

The Effect of Chlorhexidine Gluconate on Microbial Growth in Patients Undergoing Debridement for Diabetic Foot: A Randomized Controlled Study

Diyabetik Ayak Nedeniyle Debridman Uygulanan Hastalarda Klorheksidin Solüsyonunun Mikroorganizma Üremesi Üzerine Etkisi: Randomize Kontrollü Çalışma

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ABSTRACT Objective: The aim of this study was to determine the effect of chlorhexidine gluconate on microbial growth in patients undergoing debridement for diabetic foot. **Material and Methods:** The study had a randomized, controlled experimental design. The study sample included a total of 60 patients. Of 60 patients, 30 were randomly assigned into the experimental group and 30 were randomly assigned into the control group. In the experimental group, the surgical site was washed with chlorhexidine gluconate 0.05% before and after debridement in addition to routine cleaning with povidone iodine before debridement. In the control group, all the steps of the procedure performed in the experimental group were followed except for using chlorhexidine gluconate 0.05%. **Results:** The experimental and control groups were found to be similar in terms of descriptive characteristics and diabetes-related features. There was no difference in the presence of microorganisms before debridement between the experimental and control groups, but fewer species were isolated from the experimental group after debridement. The mean number of isolated species in the experimental group was 1.66±0.60 and 0.60±0.67 before and after debridement respectively. The mean number of isolated species in the control group was 1.06±0.58 and 1.10±0.75 before and after debridement respectively. **Conclusion:** It can be concluded that chlorhexidine gluconate and povidone iodine used before debridement are effective in reduction of the number of microbial species after debridement in patients with diabetic foot.

Keywords: Diabetic foot; preoperative skin preparation; infection; microorganism; nursing

ÖZET Amaç: Araştırma, diyabetik ayak nedeniyle debridman uygulanan hastalarda klorheksidin solüsyonunun mikroorganizma üremesi üzerine etkisini belirlemek amacıyla yapılmış randomize kontrollü deneysel bir çalışmadır. **Gereç ve Yöntemler:** Çalışma müdahale grubunda 30, kontrol grubunda 30 olmak üzere toplam 60 hasta ile tamamlanmıştır. Müdahale grubundaki hastalara debridman öncesi rutin uygulanan povidon iyotlu cerrahi bölge temizliğine ek olarak %0,05'lik klorheksidin solüsyonuyla yıkama yapılmış, debridman sonrası tekrar klorheksidinle temizleme yapılarak pansuman kapatılmıştır. Kontrol grubunda deney grubundan farklı olarak %0,05'lik klorheksidin glukonatlı solüsyon kullanılmamış, diğer işlemler deney grubunda olduğu gibi uygulanmıştır. **Bulgular:** Müdahale ve kontrol grubundaki hastaların tanıtıcı özellikleri ve diyabete ilişkin özellikleri bakımından benzer olduğu görülmüştür. Müdahale ve kontrol grubunda debridman öncesi mikroorganizma varlığı açısından fark bulunmazken, debridman sonrası müdahale grubunda daha az sayıda mikroorganizma ürettiği tespit edilmiştir. Müdahale grubunda debridman öncesi ve sonrası bakteri üreme ortalaması sırasıyla 1,66±0,60 ve 0,60±0,67 olarak saptanmıştır. Kontrol grubunda debridman öncesi ve sonrası bakteri üreme ortalaması ise sırasıyla 1,06±0,58 ve 1,10±0,75 olarak tespit edilmiştir. **Sonuç:** Araştırma bulgularımıza dayanarak, diyabetik ayağı olan bireylerde debridman öncesi uygulanan klorheksidin solüsyonunun debridman sonrası mikroorganizma sayısını azaltmada etkili olduğu söylenebilir.

