



## COMPARISON OF PROTEIN SYNTHESIS INHIBITING ANTIBIOTICS VERSUS CELL WALL INHIBITOR ANTIBIOTICS FOR TREATMENT OF DIABETIC FOOT.

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**ABSTRACT:** Diabetic foot infection is a form of soft tissue infection which rapidly involves the tissues of foot. It can affect all parts of foot but pressure areas of foot are commonly involved. Early diagnosis and treatment with proper antibiotic with or without surgical intervention are vital because of high morbidity. **Objectives:** To compare efficacy of protein synthesis-inhibiting antibiotics (clindamycin) versus cell wall inhibitor (imipenem) for treatment of diabetic foot infections as empirical therapy in term of clearance of infection and wound healing. **Study Design:** Randomized Clinical Trial. **Setting:** Surgical department POF Hospital. **Period:** January 2013 to January 2017. **Material & Methods:** Total of 94 patients of diabetic foot infection were included in the study through non-probability consecutive sampling. Divided into two groups each have 47 patients. In group A patients were given intravenous (i/v) imipenem while in group B intravenous (i/v) clindamycin was given. Pre and post treatment culture from wound was taken and healing observed in form of granulation tissue. **Results:** Group A patients (imipenem group) wound healing occurred in only 9 (19.1%) patients and in group B (clindamycin group) treatment was effective in 34 (72.3%) patients (P=0.001). Clearance of infection occurred in 31.91% (15) in group A and 80.85% (38) in group B (P=0.001). **Conclusion:** Protein synthesis inhibitor antibiotics have shown increased efficacy for control of infection and healing as compared to cell wall inhibitor antibiotics.

**Key words:** Cell Wall Inhibitors Antibiotics, Diabetic Foot Infection, Protein Synthesis Inhibiting Antibiotics.

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### INTRODUCTION

Diabetic foot diseases affect 6% of patients with diabetes mellitus.<sup>1</sup> Diabetic foot wound infection is the most common cause of admission related to diabetes mellitus and account for 80% of non-traumatic lower limb amputations. A study in 2008 shows that half of recent onset of diabetic foot ulcer are infected on presentation.<sup>2</sup> Most common cause of diabetic foot infection is foot ulcer, followed by foot callus and foot deformity.<sup>3</sup>

Most common bacteria involved in diabetic foot infection include staphylococcus aureus (17%), Proteus (15%), pseudomonas aeruginosa (13%), group B Streptococcus (11%) and Bacteroides s (1%).<sup>4-7</sup>

Early administration of antibiotics is required

in diabetic foot infection to avoid progression of infection. Tissue sample or abscess from the wound must be taken for culture and sensitivity. Empirical antibiotic should be started without waiting for culture and sensitivity report. Empiric antibiotic should base on the severity of the infection and the local prevalence of microbial organisms.<sup>8</sup>

There are some criteria for empirical antibiotics in diabetic foot, first it should cover staphylococcus aureus and methicillin resistant staphylococcus aureus (MRSA) should be considered, second it should have coverage of pseudomonas aeruginosa, it is one of common organism in diabetic foot, third obligatory anaerobes should be considered but rarely they are sole agent in diabetic foot usually are part of mixed infection

with pseudomonas. One clue of their presence is feculent odour.<sup>9</sup>

Some studies show use of clindamycin for MRSA and pseudomonas.<sup>9</sup> While some studies show that imipenem is most effective.<sup>5,10</sup> Few studies shows vencomycin<sup>11</sup> or piperacilline is a better choice.<sup>12</sup>

Aim of our study is to evaluate better empirical antibiotic for diabetic foot in our setup based on antibiotic resistance and its response to wound healing.

