
Original article**Clinical study on the efficacy of orally administered crushed fresh garlic in controlling *Pseudomonas aeruginosa* infection in burn patients with varying burn degrees****Abdolazim Ghalambor¹, Mohammad Hassan Pipelzadeh²**¹*Taleghani Burn Centre, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*²*Department of Pharmacology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran***Received:** September 2008**Accepted:** February 2009

Abstract

The aim of the present study was to evaluate the effectiveness of orally administered crushed fresh garlic cloves in the control of *Pseudomonas aeruginosa* burn wound infection among patients with different burn sizes. A total of 140 burn patients, divided into three groups according to their burns sizes: >70%, <70>45% and <45>20% of total body surface area (TBSA) were serially and randomly allocated into two equal number of control and treatment subgroups and matched for age, sex, area and cause of burn. Treatment group received two crushed garlic cloves mixed with yogurt with their daily lunch meal, while control group received plain yogurt only. The time *P. aeruginosa* of development of burn wound infection was considered as end-point for study among the selected groups. The results showed that the number of patients who developed *P. aeruginosa* burn wound infection was significantly reduced among the garlic-treated group with <45% but >20% of TBSA in the first week of hospitalization. No significant differences in other groups of patients were recorded. It seems that fresh crushed garlic cloves can be used as a supplementary herbal medicinal agent in delaying of *P. aeruginosa* burn wound infection in patients with moderate burn injuries.

Keywords: *Pseudomonas aeruginosa*, Burn wound size, Fresh garlic clove, Burn wound infection

Introduction

Perhaps no other subject has attracted so much attention in the medical literature as the control of infection, especially among burn injuries. Such patients are at a high risk for infection due to the nature of the burn injury itself, the immunocompromising effects of burns, prolonged hospitalization, intensive diagnostic, and therapeutic interventional procedures [1]. On the other hand, survival of burn patients is largely

dependent upon prompt and efficient control of infection. This not only limits wound contracture but also speeds up wound healing. The best management of infections is to prevent patients from becoming infected in the first place and early wound closure with application of skin grafts [2].

Garlic is a widely distributed plant used in all parts of the world not only as a spice but also as a popular medicinal plant remedy for several diseases such as wounds,

infections and ulcer for thousands of years. A wide range of microorganisms including bacteria, fungi, protozoa and viruses have shown to be sensitive to crushed garlic preparations [3,4]. Moreover, garlic is known to reduce blood sugar, lipid and cholesterol levels, [5] and is useful in anticancer and aging prevention [6]. These unique properties of garlic may be clinically important. Because the daily intake for a prolonged period neither leads to serious side effects nor produce any usual complications with some drugs.

The Egyptians used garlic as an ancient folk medicine many centuries ago. It is only since the 19th century that researchers have prompted to test its antimicrobial and antifungal effects scientifically [7,8]. Recently, topical application of 10% (v/v) garlic extract on *P. aeruginosa* infected burns in animals showed this extract to be equally effective as 1% silver sulfadiazine in extending the survival of mice and in reducing bacterial counts in various organs in mice [9]. However, garlic, in its fresh, crushed-clove form, is a potent irritant. For example, if the crushed-clove is applied topically under pressure bandage severe dermal reaction and deep chemical burns can develop [10].

The primary cause of mortality among burn patients, mainly after the second week post burn, is believed to be a consequence of wound sepsis; the most common implicated agent is the resistant strains of Gram-negative *P. aeruginosa* [11,12]. Despite great progress in control of infection caused by the use of a variety of new products such as silvadine, sulfadiazine and a myriad sliver products, infection with this organism still holds a nearly unchanged position in the rank order of pathogens causing intensive-care unit-related infections and increasing degrees of resistance continually being reported for more than four decades and continues to represent the third most frequent organism associated with wound infection [13].

Although much has been reported on the medicinal properties of garlic [14,15] not much is known about its usefulness in treatment of burn patients with different burn surface areas. The aim of the present study was, therefore; to evaluate the effectiveness of orally administered fresh crushed garlic clove (*Allium sativum* L.) in the control of *P. aeruginosa* wound infections among hospitalized burn patients with varying percentages of TBSA.

Patients and Methods

Patients

This study was conducted at Taleghani Burn Centre affiliated to Ahvaz Jundishapur University of Medical Sciences, during the periods between January and June 2007. 140 newly admitted burn cases (46 males, 94 females), having the set criteria of inclusion, with second or third degree burns with more than 20% TBSA, were the subjects of this study. Second degree wound is characterized by blister formation and the damage extending through the epidermis to the underlying dermal layer, while third degree burns go deeper and affect the underlying tissues, with a charred appearance due to blood clots in the blood vessels [1]. Patients had no wound infection at the time of admission, and had referred to the hospital within six hours of burn accident, were included in this study. None of the subjects received prophylactic antibiotics before confirmed cultured specimen and antimicrobial sensitivity assessment.

