



**ORIGINAL RESEARCH PAPER**

**Surgery**

**ROLE OF OZONE THERAPY & SYMPATHETIC BLOCK AS A COMBINATION THERAPY FOR LOWER EXTREMITY DIABETIC ULCER**

**KEY WORDS:** Ozone therapy, Sympathetic block, Diabetic foot ulcers

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**ABSTRACT**

Diabetic foot ulcers are one of the most common cause of morbidity and mortality in developing countries like India due to illiteracy, bare foot walking, low socioeconomic status and inadequate facilities for diabetes care. Treatment of diabetic foot ulcers needs multidisciplinary team approach with treatment modalities like daily dressings, debridement, antibiotic coverage, blood glucose control and management of peripheral arterial insufficiency. Traditional modalities usually fail to provide adequate management thus, resulting into chronic wounds and amputations. This also takes toll on life of patients due to economic burden faced by them. Medical Ozone and Sympathetic block, both have properties which cause vasodilation with improved oxygenation making it beneficial in speeding up recovery process with better quality of pain management. When both these modalities used in combination better results were yielded.

**INTRODUCTION**

Diabetes mellitus is a metabolic disease characterized by hyperglycaemia resulting from defects in insulin secretion or insulin action or both. Complications associated with diabetes mellitus arise mainly due to the disruption of the vascular system, resulting in inadequate circulation to the peripheral body thus, placing the foot at higher risk of ulceration and infection. In developing countries like India rate of morbidity and mortality is high due to illiteracy, bare foot walking, low socioeconomic status and inadequate facilities for diabetes care.[1] This study was carried out with the aim to evaluate the role of unconventional treatment modalities like sympathetic block and ozone therapy for the treatment of diabetic foot ulcers as their vasodilatory and hypoglycemic properties results in faster healing with better pain management.

**MATERIALS & METHODS**

Source of data - All eligible cases admitted with complaints of diabetic foot ulcers in Surgical ward at D.Y. Patil Hospital and Research Institute, Kolhapur during the study period.

Study design: Prospective Longitudinal Study.

Sample size: 60 Patients

Study period: September 2016 to September 2018 Inclusion criteria

1. Patients with informed, written and valid consent, willing to participate in study.
2. Diabetic foot ulcer of Wagner's Classification of ulcers 1, 2 and 3
3. Ulcers of size not more than 10x10 cm.

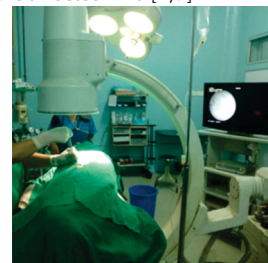
**EXCLUSION CRITERIA**

1. Ulcers with Gangrene
2. Presence of uncontrolled co-morbidities

With informed written and valid consent, 60 diabetic patients with lower limb ulcers were included in this study. Local examination of wound, with characteristics like location, extent, size, shape, edge, margin, wound area, surrounding skin, discharge and edema is done. Along with it all the routine lab investigations, importantly FBS, PPBS, HBA1C, urine ketone, serum acetone are sent. Wagner's Classification is taken into consideration for classification of ulcers. After initial assessment, patients are subjected to sympathetic block and ozone therapy sessions, 5 sessions of sympathetic block (on every 5<sup>th</sup> day) and 10 sessions of ozone therapy (on every 3<sup>rd</sup> day) within a period of 30 days. Additionally periodic surgical debridement, daily dressing with antibiotic coverage is provided to ensure faster healing. Glycaemic control is obtained. Ulcer examination is done at the beginning of study and on days 10, 20 and 30 of follow-up. Complete healing of ulcer is considered as the end point of study.

