Original Article

Comparison between Sodium hypochlorite (NaOCl 0.05%) and Povidone iodine (10%) In treating Poly microbial diabetic foot ulcer infection (DFUI) instead of using antibiotics

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Abstract

Introduction: Diabetes is a major health issue in Bangladesh, with 8% of the population claiming 3% of all deaths. Diabetic foot ulcer (DFU) is a common complication of DM, with 9-26 million patients worldwide each year. High blood sugar levels and smoking can lead to DFU-I and foot-related complications, leading to amputation. MDR-resistant micro-organisms can form biofilm in infection-wound sites, making it diflcult to clean. Systemic antibiotic use can lead to increased mucosal permeability and hyper inflammation (collateral damage). This study aimed to provide cost-effective treatment for DFU-I to establish evidence of its usefulness and cure rates, with NaOCl 0.05% as the ideal and cost effective alternative.

Objective: To compare two locally applied antiseptic applications (NaOCl 0.05% Vs. Povidone Iodine 10%) as the treatment outcome of DFU-I in clearing polymicrobial infection by enhancing healing process.

Methodology: This cross-sectional observation study (clinico-epidemiological) was conducted among 41 adult diabetic foot ulcer infection patients (DFU-I). Patients of DFU-I studied at 4P Diabetes Care at daytime oflce hours (9AM to 9 PM except Fridays) during January 2021 to July 2022. Data were collected by using a hybrid designed questionnaire (close and open ended).

Results: Most of these patients (42%) belonged between 51-60 years age group who suffered from diabetes for <10 days, followed by 39% for 10-19 days, and 19% for >=20days, respectively. Of 41 patients, 46% had been diagnosed with ulcer on anterior, dorsal, foot; 32% patient on phalanges and 22% on ankle. More than half (54%) of all DFU-I patients took <24 hours to cover disinfection process. Finding also showed that, 41% patient took >21 days, 22% patient took 18-21days and 37% patient took <17days for healing their wound. Our study revealed a significant relation between treatment and age groups of patients (p=0.03), period of DM (p=0.05), having co-morbidities (p=0.02), disinfection hours (p=0.03) and healing time, respectively.

Conclusion: This study found that Sodium hypochlorite 0.05% was more effective, quicker and cheaper in treating polymicrobial diabetic infections than that of with 10% povidone iodine. However, this preliminary finding should not be taken as final until more advanced studies are conducted to accept or refute this study.

Key Words: Diabetics, Foot Ulcer, Treatment, Sodium hypochlorite, Povidone Iodine

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Introduction:

According to 2016-WHO report, 8% of total population of Bangladesh, i.e., 12.9 million people remains affected by diabetes claiming 3% of total deaths.[1] which are being rampant in DM-prevalence Bangladeshi population, observed over time.[2]

Common complications of poorly controlled diabetes mellitus (DM) is diabetic foot ulcer (DFU) the global annual estimates of which remain 9-26 million diabetic patients (6.3%)[3] being higher in males and type 2 diabetic patients than type one.[3] Contributing factors of

DFU-infections (DFU-I) are: poor foot care, peripheral vascular diseases, neuropathy, poor glycemic control, and/or poor foot hygiene[4] However, high blood sugar levels and smoking increases DFU-I [5] and increased risk of foot-related complications often leading to lower limb amputation.[6-7]

Diabetic foot ulcer infection (DFUI) is often caused by multifactorial etiologies and diabetes, which is the leading cause of non-traumatic lower-extremity amputations worldwide[6] and can be of mono- or poly-microbial nature that may cause multidrug resistant (MDR) micro-organisms in frequently forming biofilm in infection site making the infection-wound more diflcult to clean using antibiotics and antimicrobial drugs. On the other hand, antibiotics must be limited to use in avoiding kidney failure and other adverse effects, systemically. Further, antibiotic causes dysbiosis of our nongenomic self that is our beneficial microbiota, and, administering antibiotic for local DFUI is not cost effective, too. Mentioning the gaps in global data in diabetes education, preventive measures, glycemic control, comorbidities, Rebecca Sorber et al apprehended that without a multidisciplinary assessment for treating DFU-I it can lead to serious consequences, such as DF-ulcer recurrence.[7]

This study, was thus, designed to give virtually cost-effective treatment for DFU-I to establish he evidence of its usefulness and cure. Since systemic antibiotics are often not effective in clearing surface infection and may form biofilm of DFU and can cause non-genomic self- micro-biota being essential for our survival.[8]

Gut microbiota dysbiosis by systemic antibiotic use causes increased mucosal permeability and hyperinflammation (collateral damage). So, eradication of polymicrobial infection of diabetic foot ulcer with local use of antiseptic like NaOCl 0.05% is ideal and cost effective than that of with 10% povidone iodine. NaOCl 0.05% does not hamper in healing process by killing growing fibroblasts, where povidone iodine may also cause hypothyroidism and can make the kidney injured.[9] However, NaOCl had been used since pre-antibiotic era during the 1st world war but became relevant still today when antimicrobial resistance (AMR) and collateral damage to human non-genomic self/healthy microbiota by using various antimicrobial drugs.

