



STUDY ON INSULIN AND ORAL HYPOGLYCEMIC AGENTS USED IN THE TREATMENT OF TYPE-2 DIABETIC WOUND HEALING – A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Diabetic foot ulcer can lead to gangrene and even require limb amputation due to a number of pathological consequences, including neuropathy, peripheral vascular disease, foot ulceration, and infection with or without osteomyelitis. Diabetes-related wound healing has been reportedly treated with insulin and oral hypoglycemic medications. A prospective observational study was conducted to analyze the usage of insulin and oral hypoglycemic agents used in treatment of diabetic wound healing in Cuddalore Government Medical College and Hospital. The review of treatment charts and wound healing of diabetic foot ulcer patients from October 2023- March 2024 was done. By using Descriptive statistical analysis, the gathered data was examined. In our study, 50 – 59 years old patients were highly affected by diabetic foot ulcer (male > female). Most commonly Insulin and oral hypoglycemic agents combination therapy was used to treat diabetic wound healing (44.7%). It has better wound healing effect than monotherapy of oral anti-diabetic drug or insulin therapy.

KEYWORDS : Surgery; Diabetic foot ulcer; Insulin.

INTRODUCTION

Diabetic foot is a group of conditions where tissue changes or ulcers due to micro-trauma are caused by neuropathy, ischemia, and infection⁽³⁾. A group of metabolic diseases known as diabetes mellitus (DM) are typified by hyperglycemia, inadequate or excessive insulin secretion, or glucagon secretion. It is a chronic, non-communicable illness with multiple underlying causes. Adult mortality and the greatest degree of impairment are caused by this disorder⁽⁴⁾. With increased levels of pro-inflammatory cytokines and proteases as well as decreased growth factor expression, chronic diabetes wounds are stuck in a chronic inflammatory state⁽²⁾.

Therefore, despite the fact that over 70% of diabetic patients consistently use anti-diabetic drugs-which cost more than \$50 billion annually-little is known about how these medications affect the results of wound healing, either directly by influencing the cells that aid in the healing of wounds or indirectly by influencing the systemic mechanisms that influence the healing process⁽²⁾.

Diabetes is characterized by decreased insulin activity. Glycemic control is achieved with systemic insulin treatment. Given that insulin is essential for protein synthesis, glucose metabolism, and the proliferation and differentiation of several cell types, suggested that the hormone may have an impact in the wound-healing processes⁽²⁾.

INSULIN

Rapid-acting insulin: Within 15 minutes of injection, this form of insulin begins to function. Its effects last for three to five hours, and it takes sixty minutes to reach their peak. Short-acting insulin: It takes this kind between thirty and sixty minutes to start acting in your bloodstream. Its effects can last for three to six hours after it peaks in two to three hours. It is also called regular-acting insulin.

Intermediate-acting insulin: The intermediate kind takes two to four hours to begin functioning. It operates for 12 to 16 hours, reaching its peak in 8 hours. Long-acting insulin: This kind requires the longest to begin operating. It may require two to

four hours for the insulin to enter your bloodstream.

Pre-mixed: This is a blend of two distinct forms of insulin: one that regulates blood sugar during meals and another that does so in between meals⁽⁵⁾.

Oral Hypoglycemic Agents:

1. Biguanides - Metformin.
2. Thiazolidinediones - Pioglitazone, Rosiglitazone.
3. Meglitinides - Repaglinide, Nateglinone.
4. Sulfonylureas - Glipizide, Glimepiride, Glyburide, Gliclazide.
5. Alpha glucosidase inhibitor - Acarbose, Voglibose, Miglitol.
6. DPP-4 inhibitors - Vildagliptin, Linagliptin, Sitagliptin, Saxagliptin, Alogliptin.
7. SGLT 2 inhibitors - Dapagliflozin, Canagliflozin, Ipragliflozin.
8. Dopamine D2 receptor agonist - Bromocriptine⁽¹⁾.

Wagner- Meggitt Classification Of Diabetic Foot:

- Grade 0: Foot symptoms like pain only
- Grade 1: Ulcerations on the skin and subcutaneous tissue that are superficial
- Grade 2: Deep ulcers involving ligaments, muscles and tendons
- Grade 3: Bone related ulcer
- Grade 4: Forefoot gangrene
- Grade 5: Full-foot gangrene⁽⁸⁾.