Anahtar Kelimeler: Diyabetik ayak; preoperatif cilt hazırlığı; enfeksiyon; mikroorganizma; hemşirelik

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With a recent rise in diabetes cases, diabetes-related complications have increased. One of these complications is diabetic foot. It is a condition frequently encountered, slowly progressing, leading to losses of workforce and organs, treated at high costs and severely disrupting the quality of life.^{1,2} It is also considered an important health problem due to resultant amputations and a high mortality.^{1,3}

Up to one-third of the half billion people with diabetes worldwide will develop a diabetic foot ulcer over the course of their lifetime.³ The lifetime risk of developing a diabetic foot ulcer is between 19% and 34%. Recurrence is common after initial healing; approximately 40% of patients have a recurrence within 1 year after ulcer healing, almost 60% within 3 years, and 65% within 5 years. Infection develops in 50%-60% of ulcers and is the principal pathology that damages diabetic feet.¹ Approximately 20% of infected ulcers lead to an amputation. In patients with diabetes, the risk of death is twice as high in patients with foot ulcers compared with those without.^{1,4} Around 10% of patients die within 30 days of a major amputation, and more than 70% of the patients with diabetes-related amputations will die within 5 years.⁴

Surgical debridement has been included in many guides and algorithms about the care for diabetic foot ulcers. It is considered as part of not only care standards but also effective cure.⁵ Using debridement to control infection is recommended based on Level II evidence in the guides for the treatment of diabetic ulcers prepared by the Wound Healing Society.⁶ However, evidence about the role of surgical debridement in improvement of healing is insufficient although the debridement seems to be a reasonable method to remove infected tissues and reveal healthier ones.⁵

While surgical site infections are multifactorial, it is known that a preoperative skin preparation is effective in reduction of postoperative wound infections. Many different solutions including alcohol, chloroxylenol, chlorhexidine and iodophors have been used for preoperative skin preparation.⁷ Chlorhexidine is an antiseptic agent accepted worldwide in that it has a fast bactericidal effect, prevents bacterial and fungal activity even in very low con-

centrations and has a very low toxicity.⁸ Since chlorhexidine is not a chemical that can dissolve in water on its own, chlorhexidine gluconate is preferred.⁹ Chlorhexidine gluconate is the preferred agent for both hand and surgical/invasive procedure site antiseptics.¹⁰⁻¹⁴ Chlorhexidine has been widely used for hand hygiene to prevent transmission of nosocomial pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA).¹⁴ It has been reported that using chlorhexidine is more effective in prevention of infections than using other antiseptic solutions.¹⁰⁻¹⁴ However, concentrations of the products used in the studies are different and high quality evidence has not been obtained. Despite many studies conducted so far, there is not an agreement on the cleaning technique and solution and its concentration that should be used.⁷ In the literature, no study was found in which chlorhexidine was used in diabetic foot.

Diabetic foot ulceration is a major health problem and its management involves a multidisciplinary approach.¹⁵ Healthcare providers have a responsibility for prevention of infections in patients by taking necessary precautions. It is very important to keep infections under control by utilizing appropriate interventions in patients with diabetic foot since it decreases infection-related mortality, hospitalizations, length of hospital stay, hospital costs and rates of extremity amputations.¹⁶ In the present study, we hypothesized that using chlorhexidine gluconate 0.05% before debridement is effective in reduction of microbial growth after debridement in patients with diabetic foot.

MATERIAL AND METHODS

The study was carried out in the orthopedics and traumatology inpatient clinic and the operation room of a university hospital. Sixty patients with a Stage 3 lesion were included in the study by obtaining statistical consultancy during sample selection. Out of 60 patients, 30 were randomly assigned into the study group and 30 into the control group. In the power analysis conducted after the study, statistical power and effect size of the study were found to be 0.90 and 0.83 respectively ($p=0.05$, $d=0.83$).

As part of routine practice in the clinic where the present study was carried out, patients with diabetic wound have debridement or amputation depending on the depth and width of the wound, the presence of an infection and vascular structures. Patients scheduled to have debridement undergo local, general or spinal anesthesia. During debridement, first, the wound site is washed with sodium chloride and then disinfected with povidone iodine 10%. Afterwards, debridement is performed by an orthopedic surgeon. After debridement, specimens are obtained from deep tissues and sent to the laboratory. Finally, the wound site debrided is washed with sodium chloride, cleaned with povidone iodine and closed with a dressing.