In this clinical observational study, we tried to determine which among the two **antiseptics** between diluted Sodium hypochlorite (NaOCl 0.05%) and Povidone iodine 10% remains better and more effective in healing DFU-I without using antimicrobial drugs that also delays the healing process by killing nearly 90% of growing fibroblasts. However, Iodine absorbed from wound site may cause hypothyroidism and kidney injuries, ***per se***. **10-11**

I. Background

Diabetic foot ulcer (DFU) has diverse pathology from neurological, vascular, hormonal, dehydration, dermopathy to many etiopathology to form DFU, bring or more prevalent among immunocompromised patients. The common complication of poorly controlled diabetes mellitus (DM) remains diabetic foot ulcer infection (DFU-I). Poor foot care, peripheral vascular disease, neuropathy, poor glycemic control &/or poor foot hygiene remains the main contributing factors of DFU-I.[5]

Diabetic foot ulcer infection (DFUI) is polymicrobial or monomicrobial by multidrug resistant micro-organisms frequently form biofilm in infection site and becomes diflcult to clean infection by antibiotics and antimicrobial drugs. Antibiotics has limitation in kidney failure, other adverse effect if given systemically. Antibiotic causes dysbiosis of our nongenomic self that is our beneficial microbiota. Antibiotic administration for local DFUI is not cost effective too. This study is designed to give virtually cost-effective treatment for DFUI and to establish evidence. A common complication of patients with poorly controlled diabetes mellitus (DM) is diabetic foot ulcer infection (DFUI). Poor foot care, peripheral vascular disease, neuropathy, poor glycemic control, and/or poor foot hygiene are the main contributing factors.[5]

Foot ulcers, which can cause severe tissue and bone damage, are the starting point for lower leg and foot removals. Diabetes increases the risk of needing lower limb amputation, and high blood sugar levels and smoking can also increase the risk of foot-related complications.[6]

DFUs are foot lesions that may affect the skin, soft tissue, and bone in lower limbs, causing an aggravating infection in diabetic patients that can lead to major amputations. This is often caused by multifactorial etiologies and diabetes, which is the leading cause of non-traumatic lower-extremity amputations worldwide.[6]

Data gaps in diabetes education, preventive measures, glycemic control, comorbidities, and multidisciplinary assessment and treatment of ulcers can lead to serious consequences, such as ulcer recurrence. [7] Foot ulcers are estimated to affect 9.1 million to 26.1 million people with diabetes annually.[3] The global prevalence of DFUs is 6.3%, higher in males than females, and higher in type 2 than type 1 diabetic patients.[4]

Systemic antibiotics are not effective in clearing surface infection with biofilm formation of diabetic foot ulcers rather causes to our non-genomic self that is our microbiota which is essential for our survival.[8] Gut microbiota dysbiosis by systemic antibiotic use causes increased mucosal permeability and hyperinflammation (collateral damage). So, eradication of polymicrobial infection of diabetic foot ulcer with local use of antiseptic like NaOCl 0.05% is ideal and cost effective than 10% povidone iodine as NaOCl 0.05% does not hamper healing process by killing growing fibroblasts. Moreover, povidone iodine causes hypothyroidism and kidney injury.[9-10]

This NaOCl was used in pre-antibiotic era of first world war became relevant today when antimicrobial resistance and collateral damage to our non-genomic self (Healthy Microbiota) of human race caused by various antimicrobial drugs. This observational study effectively cleared all infection within short span of moments by diluted Sodium hypochlorite without damaging by antimicrobial drugs as well as Povidone iodine 10% which delays healing process by killing nearly 90% of growing fibroblasts thus delaying healing process. Iodine absorbed from wound site may cause hypothyroidism and kidney injury.[11-12]

Diabetic foot ulcers infection (DFUI) are among the most common complications of patients with poorly controlled Diabetes Mellitus (DM), as a result of poor glycemic control, poor foot care, underlying peripheral vascular disease, and/or neuropathy. [13]

These underlying pathophysiological grounds in adjunct to co-existent factors may also predispose to more than half of the ulcers becoming infected. Infected DFUI causes patient suffering seriously and at the cost of significantly increases individual cost of OOP (out of pocket) and also create much burden to country's healthcare system. Other than economical, psychological and social burdens, DFUI also places a huge physical burden on the patient, since it a common cause of amputation of the lower extremities, globally.[13] It is therefore, remains critical to be aware of in time early interventions for DFUI. However, DFUI must be easily available, accessible, affordable and low-cost yet and cost-effective treatment/management for the patient, at large.