Lumbar sympathetic blocks are given in three stages; diagnostic block, prognostic block and therapeutic block. A needle is inserted

aiming towards the anterior aspect of the vertebral bodies of L2 or L3 under C-Arm guidance (Figure.1). Then medication is injected from here to achieve lumbar sympathetic blockade. Lidocaine 1% is preferred for diagnostic blocks, while bupivacaine 0.25–0.5% is preferred for other blocks. Neurolytic solutions like phenol and alcohol are used for therapeutic block. Patient's vitals are monitored throughout the session. The greatest indication of a successful lumbar sympathetic block is a 2°C to 3°C rise in the temperature of the affected limb.[2,3]



**Figure.1 Lumbar Sympathetic Block**



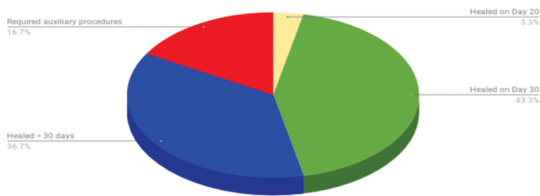
**Figure.2 Ozone Therapy**

Ozone is generated by a controlled flow of oxygen passed through a corona discharge in the ozone generator. Channel coming through ozone generator is connected to a low-pressure plastic bag enclosing affected limb. [4] After connecting inflow another channel for outflow is created and connected to ozone destructor (Figure.2). While connecting inflow channel, care must be taken in positioning of channel in order to maximize flow over wounded area. At the beginning ozone is supplied at concentration of 20–30µg/ml which is after raised to 80–100µg/ml. Session is continued for 30 minutes.

Before initiating the treatment and at the end of study patients are asked to report their pain with the Numeric Rating Scale (NRS) for pain, with 0 representing one pain extreme (e.g., "no pain") and 10 representing the other pain extreme (e.g., "pain as bad as you can imagine" and "worst pain imaginable").[5]

**OBSERVATIONS AND RESULTS**

60 patients were included in study among them 19 patients had Grade 1 Ulcers, 22 patients had Grade 2 Ulcers and 19 Patients had Grade 3 ulcers (by Wagner's classification). Out of 19 patients (31.66%) of Grade 1 ulcers 16 patients (26.66%) had complete wound healing within 30 days period while 3 patients (5%) needed more than 30 days for complete wound healing. i.e. 100% Grade 1 patients resulted in complete healing of ulcer. In 22 patients (36.66%) of Grade 2 ulcers, 12 patients (20%) had complete wound healing within 30 days period and 10 patients (16.66%) needed more than 30 days for complete wound healing i.e. 100% Grade 2 patient also resulted in complete healing of ulcer. 19 patients (31.66%) had Grade 3 ulcers, 9 patients (15%) had complete wound healing but took more than 30 days for the same and 10 patients (16.66%) required auxiliary procedures. Out of which, only 3 patients needed below knee amputation & in rest of cases extent of amputation remain limited to toes



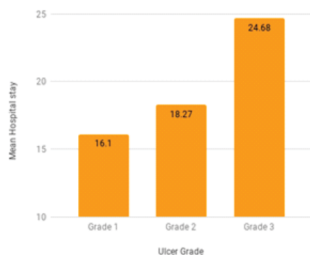
**Chart.1 Distribution Of Patients According To Time Taken By Ulcer To Heal.**

It is evident from Chart.1 that out of 60 patients 2 patients (3.33%) had complete wound closure by Day 20 while 26 patients (43.33%) had complete wound closure by day 30. That means total 28 (46.66%) ulcers had complete healing within 30 days period. In remaining patients, 22 patients (36.66%) complete wound healing was final outcome while 10 patients (16.66%) needed further surgical interventions. When calculated cumulatively, it was noted that among all patients, 28 patients (46.66%) consisting of Grades 1,2 and 3 by Wagner's Classification had complete wound healing within 30 days period while 22 patients (36.66%) needed more than 1 month for complete wound healing & Only 10 patients (18.33%) needed auxiliary procedures.