INCLUSION CRITERIA

The study included patients who could speak and understand Turkish, had a Stage 3 lesion according to Meggitt-Wagner classification (abscess formation in the soft tissue in addition to deep ulcer in the foot), volunteered to participate in the study, signed the informed consent form, and did not have a hearing problem or an allergy/sensitivity to antiseptic solutions.¹⁷ A simple computer-based randomization list was prepared before initiation of the study. The patients fulfilling the inclusion criteria were assigned into experimental and control groups according to this list.

DATA COLLECTION TOOLS

Data was collected between April-September 2017 using the descriptive characteristics form and an infection assessment form.

DESCRIPTIVE CHARACTERISTICS FORM

The descriptive characteristics form was created by the researchers and composed of 16 questions about sociodemographic and diabetes-related features of the patients. The longest length and the longest width of the ulcer debrided were measured by using a millimeter paper and obtained length and width were multiplied to determine the size of the ulcer, which was recorded in cm² in the form.

INFECTION ASSESSMENT FORM

The infection assessment form includes the bacteria isolated before and after debridement. Bacteria isolated from the surgical site before and after debride-

ment were recorded in the infection assessment form created by the researchers.

DATA COLLECTION

Specimens were collected from soft tissue through curettage. First, the patients underwent local, general or spinal anesthesia before debridement. Next, the surgical site was cleaned and ulcerated tissue was removed from the region which would be debrided. Then the soft tissue specimen was obtained from the ulcerated layer between the living tissue and the infected area through curettage. After that, the specimen was inoculated in blood eosin methylene blue media and incubated at 35 °C under aerobic conditions for 24 hours. Since analyses were made on tissue specimens, quantification could not be performed and microbial colonies could not be determined. Instead, only the presence or absence of growth of microbial species was identified.

A simple computer-based randomization list was prepared before initiation of the study. The patients fulfilling the inclusion criteria were assigned into experimental and control groups according to this list.

In the experimental group, first, the researcher cleaned the wound site with 10 cc chlorhexidine gluconate 0.05% for 2 minutes and then waited for 3 minutes until chlorhexidine gluconate 0.05% could exert its effect. Second, the researcher washed the wound site with 10-20 cc sodium chloride. Third, the patient was sedated by the anesthetist. Fourth, the surgical site was disinfected with povidone iodine 10% and debridement was performed by an orthopedic surgeon. Fifth, tissue specimens were obtained from the ulcer layer through curettage and sent to the laboratory by the researcher. Sixth, the debrided area was washed with 5-10 cc chlorhexidine gluconate 0.05% and then cleaned with 10 cc sodium chloride. Finally, povidone iodine was used and a dressing was put on the wound. Then the patient was sent to the ward. The dressing was removed 24 hours after debridement by the researcher and the debrided area was washed with 10-20 cc sodium chloride. After that, soft tissue specimens were obtained from the area between the living tissue and infected tissue through curettage. Obtained specimens were put in tubes without a fixative and sent to the laboratory.

In the control group, all the steps of the procedure performed in the experimental group were followed except for using chlorhexidine gluconate 0.05%.

DATA ANALYSIS

Obtained data was analyzed with chi-square test and dependent and independent t-tests by using the SPSS Version 24.0 (IBM, Armonk, NY). $p < 0.05$ was considered statistically significant.

ETHICAL CONSIDERATIONS

The research was conducted in accordance with the principles of the Declaration of Helsinki. Before initiation of the study, ethical approval was obtained from the ethical committee of Erciyes University Clinical Research Ethic Committee (date: April 18, 2014; no: 2014/256) and written permission was taken from the hospital where the study was conducted. The participants were informed about the

study, assured that their names would be kept confidential and their written informed consent was obtained.

RESULTS

The mean age of the patients in the experimental and control groups was 65.76 ± 9.70 and 65.96 ± 10.13 years respectively and 66.7% of all the patients were aged 51-70 years. Descriptive characteristics of the patients did not differ between the groups ($p > 0.05$) (Table 1).