Several papers were reported on the economic analyses of costs and treatment outcome aimed to get relief DFU from such infection that includes systemic and topical antimicrobial therapies, debridement of slough and dressing of the wound. One of the best topical antimicrobials available to treat infected DFUI remain are 10% Povidone iodine solution, Chlorhexidine, Acetic acid 5%, Hydrogen peroxide, etc., but not without limitation.[14] Some of these have been linked to toxic effects on granulation tissue, cartilage damage, of bullae formation and inhibition of fibroblast growth. On the other hand, systemic antibiotics may cause serious microbiota damage/collateral damage .[15-16]

In these regards, cost-effective DFUI interventions have been repeated earlier given the higher DFUI prevalence and its accompanying burden suggestions that it is essential to compare available treatments to focus on the potentially cost-effective interventions towards reducing the burden. We thus aim to compare two readily available and commonly used topical antimicrobials, [10% Povidone Iodine solution vs Diluted Sodium Hypochlorite (0.05%)]. However, Diluted Sodium Hypochlorite was evidenced to be the least injurious to fibroblast growth; we prefer to go for this later than the former one.[17]

I. 1 Pathophysiology

Diabetes Mellitus (DM) has many complications and these are rapidly becoming the world's most significant cause of morbidity and mortality, and one of the most distressing is Diabetic Foot Ulcer (DFU). Chronic wound complications are a growing concern worldwide, and the effect is a warning to public health and the economy. The etiology of a DFU is multifaceted, and several components cause added together create a suflcient impact on ulceration: neuropathy, vasculopathy, immunopathy, mechanical stress, and neuroarthropathy.[18] There are many classifications of the diabetic foot. About 50% of patients with foot ulcers due to DM present clinical signs of infection. It is essential to manage multifactorial etiology of DFU to get a good outcome.[19]

I. 2 Diabetic foot Attack

The "diabetic foot attack" is one of the most devastating presentations of diabetic foot disease, typically presenting as an acutely inflamed foot with rapidly progressive skin

and tissue necrosis, at times associated with significant systemic symptoms. Without intervention, it may escalate over hours to limb- threatening proportions and poses a high amputation risk. There are only best practice approaches but no international protocols to guide management. Immediate recognition of a typical infected diabetic foot attack, predominated by severe infection, with prompt surgical intervention to debride all infected tissue alongside broad-spectrum antibiotic therapy is vital to ensure both limb and patient survival.[20]

I. 3: Details of Diabetic Foot Ulcers

DFUs are defined as foot lesions (ulcers) that may affect the skin, soft tissue, and bone in lower limbs, causing an aggravating infection in diabetic patients that can lead to very serious consequences such as lower-limb amputations. DFUs are caused by multifactorial etiologies as part of the micro vascular complications of diabetes mellitus that can lead to major amputations, in most cases by the lack of the timely and correct management of diabetic feet. Indeed, diabetes is the leading cause of non-traumatic lower-extremity amputations worldwide.[6]

These serious consequences are mostly due to the absence of data on many subjects including diabetes education, preventive measures, glycemic control, comorbidities, inappropriate multidisciplinary assessment and treatment of ulcers, and later treatment failures in the prevention of ulcer recurrence.[7] Based on the 2015 prevalence data from the International Diabetes Federation, it is estimated that foot ulcers develop in 9.1 million to 26.1 million people with diabetes annually worldwide.[3] A systematic review and meta-analysis of the global prevalence of DFUs showed that the global prevalence of DFUs was 6.3%, higher in males than in females, and higher in type 2 than in type 1 diabetic patients.[4]

In Mexico, there are around 12 million cases of diabetes mellitus, and since the overall prevalence of DFUs is 6%, it is estimated that more than 700,000 people are affected with any grade of DFUs. DFU treatment has a high cost worldwide. In the United States (US), this cost ranges from $8000 to $17,000, depending on the grade of infection and type of amputation, with the cost rising to $43,000 in the case of partial amputation to $63,100 after major amputation.[21]

All of these costs not only affect the patient's economic and psychological status but also the family's economy, the patient's disability and diminished quality of life, and the finances provided by the government and health insurance intended for diabetes treatment. In patients with diabetes, it is reported that, in most cases (60–80%), the ulcers become less aggressive, and, with the proper care, they heal. On the other hand, about 10% to 15% of these ulcers remain active and 5% to 24% lead to limb amputation in approximately 6–18 months.[22]

