

## Antibacterial Effect of Low Level Laser Therapy in Infective Diabetic Foot Ulcers

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### Abstract:

**Background:** Patients with diabetes mellitus frequently present with foot infections as a complication, which are up to 20% of hospital admissions. On treatment of the wounds with low level laser therapy (LLLT) major changes (Increased granulation tissue, fibroblast proliferation, collagen synthesis, early epithelialization and enhanced neovascularisation) can be seen. The objective of study was to assess anti-infective property of LLLT in diabetic infections. **Methodology:** The present randomized controlled trial was conducted in Department of Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on 60 patients with infected diabetic foot ulcers for the duration of one year. Patients were divided into two groups using computerized randomization chart. Group I received conventional dressing with betadine and group II received LLLT along with conventional dressing. Both groups received empirical oral antibiotic (Ciprofloxacin-Tinidazole) for two days and culture sensitive antibiotic later. The wound culture was repeated on fifth day and tenth day of treatment. **Results:** In this study control group had 25 males and 5 female and study group had 23 males and 7 females. Twenty four (24 that is 80%) patients had positive ulcer culture in control group and culture negative ulcer were 6 (20%) on tenth day. In study group culture positive ulcers were 20 (66.66%) and culture negative ulcers were 10 (33.33%) ( $p=0.3811$ ). **Conclusions:** The wound subjected to LLLT with conventional therapy showed decreased infection rate at 10<sup>th</sup> day of culture as compared to conventional dressing group alone.

**Key Words:** Diabetic foot infection; Diabetes mellitus; Diabetic ulcers; Helium-Neon Laser; Low level laser therapy (LLLT).

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### I. Introduction

Diabetes mellitus (DM) is a common metabolic disorder. Its phenotype is same as of hyperglycemia. Secondary pathophysiological changes are seen in multiple organ systems due to the metabolic dysregulation in DM. This leads to a burden on the health care system and on the individual with diabetes. End-stage renal disease (ESRD), nontraumatic lower extremity amputations, and adult blindness are generally seen in cases of Diabetes mellitus [1].

Microvascular (Retinal, renal, possibly neuropathic), macrovascular (Coronary, peripheral vascular), and neuropathic (autonomic, peripheral) complications are seen with Type 2 diabetes mellitus. The disorder is characterized by hyperglycemia [2].

Over the past two decades, the prevalence of DM has risen. The rise is estimated to be from 30 million cases in 1985 to 177 million in 2000. More than 360 million individuals are expected to have diabetes by the year 2030 [3]. The prevalence of type 2 DM is more than type 1 DM. This increase in type 2 DM is said to be because of obesity and reduced activity levels. These high rates are seen most in Asia accounting for 6 of the top 10 countries. The Centers for Disease Control and Prevention (CDC) in the United States, has shown 7% of the population, had diabetes in 2005 (~30% of individuals with diabetes were undiagnosed). Approximately 1.5 million individuals (>20 years) were newly diagnosed with diabetes in 2005. In 2005, the prevalence of DM in the United States was estimated to be 0.22% in those <20 years and 9.6% in those >20 years. In individuals >60 years, the prevalence of DM was 20.9%. Men and women throughout most age ranges (10.5% and 8.8% in individuals >20 years) have shown similar prevalence rates although it is slightly greater in men >60 years [4]. Worldwide estimates show that individuals in the 45–64 age groups will have the greatest number of diabetes cases in 2030. In India the estimation for the number of diabetes patients in the year 2000 was 31.7 million and is expected to increase to 79.4 million by 2030 [5].

Several epidemiological studies in migrant Indians and India itself show that, the population has a high genetic predisposition for diabetes, which is precipitated by environmental factors such as urbanization [6]. The prevalence of diabetes is four to six fold lower in rural areas, which is probably attributed to a conventional lifestyle which has beneficial effect on glucose tolerance (IGT). According to the National Urban Diabetes Survey which was done in six cities, a 12% age standardized prevalence rate for diabetes was seen. The survey also showed that there was a minimal male preponderance and impaired glucose tolerance that was 14% .

Subjects under the age of 40 years, had a prevalence of five percent for DM and 13% prevalence of impaired glucose tolerance.

Around 20% of diabetes-related hospital admissions present with foot infections as a frequent complication [7]. Unless prompt treatment is carried out the infectious agents are may ultimately lead to amputation of the infected foot.

The risk of developing a foot ulcer in a diabetes patient is estimated to be 15% [8]. Recent studies have shown an incidence ranging from 1.0% to 4.1% and prevalence from 4% to 10%. This suggests that the lifetime incidence may be as high as 25% [9]. When diabetic persons are compared with nondiabetic person's lower extremity disease are seen twice as more. These diseases include peripheral arterial disease, peripheral neuropathy, foot ulceration, or lower extremity amputation. These diseases i.e lower extremity disease affect around 30% of patients with diabetes who are older than 40 years [10]. Following foot ulcers the patient undergoes emotional, physical, productivity, and financial losses.