All the patients in the experimental and control groups had Type II diabetes and duration of diabetes was longer than 20 years in 53.3% of the experimental group and 43.3% of the control group. Duration of insulin therapy was 20 years and longer in 23.1% of the experimental group and 30.8% of the control group. The groups were similar in terms of the duration of diabetes and insulin therapy ($p > 0.05$) (Table 2).

TABLE 1: The distribution of descriptive characteristics of groups.

| Descriptive characteristics | Experimental group n=30 | | Control group n=30 | | p value |
|-------------------------------|-------------------------|------|--------------------|------|---------|
| | Number | % | Number | % | |
| Gender | | | | | |
| Female | 10 | 33.3 | 7 | 23.3 | 0.390 |
| Male | 20 | 66.7 | 23 | 76.7 | |
| Age (year) (X±SD) | 65.76±9.70 | | 65.96±10.13 | | |
| Age groups (yrs) | | | | | |
| 51-70 | 20 | 66.7 | 20 | 66.7 | 1.00 |
| 71 and above | 10 | 33.3 | 10 | 33.3 | |
| Smoking status | | | | | |
| Current | 4 | 13.3 | 3 | 10.0 | 0.730 |
| Former | 12 | 40.0 | 15 | 50.0 | |
| Never | 14 | 46.7 | 12 | 40.0 | |
| Yr of smoking | | | | | |
| < 20 yr | 3 | 10 | 4 | 13.3 | 0.571 |
| >20 yr | 13 | 43.3 | 14 | 46.6 | |
| Average smoking level | | | | | |
| <20 cigarettes/day | 11 | 36.6 | 13 | 43.3 | 0.560 |
| 20->20 cigarettes/day | 5 | 16.6 | 5 | 16.6 | |
| Alcohol drinking status | | | | | |
| Current | 2 | 6.6 | 0 | 0.0 | 0.353 |
| Former | 4 | 13.3 | 4 | 13.3 | |
| Never | 24 | 80.0 | 26 | 86.7 | |
| Accompanying chronic diseases | | | | | |
| Yes | 22 | 73.3 | 24 | 80.0 | 0.542 |
| No | 8 | 26.7 | 6 | 20.0 | |

SD: Standard deviation.

The most frequent etiological cause of diabetic foot in both the experimental and control groups was trauma (66.7% of both groups). The groups were found to be similar with respect to features of diabetic foot (Table 3).

Microbial growth was present in 86.7% of the experimental group and 80.0% of the control group before debridement ($p>0.05$) and 46.7% of the experimental group and 83.3% of the control group after debridement ($p<0.05$). The most frequent mi-

TABLE 2: Distribution of groups according to diabetes-related characteristics.

| Diabetes-related characteristics | Experimental group n=30 | | Control group n=30 | | p value |
|----------------------------------|-------------------------|-------|--------------------|------|---------|
| | Number | % | Number | % | |
| Duration of illness | | | | | |
| 1-5 years | 0 | 0.0 | 1 | 3.3 | 0.247 |
| 6-10 years | 7 | 23.3 | 2 | 6.7 | |
| 11-20 years | 10 | 33.3 | 11 | 36.7 | |
| >20 years | 13 | 43.3 | 16 | 53.3 | |
| Insulin treatment | | | | | |
| Yes | 26 | 86.7 | 26 | 86.7 | 1.00 |
| No | 4 | 13.3 | 4 | 13.3 | |
| Duration of insulin treatment | | | | | |
| 1-5 years | 4 | 15.4 | 3 | 11.5 | 0.690 |
| 6-10 years | 3 | 11.5 | 1 | 3.8 | |
| 11-20 years | 13 | 5.0 | 14 | 30.8 | |
| >20 years | 6 | 23.1 | 8 | 26.6 | |
| Type of diabetes therapy | | | | | |
| Insulin | 26 | 100.0 | 24 | 92.3 | 0.149 |
| Oral antidiabetic drug | 0 | 0.0 | 2 | 7.7 | |