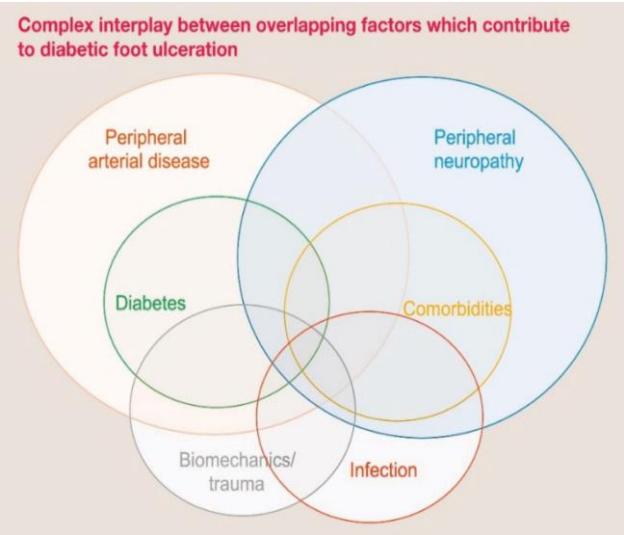
As many as 40% of patients have a recurrence within one year after ulcer healing, almost 60% have a recurrence within three years, and 65% have a recurrence within five years, making a previous incident of a foot ulcer the strongest predictor for diabetic foot ulceration. The median time to healing without surgery is about 12 weeks. The five-year risk of death in diabetes patients is 2.5 times higher in those with DFUs than without them, and the five-year mortality after diabetes-related amputations exceeds 70%, which is worse than in many common cancers.[23]

I. 4 Association between DM and DFU

A diabetic foot ulcer is an open sore or wound on the foot of a person with diabetes, most commonly located on the plantar surface, or bottom of the foot. Diabetic foot ulcers occur in approximately 15% of persons with diabetes. Of those who develop a foot ulcer, 6% will be hospitalized due to infection or other ulcer-related complication. The risk of foot ulceration and limb amputation increases with age and the duration of diabetes.[24]

I. 5 Risk factors for DF:

The main risk factors for the development of DF and the series of injuries that lead to gangrene and amputation are:



- Peripheral neuropathy
- Inadequate hygiene
- Deformities
- Old age
- High plantar pressure
- Inadequate metabolic control
- Hyperkeratosis
- Smoking
- Prior amputation
- Onychomycosis with toe nail deformity
- Inadequate shoes
- Proprioceptive loss

I. Treatment of Diabetic Foot Ulcer- Infections (DFU-I)

II.1: Treatment modalities of (DFU-I)

Successful treatment of diabetic foot ulcers consists of addressing these three basic issues: debridement, ofloading, and infection control.

SODIUM HYPOCHLORITE:

Sodium hypochlorite (NaOCl) is a solution made from reacting chlorine with a sodium hydroxide solution. These two reactants are the major co-products from most chlor-alkali cells. Sodium hypochlorite, commonly referred to as bleach, has a variety of uses and is an excellent disinfectant/antimicrobial agent. **Hypochlorite** is an antimicrobial used to treat and prevent infections of the skin and tissue. Sodium hypochlorite topical is an antibiotic that fights bacteria. Sodium hypochlorite topical is used to treat or prevent infections caused by cuts or abrasions, skin ulcers, pressure ulcers, diabetic foot ulcers, or surgery. **Hypochlorite** is an antimicrobial used to treat and prevent infections of the skin and tissue

Mechanism of action:

Sodium hypochlorite mediates its antimicrobial action by reacting with fatty acids and amino acids. Via saponification reaction, it acts as an organic and fat solvent, degrading fatty acids to form fatty acids and glycerol. This reduces the surface tension of the remaining solution. Sodium hypochlorite may react with amino acids to neutralize them and form water and salt. Hypochlorous acids (HOCl) present in sodium hypochlorite solutions may act as solvents in contact with organic tissue to release chlorine, which forms chloramines when combined with the protein amino group that disrupt cell metabolism Chlorine in the solution is a strong oxidant that inhibits essential bacterial enzymes leading to an irreversible oxidation of SH groups 1. Eventually Hypochlorous acid and hypochlorite ions degrade and hydrolyze amino acids.

II. 2: Pathway from Treating DFU-I to Ultimate Amputation:

Lower leg and foot removals begin with foot ulcers. An ulcer that won't heal causes severe damage to tissues and bone. It may require surgical removal (amputation) of a toe, a foot or part of a leg. People living with diabetes have an increased risk of needing lower limb amputation. Wounds or ulcers that do not heal are the most common reason for amputation. Factors such as high blood sugar levels and smoking can increase the risk of foot-related complications, which can lead to a need for amputation.