## MATERIAL & METHODS

The study was started after taking approval from hospital ethics committee. This randomized clinical trial, conducted from 2013 to 2017 in surgical department of P.O.F's Hospital Wah Cent. Total of 94 patients of both gender age from 20 to 70 years with moderate diabetic foot infection were included in the study through non-probability consecutive sampling. Moderated diabetic foot is diagnosed clinically by consultant surgeon following Infectious Diseases Society of America (IDSA) and International Working Group on the Diabetic Foot (IWGDF) classification. After admission patients are divided into two equal groups A and B. In group A (n=47) patients were given i/v imipenem while in group B (n=47) i/v clindamycin was given for 5 days.

Patients with mild or sever diabetic foot infection, chronic limb ischemia, renal failure and patients receiving radiation therapy or chemotherapy were excluded from the study.

Informed written consent was taken from each patient. Patients were randomly divided into two groups by using computer generated tables. One group received injection imipenem 500 mg I/V 8 hourly and the other group received injection clindamycin 600 mg I/V 8 hourly. All patients from both groups underwent surgical debridement and abscess drainage if required, tissue or abscess was taken from every patient before starting the antibiotic for culture and sensitivity. Dressing was changed every day. During treatment blood sugar levels were maintained by insulin and monitored

by BSF and BSR. Tissue culture was taken on 5th day to confirm eradication of organism, after the wound examination was done by consultant surgeon for formation of granulation tissue. Findings were documented in predesigned Performa.

The data was entered in SPSS version 21. Descriptive statistics were used to calculate means  $\pm$  standard deviation for age. Frequencies with percentage were calculated for gender, type of organisms and efficacy. Chi-square test was used to compare the two groups in term of efficacy. P value  $< 0.05$  was considered significant. Effect modifiers like age, gender and type of organisms were controlled using stratification. Post stratification Chi-square test was applied.

## RESULTS

In our study total of 94 patients suffering from moderate diabetic foot infection were included, divided into two equal groups of 47 patients each. Group A patients received cell wall inhibitor antibiotics (imipenem) and group B patients received protein synthesis inhibitor antibiotics (clindamycin). Patients included in group A had mean age of  $53.46 + 5.88$  years. Minimum age was 41 years and maximum age was 64 years. Patients included in group B had mean age of  $54.36 + 5.38$  years. Minimum age was 44 years and maximum age was 66 years.

In Group A out of 47 patients; 31 (66%) were male and 16 (34%) were female and in group B, 32 (68%) were male and 15 (32%) were female.

Among patients in group A, 66 % ( 31) showed staphylococcus aureus monomicrobial and 34 % ( 16) showed pseudomonas aeruginosa, staphylococcus aureus, proteus, and klebisella polymicrobial. Among patients in group B, 68% (32) patients were staphylococcus aureus positive monomicrobial and 32% (15) patients had pseudomonas aeruginosa, staphylococcus aureus, proteus, and klebsiella polymicrobial. In group A 9 (19.1%) had granulation tissue at 5<sup>th</sup> day and in group B 34(72%) patient had granulation tissue formation ( $p=0.0001$ ), so

having effective treatment in term of wound healing. (Table-I).

Clearance of infection occur in 31.91% (15) in group A and 80.85% (38) in group B (P=0.0001). (Table-V).

Results were stratified on basis of gender, age and type of organisms.

Group of Patient	Complete Healing of Wound		Total	P-Value
	Yes	No		
Cell Wall inhibitor antibiotic	09	38	47	0.0001
Protein synthesis inhibiting antibiotic	34	13	47	
Total	43	51	94	

**Table-I. Comparison of treatment in both groups. n = 47**

Gender of Patient		Complete Healing of Wound		Total	P-Value
		Yes	No		
Male	Cell Wall inhibitor antibiotic	04	27	31	0.0001
	Protein synthesis inhibiting antibiotic	23	09	32	
Female	Cell Wall inhibitor antibiotic	05	11	16	0.019
	Protein synthesis inhibiting antibiotic	11	04	15	