Diabetic foot ulcers are wounds on the feet. These wounds occur due to high blood sugar levels associated with diabetes. When untreated these ulcers do not heal and lead to infection. In cases of diabetic neuropathy ulcerations may be complicated by infection and gangrene, with a subsequent risk of amputation. In order to avoid the unfortunate complication of amputation the surgeon needs to identify and manage these problems early enough.

The fundamental pathophysiological factors that lead to diabetic ulcer remain unclear. Neuropathy, ischaemia and infection are considered to be the most important factors. These ulcers are known to be resistant to conventional treatment and may lead to severe complication if not treated properly. Animal, human and invitro cellular studies have shown beneficial effect of low level laser therapy (LLLT) on wound healing and LLLT can play major, adverse effect free, role in healing chronic diabetic ulcers which are resistant to conventional mode of treatment.

Use of LLLT when applied to soft tissue invitro and invivo has shown stimulation of specific healing processes. The major changes seen LLLT is used for treatment include increased granulation tissue, increased fibroblast proliferation, increased collagen synthesis, early epithelialization and enhanced neovascularisation.

In view of no study regarding the anti-infective property of LLLT in diabetic infections the present study was undertaken to know whether Low Level Laser Therapy given daily with clustered probe at 60 mW at 5 KHz frequency, for two minutes at a dose of two to four J/cm<sup>2</sup> along with conventional treatment compared to conventional therapy alone, is effective in reducing the infection.

## **II. Methodology**

The present randomized clinical trial was carried out at Department of Surgery, Jawaharlal Nehru Medical College and KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum for a period of one year on 60 patients with chronic diabetic ulcer of lower extremities. The sample size was calculated based on patient data at hospital for the last three consecutive years.

### *Selection Criteria*

#### **Inclusion criteria**

- Type 1 and 2 diabetes patient between 18 to 65 years with duration of the ulcer of more than four weeks.
- Culture positive ulcer on admission.
- Fasting blood glucose levels measured on two occasions 24 hours apart between 140 mg/dl to 200 mg/dL

#### **Exclusion criteria**

- Pulseless limb, immunocompromised patients, associated osteomyelitis.
- Cardiac conductivity disorders, skin malignancy, diabetic ketoacidosis and cellulitis.
- Serum creatinine > 2, diabetic gangrene.

#### **Procedure**

The study was approved by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belgaum. After finding the suitability as per inclusion and exclusion criteria patients were selected for the study and briefed about the nature of the study, the interventions used and written informed consent was obtained. Further, descriptive data of the participants like name, age, sex, detailed history, were obtained by interviewing the participants and clinical examination and necessary investigations like complete blood count, blood urea and serum creatinine and culture of the ulcer on admission were recorded on predesigned and pretested proforma. Duplex scan was not done for the study subjects. Further the patients were divided into two groups using a computerized randomization chart.

Both the groups were given empirical antibiotic (Tab. Ciprofloxacin-Timidazole) for two days and culture sensitive antibiotics after two days. Group I received standard treatment that is conventional dressing with betadine. In group II patients received LLLT along with conventional dressing. Specification for LLLT

- Duration – 10 days.
- Frequency – 5 KHz.
- Cluster probe – 60 mW.
- Dose – 12 J/cm<sup>2</sup> daily.

The wound culture was repeated on fifth day and tenth day of treatment.

*Statistical Methods*

At the end of the study the data was tabulated and analysed using chi-square test.

**III. Results**

In this study control group had 25 males and 5 female with M: F of 5:1. Study group had 23 males and 7 females with M: F ratio 3:1. In this study more number of patient were within age group of 51 – 65 years (66.66%) (Table 1). Two patients were of Type I DM and rest had Type II DM. In the present study 43.33% of patients had history of DM for a period of 6 to 10 years and 36.66% had diabetes for 10 years or more (Table 2). In the present study number of patients with neuropathy was 21 (35%) whereas vasculopathy was present in 10% of the patients (Table 3). In our study it was observed that 46.66% of patients had ulcer on plantar aspect and 53.33% had ulcer on dorsum of foot. Trauma was the most common cause of origin of diabetic foot ulcer (65%) while only 35% had spontaneous ulcer origin.

In our study total number of patient with positive ulcer culture in control group were 24 (80%) and culture negative ulcer were 6 (20%) on tenth day. In study group culture positive ulcers were 20 (66.66%) and culture negative ulcers were 10 (33.33%). LLLT was useful in reducing infection in study group. However this effect was not statistically significant (p=0.3811) (Table 4).

Staph aureus and pseudomonas were most common infections in diabetic foot ulcers (30% and 20% respectively) (Table 5).