II. 3: Role of Starting treatment from Initial Stage to avoid amputation(s):

Using a superficial antiseptic such as sodium hypochlorite at the initial stages of foot ulcer would prove to be very much effective in saving the limb rather than not taking appropriate measures in the early stages, which will eventually lead to amputation.

Amputation itself is a very costly procedure. Starting from the routine investigation to choosing very skilled medical personnel for this surgical procedure the whole process is lengthy and takes a toll on both the patients and their attendance.

Also, such major surgical procedures come with risks, complications and medical failure. Whereas using a proper antiseptic solution to clean the debridement is cost effective, time saving, easier.

III. Aims and Objectives:

III. 1: Aims: To Compare two locally applied antiseptic applications (NaOCl 0.05% Vs. Povidone Iodine 10%) as the treatment outcome of DFU-I in clearing polymicrobial infection by enhancing healing process.

III.2 Specific Objectives:

The purpose of this study was to compare the response of clearing polymicrobial diabetic foot ulcer infection that enhance healing process by Sodium hypochlorite (NaOCl 0.05%) Vs. 10% povidone iodine.

IV. Methodology:

Research Design: Clinical Research on patients with diabetic foot ulcer infection (DFUI)

Study Type: Observational study.

Study Design:

This clinico-epidemiological study was conducted on diabetic foot ulcer patients to compare the treatment

outcome of two groups of antiseptic solutions (NaOCl 0.05% Vs. Povidone Iodine 10%) used.

Study period: January 2021 to July 2022

Place and time of selecting patients

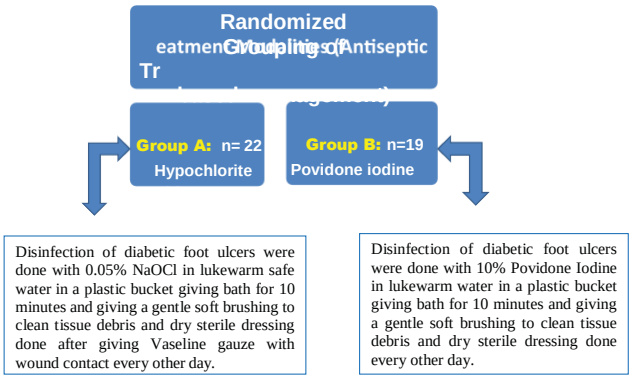
Patients of diabetic foot ulcers with infection were recruited through referral and direct patent visit to our 4P Diabetes Care at daytime oflce hours from 9AM to 9 PM except Friday.

Study population:

Total 41 adult diabetic patients with infected ulcers were enrolled sequentially over a period of one and a half year. Among them 5 patients were refused treatment by tertiary care hospital as because of critical conditions which requiring surgical treatment under general anesthesia.

Randomized Grouping of Treatment Modalities

Every patient was provided best cost-effective treatment for Diabetes as well as for comorbidities. Twenty-two patients with infected diabetic foot ulcers were placed on wound care with Sodium hypochlorite 0.05% and rest 19 patents placed on povidone iodine 10%. Diabetic foot ulcer patients were randomly assigned with-



However, the cost of other ailment treatment was borne by patients' family support.

Training on follow up methods:

After practical training of wound care- stock solutions in dark bottle given with patients' wound care volunteers. The bottles were numbered with patients' ID. Author and nurses knows which solution inside bottle. Bottles were assigned randomly from very beginning of wound care. As healing with hypochlorite 0.05% was speedy later recruitment of patients were placed on mostly hypochlorite 0.05%. Most of the volunteers were instructed to take high definition photograph of wound serially and over video conversation,

Inclusion Criteria: Those who agreed and consented to include in this wound care study after explaining pros and cons of study were included in this project

Exclusion Criteria: Those who were not agreed and consented to include in this wound care study after explaining pros and cons of study were excluded in this project

Data Management:

Data collection:

Data was collected using a hybrid designed questionnaire (structured: close ended and some open ended) was used to collect data/ information. This questionnaire was pre-tested (on 1% subject) on diabetic foot ulcer patients of Ad-din Women's Medical College and Hospital, Maghbazar, Dhaka.

Data Cleaning:

Printed out data on listed variables and tallied with the data sheet, Treated all blank cells for better database, Avoided duplication, Pointing errors, Unnecessary space was removed, Converted all texts into numbers, Checked all the spelling properly

Data Entry:

SPSS Win V.22.0 was used for entering and recoding all collected data.

Data Quality Control: For the quality assurance, each data was double-checked followed by entering the data into the PC for logical check. Data collected from each interviewee was coded and analyzed.