**Chart.2 Comparison Of Mean Wound Area**



**Chart.3 Comparison Of Mean Hospital Stay**



Mean wound area on day of admission was  $38.01 \pm 6.22 \text{ cm}^2$  which reduced to  $26.97 \pm 3.96 \text{ cm}^2$  on day 10 ,  $13.70 \pm 7.65 \text{ cm}^2$  on Day 20 and on day 30 it was  $12.45 \pm 4.47 \text{ cm}^2$ .(Chart.2) Data was analyzed with One-way ANOVA test & a reduction in mean

wound area is observed with  $P < 0.0001$  which is considered statistically significant. One of the main objectives of this study was to reduce the duration of bed stay of patients. Mean duration of hospital stay of all patients ( $n=60$ ) was  $19.61 \pm 6.32$  days specifically  $16.10 \pm 03.80$  days for Grade 1,  $18.27 \pm 05.45$  days for Grade 2 ulcers & While in Grade 3 ulcers it was  $24.68 \pm 06.31$  days (Chart.3). When compared using One-way ANOVA test, it is observed that mean hospital stay of grade 1 patients was significantly less compared to Grade 2 and Grade 3 ulcers with  $P < 0.0001$ . Pain Scores were also analyzed, which showed drastic reduction. Mean pain score at the time of admission was  $7.05 \pm 1.04$  while post-procedure pain score was  $1.18 \pm 1.24$ .

**DISCUSSION**

Diabetes mellitus is a major cause of mortality and disability due to macro vascular and micro vascular complications. Disruption of the vascular system results in inadequate circulation to the peripheral body thus placing the foot at higher risk of ulceration and infection. Diabetic foot ulcer is one of the most common complications of diabetes affecting more than 25% of people with diabetes in their lifetime and if not treated properly, can lead to complications such as infection, gangrene & amputation.[1] Treatment of diabetic foot ulcers mostly depends on traditional modalities which often results in longer hospital stay and complications mentioned before.

Many studies have been carried out till date evaluating effects of ozone therapy and sympathetic block individually. These studies have reported the use of ozone as a local applicant over the wounds as well as its use in systemic therapy and autohemotherapy. Historically, Ozone therapy has been in use since 18<sup>th</sup> century. The first therapeutic ozone applications were initiated around 1870. During World War I, ozone was used to treat wounds and gangrene decubitus ulcers.[6] As the application of ozone showed positive research, efforts were made to widen the use of medical ozone. Repeated administration of ozone in non-toxic doses play a role in the control of diabetes and its complications. Medical ozone acts by inactivating bacteria, viruses, fungi, yeast and protozoa, stimulating oxygen metabolism and by activating the immune system.[7] Fungal infections delay wound healing in diabetic foot ulcers. In these patients antifungal therapy is effective in controlling infection, but not effective in colonization on the other hand ozone therapy is better for colonization, thus preventing infection.[8]The anti-diabetic effect of ozone therapy is attributed to its antioxidant properties which causes an increase in insulin sensitivity, and prevent oxidative stress associated with diabetes. Ozone therapy can reduce the oxidative stress by normalizing the organic peroxide levels by activating superoxide dismutase. Ozone stimulates process like pentose phosphate shunt and aerobic glycolysis which are suppressed in diabetes, this makes the cellular membranes more permeable for glucose allowing more glucose to enter tissues, thus reducing hyperglycemia. Also progression of the disease is slowed down by preventing neuropathies, arthropathies, angiopathies associated with low entry of glucose into the cell. Ozone also has immunomodulating properties making it more useful in IDDM, which is characterized by the liability to chronic infections because of suppressed immunity. All these effects delay serious complications associated with diabetes, and improves the quality of life of patients with diabetic foot ulcers.[8]

Diabetic neuropathy is a common complication of both type 1 and type 2 diabetes, which affects over 90% of the diabetic patients and pain is one of the main symptoms of diabetic neuropathy. Management of diabetic neuropathy remains an enormous challenge to both the patients and the clinicians. For better pain management patients are also subjected to sympathetic blocks. A lumbar sympathetic block is the injection of medication into the sympathetic nervous system at the lumbar level. In addition to pain control these blocks increase circulation to a lower limb, thus facilitate healing in conditions such as diabetic neuropathy or slow healing wounds.[2] Sometimes a sympathetic innervation may be unnecessarily stimulated as a result of injury to the body. In this situation, poor circulation to that limb results from the prolonged constriction of the involved sympathetic nerve. If the sympathetic