**Table-II. Stratification in both groups on basis of gender.**

Age in Decades (Decades)		Complete Healing of Wound		Total	P-Value
		Yes	No		
40-49 years	Cell Wall inhibitor antibiotic	01	11	12	0.0001
	Protein synthesis inhibiting antibiotic	08	01	09	
50-59 years	Cell Wall inhibitor antibiotic	07	22	29	0.001
	Protein synthesis inhibiting antibiotic	20	10	30	
60-69 years	Cell Wall inhibitor antibiotic	01	05	06	0.031
	Protein synthesis inhibiting antibiotic	06	02	08	

**Table-III. Stratification in both Groups on basis of Age in decades.**

Type of Organism		Complete Healing of Wound		Total	P-Value
		Yes	No		
Staphylococcus aureus monomicrobial	Cell Wall inhibitor antibiotic	05	26	31	0.0001
	Protein synthesis inhibiting antibiotic	24	08	32	
Streptococcus pyogenes & Staphylococcus aureus, poly microbial	Cell Wall inhibitor antibiotic	04	12	16	0.020
	Protein synthesis inhibiting antibiotic	10	05	15	

**Table-IV. Stratification in both groups on basis of type of organisms. n = 47**

Group of Patient	Culture negative after 5 days		Total	P-Value
	Yes	No		
Cell Wall inhibitor antibiotic	15	32	47	0.0001
Protein synthesis inhibiting antibiotic	38	9	47	
Total	53	41	94	

**Table-V. Culture negative after antibiotic treatment. n = 47**

## DISCUSSION

Diabetic foot infection is defined as infection in diabetic patient below ankle characterized by signs of inflammation and/or purulence. It is the most common complication of diabetes leading to hospital admission. It is divided into mild, moderate or severe infection. Moderate and severe infections need hospitalization. The most common organism isolated is staphylococcus aureus.<sup>13</sup>

Another study conducted in 2019 for causative organism and empirical antibiotic consideration in diabetic foot infection. Study shows most common organism was staphylococcus aureus.<sup>14</sup> In our study the most common organism is staphylococcus aureus in both groups as monomicrobial as well in polymicrobial infection.

In 2019 a retrospective study was conducted to evaluate the treatment of moderate diabetic foot infection. They compared amoxicillin/clavulanate + metronidazole (group-1) with clindamycin + metronidazole (group 2) for cure of diabetic foot infection. Group one had 80% cure rate and group 2 had 100% cure rate. Our present study shows similar result as in group B clindamycin for diabetic foot Infection with healing in 72%. The difference is probably due to mitranidazole in addition to clindamycin.<sup>15</sup>

Lipsky in 1999 for evidence based antibiotic therapy of diabetic foot infection suggested that for moderate diabetic foot infection clindamycin and ciprofloxacin should be used.<sup>16</sup> Response to clindamycin in eradicating infection in moderate infections suggests its efficacy over period of time in present study.

Not direct comparison between imipenum and clindamycin is found in literature but other antibiotics are compared.

Another study conducted in 2019 for antibiotic sensitivity in diabetic foot 125 patients included in study, staphylococuss aureus and pseudomonas were the two most common organisms and linzolid was the most effective antibiotic with 100% cure rate followed by imipenum which had

75% cure rate.<sup>17</sup>

In our study 19.1% patients showed cure on imipenum including monomicrobial and polymicrobial. Which is very less as compared to international figures given above. This may be due to excessive use resulting in resistance.

A study published in 2018 microbiology and antimicrobial therapy for diabetic foot infection, author recommends clindamycine in moderate diabetic foot infection if methicillin resistant staphylococcus aureus (MRSA) is suspected and in sever diabetic foot infection clindamycin with other antibiotic.

Author also refers to a Korean study in which MRSA has high prevalence and recommended clindamycin for empirical use.<sup>18</sup>

## CONCLUSION

Debridement along with antibiotics are the key to prevent diabetic foot infection from extending into surrounding tissues. Clindamycin i.e. protein synthesis inhibitor antibiotic has shown increased efficacy for control of infection as compared to cell wall inhibitor antibiotics. More studies are needed to be carried out to compare efficacy of both group of drugs to identify more efficacious drugs for treatment of moderate diabetic foot infection.

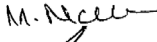


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