Data Analysis Plan:

Finally, data were analyzed using the software 'Statistical Package Social Sciences (SPSS) version, 22.0.

Results and Findings:

Table-1: Age of the respondent's

Age	Frequency	Percent
<50 years	11	26
51-60 years	17	42
>60+ years	13	32
Total	41	100.0

Table 1 shows Majority of patients' recoded age (42%) belonged to 51-60 years (n=17), followed by <50 years age group (26%) and >60+ years age group (32%).

Table-2: Duration of Diabetes Foot Ulcer- Infections

Duration of Diabetes	Frequency	Percent
<10days	17	42
10-19	16	39
>=20 days	8	19
Total	41	100.0

Table-2 yields large majority (42%) of all respondents suffered from diabetes <10 days. Following that 39% & 19% were suffered from diabetes 10-19 days and >=20days respectively (Table 2).

Table-3: Other Diagnosis among the respondent's

Other Diagnosis	Frequency	Percent
HBV, HCV, PAD, Osteosarcomas	7	17
IHD, HTN, DLPAD, CKD, CLD	22	54
NAFLD, NASH, DL	12	29
Total	41	100.0

Among all the patients, majority patients 54% (n=22) had also another disease (**ischemic heart disease**-IHD, Hypertension-HTN, Peripheral Arterial Diseases-PAD, Chronic Kidney Disease-CKD, Chronic Liver Disease-CLD) along with diabetic foot ulcer (Table 3).

Table-4: Ulcer site among the respondent's

Ulcer Site	Frequency	Percent
Anterior Dorsal Foot Heel	19	46
Phalanges	13	32
Ankle	9	22
Total	41	100.0

Of 41 patients, 46% had been diagnosed with ulcer on Anterior, Dorsal, Foot; 32% patient had been diagnosed with ulcer on Phalanges; 22% patient had been diagnosed with ulcer on Ankle (Table 4).

Table-5: Hours of disinfection performed

Disinfection Hours	Frequency	Percent
<24 hours	22	54
24-48 hours	8	19
<48 hours	11	27
Total	41	100.0

Table 5 shows, 54% patient took <24 hours for disinfection process where 19% patient took 24-48 hours and 27% patient took <48 hours for disinfection process.

Table-6: Healing time of patient

Healing time	Frequency	Percent
<17days	15	37
18-21days	9	22
>21days	17	41
Total	41	100.0

Table 6 shows among all (41) patient, 41% patient took >21 days, 22% patient took 18-21days and 37% patient took <17days for healing wound.

Table-7: Association of Treatment outcome with Patient's Age, Gender, BMI & DF-infection Duration

Table-7.1: Association of DF-infection treatment with age of patients

Treatment modalities (antiseptic used)	Age of patients			Total	Chi square test of significance (p value)
	<50 Years	51-60 years	>60+ years		
Sodium hypochlorite (NaOCl)	5	13	4	22	P=0.03
Povidone Iodine	6	4	9	19	
Total	11	17	13	41	

Table- 7.1 yielded the prevalence of using Sodium hypochlorite (NaOCl) antiseptic agent was higher among 51-60 years aged patient (n=13) than using Povidone Iodine antiseptic agent (n=4). It had been observed there has positive significant differences (p=0.03) between patients

Table-7.2 Association of DFU-infection treatment with duration of patient's diabetes

Treatment modalities (antiseptic used)	Diabetes period			Total	Chi square test of significance (p value)
	<10days	10-19 days	>=20 days		
Sodium hypochlorite (NaOCl)	4	12	6	22	P=0.05
Povidone Iodine	13	4	2	19	
Total	17	16	8	41	

Another finding also showed that Sodium hypochlorite (NaOCl) antiseptic agent also effective for those who (n=6) had a longer diabetic period (>=20days) compared to Povidone Iodine antiseptic agent. Among 8 patients who had a longer diabetic period only 2 patients had used to Povidone Iodine antiseptic agent for healing wound. There had significant difference (p=0.05) between diabetes period and treatment modalities (antiseptic used) **Sodium hypochlorite (NaOCl)** solution **and Povidone Iodine.**

In table-7.3 shows of total 41 patients, patients who had suffer from (IHD+HTN+DLPAD+CKD+CLD) diseases, mostly patients (n-16) used Sodium hypochlorite (NaOCl) Antiseptic agent which was effective for them compared to **Povidone Iodine antiseptic agent.** There had also significant difference (p=0.02) between other complications and treatment modalities (antiseptic used) **Sodium hypochlorite (NaOCl)** solution **and Povidone Iodine.**