Since susceptibility to infection is related to extent TBSA, the patients were serially and randomly divided into three main categories in relation to the burn percentage of TBSA: group A, with burn of more than 70%; group B, with less than 70% but more than 45% and group C, with less than 45% but more than 20% TBSA. The number of patients in groups A, B and C were 40, 40 and 60 respectively. Each group was further sub-grouped randomly into equal numbers of patients (matched for age, sex and cause of burn), into treatment and

control groups. Each patient in the treatment group was hospitalized in the same room as their corresponding control with almost the same burn coverage and area of body infected. The morbidity and mortality and the timing of development of *P. aeruginosa* infections were assessed.

Sampling procedure

The first 1g wound biopsy, removed with a wound puncture remover, was collected from all patients immediately after admission, and then continued every three days during the whole period of the study. The grown colonies from samples were cultured for aerobic bacteria on blood agar and Eosin Methylene Blue (EMB) agar (Highmedia, India) plates [16]. Identification and counting of bacteria were performed according to the standard bacteriologic methods. The cultured samples were stained with Gram's stain and were microscopically examined for the presence of *P. aeruginosa* [16].

In order to limit the influence of suspected confounding factors, trained health care personnel constantly provided the medical care to both treatment and control patients in the allocated category. The end-point for this study was taken as the day of development of infection with *P. aeruginosa* with microorganism count above $10^5/g$ [12].

Treatment protocol

Immediately after the admission and during the follow up, medical care was provided with the aim of prevention of burn complications as well the control of infection routinely instituted at our centre on all burn cases. These controls included the ensuring of the airway patency, pain relief, estimation of extent of depth and burn percentage TBSA, estimation of fluid requirements and wound dressing which were administrated similarly in both control and subjects who received garlic cloves. All subgroups of patients involved in the garlic treatment received, in addition to the

standard medical care provided in our centre for burn wounds, two fresh crushed-cloves of garlic (*Allium sativum* L.). The garlic was purchased from the commercial market of Ahvaz city, and were mixed with yogurt at lunch. While the corresponding control subgroups received yogurt that contained no garlic.

Ethical considerations

This study was with the approval of the ethics research committee of Ahvaz Jundishapur University of Medical Sciences. The patients signed a written consent and acknowledged their rights to withdraw from the study whenever they wished. This was an essential part of the study.

Statistical analysis

The data were statistically analyzed using Chi-squared test, with $P < 0.5$ as the level of significance.

Results

While all the 40 patients in the group with $>70\%$ TBSA burn were females (primarily due to an attempted suicide), there were 34 females (17 patients in each of control and treatment groups) out of a total of 40 patients, who were in the group with a burn covering between 70-45% caused by accidental burns primarily due to flame and boiled water, and there were an equal number of males and females in the group with $<45>20\%$ burns primarily due to accidental events.

The time and the number of patients who developed burn wound infection among the studied groups varied. All the 19 survived patients both subgroups of the burn patient with $>70\%$ TBSA and 18 (90%) of the burn wound in both subgroups of patients with $<70>45\%$ TBSA were infected within the first week of hospitalization ($P < 0.05$ relative to group $<45>25\%$ group). While, burn wound infection among the subgroups of patients with $<45>20\%$ TBSA was significantly different. 70% of patients in the control subgroup and 15% in the

garlic treated group were infected within the first week of hospitalization ($P<0.01$). However infection of burn wounds in the garlic-treated subgroup with $<45\%$ TBSA did develop on days 11 and 13 of hospitalization in seven and eight patients

respectively ($P<0.01$) (Table 1). In general significantly a fewer number of patients in the garlic-treated subgroup with $<45\%$ TBSA did developed burn wound infection (70 versus 60%, $P<0.022$) (Table 1).

Table 1: The comparison of the number of patients with different percentages of TBSA among standard treatment (control group) and those additionally given two fresh garlic cloves daily mixed with yogurt (treatment group) on development of *P. aeruginosa* burn wound infection

Day	Groups of patients with burn covering					
	>70 % of TBSA (n=40)		<70>45% of TBSA (n=40)		<45>20 % of TBSA (n=60)	
	Control (n=20)	Treatment (n=20)	Control (n=20)	Treatment (n=20)	Control (n=30)	Treatment (n=30)
1	0	0	0	0	0	0
4	17	17	7	5	12	1 ⁺
7	2	2	11	13	9	2 ⁺
10	-	-	-	-	0	7 ⁺⁺
13	-	-	-	-	0	8 ⁺⁺
Total (%)	19 (90)	19 (90)	18 (90)	18 (90)	21 * (70)	18 * (60 [#])