TABLE 3: Distribution of groups according to diabetes foot characteristics.

| Diabetes foot characteristics | Experimental group n=30 | | Control group n=30 | | p value |
|-------------------------------|-------------------------|------|--------------------|-------|---------|
| | Number | % | Number | % | |
| History of diabetic foot | | | | | |
| Yes | 23 | 76.7 | 28 | 93.3 | 0.145 |
| No | 7 | 23.3 | 2 | 6.7 | |
| Etiology of diabetic foot | | | | | |
| Neuropathy | 2 | 6.7 | 2 | 6.7 | 0.567 |
| Trauma | 20 | 66.7 | 20 | 66.7 | |
| High planter pressure | 3 | 10.0 | 1 | 3.3 | |
| Deformity | 1 | 3.3 | 4 | 13.3 | |
| Peripheral artery disease | 4 | 13.3 | 3 | 10.0 | |
| Wound size | | | | | |
| 2-4 cm | 6 | 20.0 | 4 | 13.3 | 0.710 |
| 4-6 cm | 18 | 60.0 | 18 | 60.0 | |
| >6 cm | 6 | 20.0 | 8 | 26.7 | |
| Use of antibiotics | | | | | |
| Yes | 23 | 76.6 | 27 | 90 | 0.299 |
| No | 7 | 23.3 | 3 | 10 | |
| Dose of antibiotic | | | | | |
| 2 pieces per day | 22 | 95.7 | 27 | 100.0 | 0.460 |
| >2 pieces per day | 1 | 4.3 | 0 | 0.0 | |
| Duration of using antibiotics | | | | | |
| 7-10 days | 11 | 47.8 | 13 | 48.1 | 0.982 |
| >10 days | 12 | 52.2 | 14 | 51.9 | |

TABLE 4: Distribution of groups according to pathogen microorganism development status.

| | Experimental group n=30 | | Control group n=30 | | p value |
|---|-------------------------|------|--------------------|------|--------------|
| | Number | % | Number | % | |
| Pathogen microorganism before the debridement | | | | | |
| Yes | 26 | 86.7 | 24 | 80.0 | 0.731 |
| No | 4 | 13.3 | 6 | 20.0 | |
| Pathogen microorganism after the debridement | | | | | |
| Yes | 14 | 46.7 | 25 | 83.3 | 0.003 |
| No | 16 | 53.3 | 5 | 16.7 | |

croorganism detected was *Escherichia coli* (n=13), followed by *Pseudomonas aeruginosa* (n=11), *Klebsiella pneumoniae* (n=9), *Enterococcus* (n=10), Coagulase Negative *Staphylococcus* (n=8), *Morganella* (n=3) and *Staphylococcus epidermidis* (n=1) (Table 4).

The mean number of species per patient before debridement was 1.16 ± 0.64 in the experimental group and 1.00 ± 0.64 in the control group without a significant difference ($p > 0.05$). The mean number of species per patient after debridement was 0.60 ± 0.67 in the experimental group and 1.20 ± 0.76 in the control group with a significant difference ($p < 0.05$) (Table 5).

The mean number of species per patient in the experimental group was 1.16 ± 0.64 before debridement and 0.60 ± 0.67 after debridement with a significant difference ($p < 0.05$). The mean number of species per patient in the control group was 1.00 ± 0.64 before debridement and 1.20 ± 0.76 after debridement without a significant difference ($p > 0.05$) (Table 5).

DISCUSSION

It is stated in the literature that the most frequently detected bacterium in diabetic foot infections is *S. aureus*.^{18,19} The most frequent bacterium isolated in the present study was *E. coli*. Microorganisms generally isolated in diabetic foot infections are *S. aureus*, Streptococci, Gram-negative bacteria and Anaerobes.^{19,20} Şerefhanoglu et al. reported that the most frequently isolated microorganisms were *E. coli*, *P. aeruginosa* and *Klebsiella*, which is consistent with the results of the present study.²⁰ In study by Shankar

TABLE 5: Distribution of groups according to mean of pathogen microorganism.