In table-7.4 shows among all patients n=17 patients needed only <24 hours for disinfection who had used to Sodium hypochlorite (NaOCl) antiseptic agent where only n=5 patients needed <24 hours who had used to Povidone Iodine antiseptic agent for disinfection. Nearby, n=2 patients needed >48 hours for disinfection who had used to Sodium hypochlorite (NaOCl) antiseptic agent where n=9 patients needed >48 hours who had used to Povidone Iodine antiseptic agent for disinfection. It had been yielded that there had highly positive association (p=0.03) between disinfection hours and treatment modalities (antiseptic used) **Sodium hypochlorite (NaOCl)** solution **and Povidone Iodine.**

Table-7.3: Association of treatments with other co-morbidities of patients

Treatment modalities (antiseptic used)	Other diseases			Total	Chi square test of significance (p value)
	HBV+ HCV+PAD + Osteosarcomas	IHD+HTN+DLPAD+ CKD+CLD	NAFLD + NASH +DL		
Sodium hypochlorite (NaOCl)	3	16	3	22	p=0.02
Povidone Iodine	4	6	9	19	
Total	7	22	12	41	

Table-7.4 Association of treatments with hours of disinfection

Treatment modalities (antiseptic used)	Disinfection hours			Total	Chi-square p value
	<24hours	24-48hours	>48hours		
Sodium hypochlorite (NaOCl)	17	3	2	22	P=0.03
Povidone Iodine	5	5	9	19	
Total	22	8	11	41	

Table-7.5: Association of treatments with healing time

Treatment modalities (antiseptic used)	Healing time		Total		Chi square, p value
	<17days	18-21days	>21days		
Sodium hypochlorite (NaOCl)	12	8	2	22	P<0.01
Povidone Iodine (PI2)	3	1	15	19	
Total	15	9	17	41	

In table-7.5 yielded, of 41 patients, n=12 patients needed only <17 days for healing wound using Sodium hypochlorite (NaOCl) antiseptic agent and only n=3 patients needed <17 days using Povidone Iodine antiseptic agent for healing wound. Adjacent to, only n=2 patients needed >21 days for healing wound using Sodium hypochlorite (NaOCl) antiseptic agent where n=15 patients needed >21 days using Povidone Iodine antiseptic agent for healing wound. It had been yielded that between healing time and treatment modalities (antiseptic used) **Sodium hypochlorite (NaOCl)** solution **and Povidone Iodine** had highly positive association ($p<0.01$).

Discussion:

A report from WHO in 2016, 8% of our total population in Bangladesh (12.88 million) remain affected by diabetes whereas 3% of total deaths of all-ages occurred due to diabetes.[1] According to 2016-WHO report, 8% of total population of Bangladesh, i.e., 12.9 million people remains affected by diabetes claiming 3% of total deaths which are being rampant in DM-prevalence Bangladeshi population, observed over time. [1,2]

Diabetic foot ulcer (DFU) has diverse pathology from neurological, vascular, hormonal, dehydration, dermopathy to many etiopathology to form DFU, bring or more prevalent among immunocompromised patients. The common complication of poorly controlled diabetes mellitus (DM) remains diabetic foot ulcer infection (DFU-I). Poor foot care, peripheral vascular disease, neuropathy, poor glycemic control &/or poor foot hygiene remains the main contributing factors of DFU-I.[11]

Polymicrobial biofilm formation on ulcers causing hard to eradicate this infection by systemic antibiotics. Some infections are multidrug resistant monomicrobial also cured by this NaOCl 0.05%. Systemic antibiotics if given causes our non-genomic self-injury to our healthy microbiota, by that way causes a vicious cycle to our health in many ways. As infection site of diabetic foot ulcer has less vascularity microbe's biofilm cannot be removed by systemic antimicrobial drugs. So, local disinfectant like sodium hypochlorite in diluted form is very effective tool since pre-antibiotic era as Dakin's solution.

Today in post antibiotic era it again became useful in ours research. Here we compared with povidone iodine which is used widely around the globe to clean wound, but it had some negative effects such as it might cause growing fibroblast injury thus hampering healing process, may cause hypothyroidism by Iodine absorption from wound site and it may cause kidney injury too as in radio contrast (Iodine based) renal injury. In case of NaOCl no such adverse effects rather it can be used in zidney failure patients' wound care.

Each and every patient is poor if we can give care of DFUI infection in such virtually cost free care with NaOCl, it may be a role model of DFUI care in the world.