nerve impulse is blocked, the blood vessels dilate, circulation is improved and pain relief occurs. Sympathetic Block causes vasodilation, and it is important in exposing a wound to increased blood flow, which is accompanied by necessary inflammatory cells and factors that prevent infection. Increased blood flow is a critical first step in the process of wound healing. This will bring to the affected muscle the much-needed nutrients and oxygen essential to start the reparative process. This makes the widening of blood vessels vital in healing; without vasodilation, healing will not proceed. lumbar sympathetic block therapeutically stimulates healing as heat which widens the blood vessel diameter, which increases blood flow and jump starts the healing process.[9] An ideal treatment modality should be able to control BSL level, infections & manage pain. All these aims are achieved by both elements of this combination therapy.

Another issue faced by patients with diabetic foot ulcers which increases economic burden over them is prolonged duration of hospital stay. Lengthier hospital stay leads to increase in mortality rate.[10] In India only a fraction of population is covered by health insurance while rest of the population have to bear cost of treatment by themselves. According to a survey done in 2010, only about 19 % of the population was covered health insurance including by the country's central and state government-sponsored health insurance, the number raised to only 25% when private insurance and other schemes were included. This means despite of government schemes and insurances economic burden of diabetic foot ulcers falls mostly on individual. It is estimated that by 2025, in developing countries, most of the patients with diabetic foot will fall in the age group 45 to 64 year which is a big threat to the economic productivity of the country and the income-earning ability of individuals. As India plans to achieve universal health coverage by 2022, higher costs of management of diabetes and its complications seems to be main obstacle while achieving this aim.[11] To tackle this, hospital stay should be minimized, which was reduced to  $19.61 \pm 6.32$  days (n=60) in this study.

Results obtained in this study were compared to a study conducted by Martínez-Sánchez<sup>2</sup> in 2005, in which he compared ozone therapy with antibiotic therapy for the treatment of diabetic foot ulcers. He observed full wound closure of ulcers in 39 of the 51 (77%) participants in the ozone group and 34 of the 49 (69%) participants in the antibiotic group. Here in this study among all patients 46.66% had full wound closure within 30 days period, 36.66% patients needed more than 1 month but eventually resulted in full wound closure. In total patients, 81.67% ulcers resulted in full wound closure while only 18.33% patients needed auxiliary procedures. Our results are in accordance with this study however, aforementioned study was not time bounded while this study main emphasis was to reduce hospital stay.

Another fatal outcome of diabetic foot ulcers is amputations. Depending upon grading of wound and infections which directly depends on hospital stay, extent of amputation is decided. Data suggests that approximately 39% patients end up in losing their toes or limb. This further results in psychological as well as economic disaster for the patient and his family. However, in this study only 8% patients end up with losing their limb & in 34 % patients, in which surgical interventions were done, extent of amputation was significantly reduced.

## CONCLUSION

Time taken by diabetic foot ulcer to heal after this combination therapy is significantly lower thus reducing the hospital & economic burden of patients. This therapy showed promising results in wound healing especially in grade 1 and grade 2 ulcers (by Wagner's classification). Significant reduction in wound area was observed at the end of follow-up period. 34 % patients required other surgical interventions however, extent of amputation was significantly reduced and extent remained limited to toes and Only 8% patients end up losing their limb. This combination therapy was successful in providing better quality of pain management. Considering all results, it is safe to say that ozone therapy and sympathetic block when combined together, have a definite role in the treatment of diabetic foot ulcer. This

combination when used in treatment of diabetic foot ulcers, may result in faster wound healing with better quality of pain management, making it a cost-effective modality of treatment for diabetic foot ulcer. However, this study was conducted with 60 patients. In order to make this treatment modality widely acceptable, a greater number of trials with larger sample sizes must be conducted.

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**Conflict of interest: None declared.**

**Ethical approval: The study was approved by the Institutional Ethics Committee.**

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