**IV. Tables**

**Table 1: Distribution of patients according to age**

Age (Years)	Number of patients	
	No.	Percentage
18 – 30	2	3.33%
31 – 40	7	11.6%
41 – 50	11	18.33%
51 – 65	40	66.66%
Total	60	100%

**Table 2: Distribution of patients according to duration of diabetes mellitus**

Duration (Years)	Number of patients	
	No.	Percentage
0 – 5	12	20%
6 – 10	26	43.33%
> 10	22	36.66%
Total	60	100%

**Table 3: Distribution of patients according to complications**

Complications	Number of patients	
	No.	Percentage
Neuropathy	21	35.00%
Vasculopathy	06	10.00%

**Table 4: Culture of Ulcer**

Culture	Control group		Study group	
	No.	Percentage	No.	Percentage
+	24	80%	20	66.66%
-	6	20%	10	33.33%
Total	30	100%	30	100%

p=0.3811 (Chi square test)

Table 5: Organisms

Organisms	Number of patients	
	No.	Percentage
Staph aureus	18	30.00%
Pseudomonas	12	20.00%
E. Coli	10	16.60%
P. Mirabilis	08	13.33%
Streptococci	04	6.66%
Others	08	13.33%

## V. Discussion

Foot ulceration is a complication caused by diabetic disease and is commonly infected. The source of infection is usually the contamination of the break in the skin, which may be imperceptible like cracks or fissures. Most commonly infection is polymicrobial. The most common organisms are staphylococcus aureus, pseudomonas and beta haemolytic streptococci. The diabetic state needs to be well controlled and infection should be effectively treated to achieve healing of the ulcer.

Control of infection in diabetic foot ulcers is an unbeatable challenge. Infection results in microthrombi in smaller vessels of foot. This impairs blood flow leading to ischaemia which makes eradication of bacteria difficult by antibiotics.

Low level laser therapy has shown great promise as a procedure for healing of chronic wounds. The beneficial effect of LLLT on wound healing in diabetic foot ulcers was observed in the study conducted in our institution [11]. LLLT increases hydroxyprolene level at wound site leading to faster healing as compared to conventional dressing alone.

This beneficial effect of LLLT on diabetic foot ulcers was due to its effect on wound healing dynamics, but to know whether LLLT has antibacterial effect also was the purpose of this study.

Rationale of conducting this study was to know the antibacterial effect of LLLT in diabetic foot patients. Effect of LLLT in controlling wound infections has not been studied. However LLLT has been found to increase the bacterial growth in in-vitro studies [12]. It has also been shown that LLLT improves tissue permeability resulting in increase in local antibiotic concentration [13]. This study explores the antibacterial effect of LLLT on infected diabetic foot ulcers.

The present study was conducted in JNMC and KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum to know the antibacterial effect of LLLT (Helium Neon laser media) in infected diabetic foot ulcers.

In the present study it was seen that incidence of diabetic foot ulcer was more in males (80%) as compared to females (20%). The national data source, NHDS documented higher hospital rates in males suffering from diabetic foot ulcer.

Diabetic foot ulcers are most commonly seen in 6<sup>th</sup> decade (66.66%), while 18.33% were affected in 4<sup>th</sup> decade and 11.6% were in 3<sup>rd</sup> decade, we had 2 patients (3.33%) in 2<sup>nd</sup> decade. Older the patient, more the chances of diabetic foot ulcer and more chances of infections.

In our study only 2 patients (3.33%) were of type 1 DM and rest had type 2 DM. In our study 12 (20%) patients were diagnosed with DM of less than five years duration. Twenty six (43.33%) patients were suffering from DM for the duration of 6 to 10 years. It was observed that 22 patients had history of DM for more than 10 years.

In this study 35% patients had neuropathy and 10% had vasculopathy. More than half of the patients (53.3%) had ulcer on dorsal surface of foot, remaining (46.66) had ulcer on plantar surface. Trauma was most common cause of foot ulcer in our study (65%). Thirty five percent patients had ulcers which were spontaneous in origin secondary to blister rupture or unnoticed trivial trauma.

All culture positive diabetic foot ulcer patients were included in the study. At the end of tenth day out of 30 patients in control group 24 (80%) patients had positive cultures and 6 (20%) had negative culture. Whereas in study group out of 30 patients 10 (33.3%) had negative culture, in remaining 20 (66.6%) patients culture remained positive. Although numerically study group had better infection control (10 Vs 6), it was not statistically significant, as the p value of 0.3811 derived by Chi-square test.

It was also observed that staph aureus was commonest organism accounting for 30% of wound infection; second commonest organism cultured was pseudomonas (20%).

## VI. Conclusion

The wound subjected to LLLT with conventional therapy showed decreased infection rate at 10<sup>th</sup> day of culture as compared to conventional dressing group alone. But this finding was not statistically significant. Large scale trials are required to know the anti-infective property of LLLT. Multicentre trials are required to know the anti-infective property of LLLT.

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