A common complication of patients with poorly controlled diabetes mellitus (DM) is diabetic foot ulcer infection (DFUI). Poor foot care, peripheral vascular disease, neuropathy, poor glycemic control, and/or poor foot hygiene are the main contributing factors.[11]

Foot ulcers, which can cause severe tissue and bone damage, are the starting point for lower leg and foot removals. Diabetes increases the risk of needing lower limb amputation, and high blood sugar levels and smoking can also increase the risk of foot-related complications.[6]

DFUs are foot lesions that may affect the skin, soft tissue, and bone in lower limbs, causing an aggravating infection in diabetic patients that can lead to major amputations. This is often caused by multifactorial etiologies and diabetes, which is the leading cause of non-traumatic lower-extremity amputations worldwide.[19] Data gaps in diabetes education, preventive measures, glycemic control, comorbidities, and multidisciplinary assessment and treatment of ulcers can lead to serious consequences, such as ulcer recurrence.[20] Foot ulcers are estimated to affect 9.1 million to 26.1 million people with diabetes annually.[6] The global prevalence of DFUs is 6.3%, higher in males than females, and higher in type 2 than type 1 diabetic patients.[7]

This study evaluated the response of Sodium hypochlorite (NaOCl 0.05%) to clearing polymicrobial diabetic foot ulcer infection and enhancing healing process. Effective infection clearing can prevent contiguous osteomyelitis and prevent osteotomy and limb amputations. Sodium hypochlorite (NaOCl) is a solution made from reacting chlorine with sodium hydroxide solution, containing major co-products from most chloral-alkali cells. It has a variety of uses and is an effective disinfectant/antimicrobial agent. Hypochlorite is an antimicrobial used to treat and prevent infections of skin and tissue. Hypochlorite is an antimicrobial used to treat and prevent infections caused by skin and tissue diseases, such as cuts or abrasions, skin ulcers, pressure ulcers, diabetes, and surgery.

NaOcl is superior to povidone iodine in antimicrobial action, as it acts as an organic and fat solvent, degrading fatty acids to form fatty acids and glycerol, and reacting with amino acids to neutralize them and form water and salt. Hypochlorous acids (HOCl-) present in sodium hypochlorite solutions act as solvents in contact with organic tissue to release chlorine, which forms chloramines when combined with the protein amino group that disrupt cell metabolism. Chlorine in the solution is a strong oxidant that inhibits essential bacterial enzymes leading to an irreversible oxidation of SH groups 1.

The most important idea is to compare two cost-effective DFUI interventions, Diluted Sodium Hypochlorite and Povidone Iodine solution, to reduce the burden of fibroblast growth.[15] The best topical antimicrobials available to treat DFUI are 10% Povidone iodine solution, Chlorhexidine, Acetic acid 5%, Hydrogen peroxide, but not without limitation.[5] Systemic antibiotics can have toxic effects on granulation tissue, cartilage damage, bullae formation, and fibroblast growth.[13-14]

Foot ulcers in patients with diabetes should be treated to reduce the risk of infection and amputation, improve function and quality of life, and reduce health-care costs. [23]

Using sodium hypochlorite at the initial stages of foot ulcer is effective in saving the limb, but it is costly and takes a toll on both the patients and their attendance. Antiseptic solutions are also cost-effective, time saving, and easier.

Sodium hypochlorite (NaOCl) is a solution made from reacting chlorine with a sodium hydroxide solution, two of which are major co-products from most chlor-alkali cells. It has a variety of uses and is an excellent disinfectant/antimicrobial agent. However, it does not result in an improvement in clinical outcomes, while it has promising properties that result in significant improvement in probing pocket depth and clinical attachment level. More studies are needed to confirm these observations.

Diabetic foot ulcer has diverse pathology and is easily infected by polymicrobial biofilm formation, which can be cured by NaOCl 0.05%. Systemic antibiotics can cause non-genomic self-injury to our healthy microbiota, which can lead to a vicious cycle. Local disinfectant like sodium hypochlorite in diluted form is an effective tool in post-antibiotic research.

Here we compared with povidone iodine which is used widely around the globe to clean wound, but it had some negative effects such as it might cause growing fibroblast injury thus hampering healing process, may cause hypothyroidism by Iodine absorption from wound site and it may cause kidney injury too as in radio contrast (Iodine based) renal injury. In case of NaOCl no such adverse effects rather it can be used in kidney failure patients' wound care.

Each and every patient is poor if we can give care of DFUI infection in such virtually cost-free care with NaOCl, it may be a role model of DFUI care in the world.

Conclusion:

Though findings of this study evidenced Sodium hypochlorite 0.05% as quicker and cheaper in yielding more effectiveness in treating polymicrobial diabetic infections towards speedy healing in comparison to 10% povidone iodine, this preliminary finding should not be taken as final, unless more advanced studies using larger samples are conducted to accept or refute our finding.

Conflicts of interest: None. Declared.

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