| | Pathogen microorganism before the debridement | Pathogen microorganism after the debridement | p value |
|-------------------------|---|--|--------------|
| | X±SD | X±SD | |
| Experimental group n=30 | 1.16 ± 0.64 | 0.60 ± 0.67 | 0.000 |
| Control group n=30 | 1.00 ± 0.64 | 1.20 ± 0.76 | 0.136 |
| p value | 0.321 | 0.002 | |

SD: Standard deviation.

et al. the most frequent Gram-negative microorganism was *P. aeruginosa*.²¹ In the present study, the other frequently isolated microorganisms were *Enterococcus*, Coagulase Negative *Staphylococcus*, *Morganella* and *S. epidermidis*.

Several studies have shown that using chlorhexidine 4% is more effective to achieve surgical site antisepsis than other antiseptic agents.^{10,11,14,22} In the current study, chlorhexidine gluconate was utilized in the experimental group and significantly fewer species were isolated in this group compared to the control group. Wang et al. found that chlorhexidine gluconate 4% was effective in different gene types of MRSA.¹⁴ Kaleli and Demir compared chlorhexidine gluconate 4% and povidone iodine in terms of their effects on various bacteria and found that chlorhexidine gluconate was effective in all bacteria.¹³ Darouiche et al. reported that using chlorhexidine with alcohol for cleaning the surgical site skin was more effective in prevention of surgical site infections as compared with using povidone iodine.¹¹ Chaiyakunapruk et al. also showed that chlorhexidine gluconate was more effective in prevention of

catheter-related blood circulation infections than povidone iodine.¹⁰ Goztok et al. observed that utilizing chlorhexidine gluconate 0.05% in closure of ileostomy shortened duration of recovery.²³ Çobanoğlu and Şendir evaluated the effect of chlorhexidine gluconate on healing of episiotomy and noted that chlorhexidine gluconate was an effective care product and could be used to support wound healing.²⁴

Although there have been many studies proving the effectiveness of chlorhexidine, some studies have shown that povidone iodine is more effective than chlorhexidine.²⁵⁻²⁷ McLure and Gordon examined effects of povidone iodine and chlorhexidine on 33 strains of MRSA and found that while chlorhexidine was effective in 3 strains of MRSA, povidone iodine was effective in 33 strains.²⁵ Michel and Zäch investigated effects of a few antiseptics on MRSA, *P. aeruginosa* and *E. coli* in pressure ulcers secondary to spinal injuries and reported that povidone iodine 10% was more effective than chlorhexidine 0.05%.²⁶ However, in a study by Türkyılmaz, no significant difference was found in effectiveness between chlorhexidine gluconate 4% and povidone iodine 10% used in skin preparation before cesarean-section.²⁷

LIMITATIONS

The study has 2 limitations. First, since most of the patient files did not have data about hemoglobin A1c, this criterion could not be taken into consideration in patient selection. Second, it was difficult to access the study sample. Since the patients underwent debridement repeatedly, several subjects could not be included in the study.

CONCLUSION

In conclusion, the number of species isolated before debridement was not different between the experimental and control groups, but significantly fewer species were isolated in the experimental group after debridement. Besides, the mean number of microorganisms isolated before debridement was similar in the experimental and control groups. However, it was significantly lower in the experimental group after the procedure. In light of these findings, it can be recommended that chlorhexidine gluconate and povidone iodine should be used together in surgical site cleaning before debridement of diabetic foot.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Dilek Talhaoğlu; **Design:** Dilek Talhaoğlu, Gülsüm Nihal Çürük; **Control/Supervision:** Dilek Talhaoğlu, Gülsüm Nihal Çürük; **Data Collection and/or Processing:** Dilek Talhaoğlu; **Analysis and/or Interpretation:** Dilek Talhaoğlu, Gülsüm Nihal Çürük; **Literature Review:** Dilek Talhaoğlu; **Writing the Article:** Dilek Talhaoğlu; **Critical Review:** Gülsüm Nihal Çürük; **References and Fundings:** Dilek Talhaoğlu.

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