* $P<0.05$ relative to $>70\%$ and <70 and $>45\%$ groups. ⁺ $P<0.05$ and ⁺⁺ $P<0.01$ between the <45 and $>20\%$ TBSA subgroups. [#] $P<0.05$ between the garlic treated and control subgroup with $<45\%$ TBSA coverage. Chi squared test

Discussion

In recent years, multiple drug-resistant (MDR) *P. aeruginosa* have been identified from different centers [11]. The inappropriate long-term use of antibiotic, both for prophylactic and treatment purposes and difficulty in isolation of the patients increased the development of resistance and spreading the growth of *P. aeruginosa* strains. National Nosocomial Infection Surveillance System reported a growth of resistance of this microorganism to commonly used antibiotics such as imipenem, ciprofloxacin and ceftazidime by 15, 19 and 20% between the periods of 1998-2003 [11]. This report justified the serious concern for implementation of strategies for control of infection in hospital environment especially in acute care units such as ICU and more specifically in burn units throughout the world [12, 17]. On the other hand, antibiotic resistance in *P. aeruginosa* does not only predict a poor clinical outcome but also increases the

hospitalization period with the consequence of a significant economic burden for the health system [18]. Therefore, any measures that can lead to the control of wound infection will be a welcomed measure.

In this study, we attempted to evaluate the effectiveness of fresh garlic, as a prophylactic agent in control of *P. aeruginosa* infection, in patients with different percentages of TBSA burns. We showed that two crushed-cloves given orally daily produces some efficacy in patients with burns between 45 and 20% of TBSA, and had no similar effect on burns with $>45\%$ of TBSA.

The dose employed for garlic was selected arbitrarily and based on the normal consumed quantity by some people in this area, and which was traditionally recommended for various ailments. However, would we have administered larger doses of this old medicinal plant, its usefulness in other patient groups would have been evaluated more thoroughly.

Furthermore, other parameters such as the metabolic, cardiovascular and immune status of burn patients on garlic treatment were not compared with their control patient subgroups. These aspects need to be studied further in separate studies.

It has been suggested that the mechanism by which garlic extract produces its anti-microbial actions to be mediated via changes the lipid profile of the cell membrane [19]. Furthermore, a very interesting aspect of the antibacterial activity of allicin is the apparent inability of most bacteria to develop resistance to it, because the mode action is completely different from that of other antibiotic substances [20]. It has been proposed that the development of resistance to β -lactam antibiotics is 1000-fold easier than development of resistance to allicin [20]. However, if a medicinal plant-based or a synthetic prescription drug formulation is to be employed in treatment of a given disease, then a vigorous scientifically based evidence on their safety and efficacy needs to be provide.

Despite the employment of various techniques in the control of infection as well as the current use of broad-spectrum antibiotics and aggressive diagnostic and therapeutic techniques, *P. aeruginosa* wound infection occurs in 10-50% of patients with burns, and with a mortality rate of 80% [21]. In other studies *P. aeruginosa* was reported to be the causative agent in 65-71% of the sepsis [11, 22]. In our study, the rate of *P. aeruginosa* wound infection was found to be related to the burn wound surface area. These findings were anticipated, since the rate of mortality and morbidity are directly related to the size of burn wound [1].

In this pilot clinical trial, we have shown that two crushed garlic cloves, mixed with yogurt at lunchtime, is partially an effective medicinal plant in delaying burn wound infection with *P. aeruginosa* and in reducing the need for antibiotics in some burn patients. These findings contradict those reported by Ankri and Mirelman [3] who suggest that multiple drug resistant strains of

P. aeruginosa are resistant to allicin. There are possibly three reasons for these discrepancies. Firstly, they tested allicin, the active constituent of garlic in an *in vitro* condition on the isolated microorganism, while we employed fresh crushed garlic cloves in uninfected burn patients. Secondly, the strain tested in their study was MDR mucoid type, while in our study, the pathogenic strains *P. aeruginosa* were mostly non-MDR type since they responded to third generation cephalosporins and imipenm. In our study, only 2% of the isolated cultures were MDR which were treated with a combination of two antibiotics regimen such as gentamycin plus ceftazodime/imipenem or amikacin plus ceftazidime/imipenem. Furthermore, the purpose of our study was to evaluate the efficacy of garlic in prevention of burn infection in the first place, rather than to test its efficacy as an antimicrobial agent.

What is the relevance of these findings to clinical practice? Since the development of infection, especially with multiple drug-resistant *P. aeruginosa* strains, has serious consequences on the course of the burn wound healing and the treatment outcomes, employment of various prophylactic strategies seems to be a more logical approach in the prevention of the development of burn wound infections. Taking all possible confounding factors for the development of burn infection into consideration, garlic was found to be partially useful in delaying the development of infection in a selected number of burn patients with <45>20% of TBSA. It seems that this ancient folk medicine may have a role to play in the treatment of one of the common underlying causes of morbidity and mortality in the 21st century.

