25 days and wounds healed completely without any adverse effects in 69 cases (98.57%) in 6 to 25 days except for mild irritation for 2–3 minutes in 20 cases, especially those cases with superficial incisions. In 12 cases (17.14%) with wound gaping, citric acid ointment was applied till the wound showed formation of healthy granulation tissue. In these cases, the wounds were closed by suturing after formation of healthy granulation tissue (Figures 1–3). In one case of postoperative abdominal wound infected with multiple antibiotic-resistant *P. aeruginosa* and *Staph. aureus*, in spite of 13 days of continuous daily application of citric acid, no signs of healing were seen. The re-culture of pus sample from this patient yielded *Candida albicans* in significant number. Hence, an oral antifungal agent (Tablet Fluconazole 150 mg per day for seven days) with local wound care using 3% citric acid was started that resulted in healing of this wound after 10 days.

Citric acid was found effective in the control of these infections caused by notorious nosocomial pathogens including *P. aeruginosa* and *Staph. aureus* and all the 70 cases of surgical site infections were healed completely. No adverse effects were noted in any of the patients, except for mild to moderate irritation in some patients after application of the citric acid ointment to wound.

Discussion

The incidence of nosocomial infections of surgical wounds is as high as 10%. These infections complicate illness, cause anxiety, increase patient discomfort and can lead to death[10]. The multiple antibiotic resistance in microbes involved in these infections is a serious problem. To combat the situation of multiple antibiotic resistance, there is a need of alternative therapies.

The use of citric acid as a topical agent for effective elimination of *P. aeruginosa* and other nosocomial pathogens from a variety of chronic wounds has been reported previously[3-5]. Considering its antimicrobial activity against various bacteria commonly involved in various types of acute and chronic wounds, an attempt was made to study the effect of citric acid against nosocomial pathogens involved in surgical site infections and to use it in the treatment of surgical site infections caused by different bacteria. Citric acid was found effective against these pathogens in *in vitro* studies and was also found effective in the elimination of organisms from the operative site and accelerated the healing process of wounds leading to complete closure of postoperative wounds in 6 to 25 applications.

These results show that the citric acid is also active against multiple antibiotic resistant nosocomial pathogens and effectively eliminates these pathogens from surgical infection site without any adverse effects; hence it can be safely used in the treatment of surgical site infections caused by multiple antibiotic resistant nosocomial pathogens, including *P. aeruginosa* and *Staph. aureus*.

These results are encouraging and suggest the opportunity to design a study involving large number of cases of surgical site infections with relevant control groups to confirm these preliminary findings and reach more useful and concrete conclusion.

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