This study was merely a small inroad towards prevention of one of the most difficult conditions that has haunted humankind over the centuries. Although the exact role of garlic in the control of infection in burn patients with high percentage of TBSA remains to be seen, this study,

demonstrated that the administration of two garlic cloves daily delayed the development of *P. aeruginosa* wound infection, and hence reduced the need for antibiotic administration. Prudently, further studies to evaluate the efficacy of this method in reducing the mortality rate on a larger number of patients is warranted.

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References

- 1) Sharma BR. Infection in patients with severe burns: Causes and prevention thereof. *Infectious Diseases Clinics of North America* 2007; 21: 745-759.
- 2) Ong YS, Samuel M, Song C. Meta-analysis of early excision of burns. *Burns* 2006; 32: 145-150.
- 3) Ankri S, Mirelman D. Antimicrobial properties of allicin from garlic. *Microbes and Infection* 1999; 2: 125-129.
- 4) Arora DS, Kaur J. Antimicrobial activity of spices. *International Journal of Antimicrobial Agents* 1999; 12: 257-262.
- 5) Augusti KT, Mathew PT. Lipid lowering effect of allicin (diallyl disulfide oxide) on long-term feeding in normal rats. *Experientia* 1974; 30: 468-470.
- 6) Milner JA. Garlic: its anticarcinogenic and antitumor properties. *Nutrition Review* 1996; 54: S83-S86.
- 7) Ali M, Thomson M, Afzal M. Garlic and onions: their effect on eicosanoid metabolism and its clinical relevance. *Prostaglandins, Leukotrienes and Essential Fatty Acids* 2000; 62: 55-73.
- 8) McNamara DB, Agrawal KC, Kadowitz PJ. The pharmacological effects of allicin. International Garlic Symposium: Pharmacy, pharmacology and Clinical Application of *Allium sativum*. *Cardiology in Practice* 1991; Supplement 6.
- 9) Erzanlou M, Arab R, Alaei R. Investigation on efficacy of garlic extract (*Allium sativa*) against burn wound infection by *Pseudomonas aeruginosa* in burned animal model. *International Journal of Antimicrobial Agents* 2007; 29: S505-S506.
- 10) Friedman T, Shalom A, Westreich M. Self-inflicted garlic burns: our experience and literature review. *International Journal of Dermatology* 2006; 45: 1161-1163.
- 11) National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *American Journal of Infection Control* 2004; 32: 470-485.
- 12) Gang RK, Bang RL, Sanyal SC, Mokaddas E, Lari AR. *Pseudomonas aeruginosa* septicemia in burns. *Burns* 1999; 25: 611-616.
- 13) Andrade SS, Jones RN, Gales AC, Sader HS. Increasing prevalence of antimicrobial resistance among *Pseudomonas aeruginosa* isolates in Latin American medical centres: 5 year report of the SENTRY Antimicrobial Surveillance Program (1997-2001). *Journal of Antimicrobial Chemotherapy* 2003; 52: 140-141.
- 14) Trautmann M, Lepper P M, Haller M, Ulm S, Germany K. Ecology of *Pseudomonas aeruginosa* in the intensive care unit and the evolving role of water outlets as a reservoir of the organism. *American Journal of Infection Control* 2005; 33: S41-S49.
- 15) Broekaert WF, Van Parijs J, Leyns F, Joos H, Peumans WJ. A chitinbinding lectin from stinging nettle rhizomes with antifungal properties. *Science* 1989; 245: 1100-1102.
- 16) Finegold SM, Martin WJ. Diagnostic microbiology. Chapter 22. 6ed. Toronoto, The CV Mosby Co, St Louis, 1982: 249-263.
- 17) Eyal AS, Kemp M, Luvhengo T. A 10-year audit of burns at Kalafong hospital. *Burns* 2007; 33: 393-395.
- 18) Modjarrad K, McGwin G Jr, Cross JM, Rue LW 3rd. The descriptive epidemiology of intentional burns in the United States: an analysis of the National Burn Repository. *Burns* 2007; 33: 828- 832.
- 19) Cammue BPA, Thevissen K, Hendriks M, et al. A potent antimicrobial protein from onion seeds showing sequence homology to plant lipid transfer proteins. *Plant Physiology* 1995; 109: 445-455.
- 20) Ghannoum MA. Studies on the anticandidal mode of action of *Allium sativum* (Garlic).

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- Journal of General Microbiology* 1988; 134: 2917-2924.
- 21) Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. *Clinical Infectious Disease* 2004; 39: 309-317.
- 22) Carmeli Y, Troillet N, Karchmer AW, Samore MH. Health and economic outcomes of antibiotic resistance in *Pseudomonas aeruginosa*. *Archives of Internal Medicine* 1999; 159: 1127-1132.
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