METHODOLOGY

Study site was hospital based and involves surgery patients in the department of surgery at Government Cuddalore Medical College and Hospital (GCMCH), a 1250 bedded tertiary care teaching hospital located in rural South India, Chidambaram.

Study period involves 6 months [October 2023 to March 2024] with a Prospective Observational study design. Proforma (Data collection form) was developed for the data collection purpose.

Data collected from case sheets of diabetic foot ulcer patients

(In-patients only) and personal interaction with patients of Government Cuddalore Medical College and Hospital.

Selection criteria for the study includes patients of either gender with Type II diabetes, patients aged between 30 and 70 years, patients with normal range of laboratory findings and patients having Wagner's classification of diabetic wound grade 1 to 3 were included in this study. Patients with other comorbidities, patients with Wagner's classification grade 4 and 5, patients who were over 70 years and younger than 30 years were excluded from this study.

A total of 85 diabetic foot ulcer patients were observed and the gathered data was analyzed using a suitable statistical tool and Spreadsheet had been used to generate tables to provide significant results.

RESULT AND DISCUSSION

Based on selection criteria, 85 patients were included in this study.

Gender Wise Distribution:

Table 1: Gender Wise Distribution

S. No	Gender	No. of patients	Percentage (%)
1.	Male	54	64
2.	Female	31	36

In our study, 85 patients were enrolled. Among these patients, male patients are 54 (64%) and female patients are 31 (36%). In our study, the prevalence of diabetic foot ulcer found to be 28% more in male patients than in female patients.

Age Wise Distribution:

Table 2: Age Wise Distribution

S. No	Age group (years)	No. of patients	Percentage (%)
1.	30-39	09	10.5
2.	40-49	15	17.7
3.	50-59	35	41.2
4.	60-70	26	30.6

Higher prevalence of diabetic foot ulcer was reported in patients among the age group of 50-59 years i.e., 35 (41.2%) patients, followed by 60-70years 26 (30.6%) patients and then 40-49 years 15 (17.7%) patients.

Distribution Based On Wagner's Scale:

Table 3: Distribution Based On Wagner's Scale

S. No	Grade	No. of patients	Percentage (%)
1.	Grade-0	-	-
2.	Grade-1	22	26
3.	Grade-2	37	43.5
4.	Grade-3	26	30.5

Wagner's scale was used to grade the 85 patients who were enrolled in this study and had been diagnosed with diabetic foot ulcer.

Most of the ulcer was predominantly grade 2 to 3. This suggests decreased awareness of foot care among the study population.

Distribution Of Hypoglycemic Drugs:

Table 4: Distribution Of Hypoglycemic Drugs

S. No	Drugs	No. of patients	Percentage (%)
1.	Insulin	29	34.1
2.	Oral hypoglycemic agents	18	21.2
3.	Both	38	44.7

In our study, 29 (34.1%) patients were treated with insulin, 18 (21.2%) patients were treated with oral hypoglycemic agents and 38 (44.7%) patients were treated with both insulin and oral hypoglycemic agents.

Distribution Of Insulin:

Table 5: Distribution Of Insulin

S. No	Insulin	No. of patients	Percentage (%)
1.	Human Actrapid	29	43.2
2.	Human Monotard	18	26.9
3.	Human Mixtard	20	29.9

In our study, Insulin was used to treat 67 patients. Out of 67 patients, 29 (43.2%) patients treated with Human Actrapid and 18 (26.9%) patients treated with Human Monotard and 20 (29.9%) patients were treated with Human Mixtard.

Distribution Of Oral Hypoglycemic Drugs:

Table 6: Distribution Of Oral Hypoglycemic Drugs

S. No	Drugs	No. of patients	Percentage(%)
1.	Metformin	18	32.2
2.	Glimepiride	0	0
3.	Metformin and Glimepiride	27	48.2
4.	Metformin and Glibenclamide	05	8.9
5.	Pioglitazone + Metformin + Glimepiride	02	3.5
6.	Voglibose + Metformin + Glimepiride	03	5.4
7.	Dapagliflozin + Sildagliptin	01	1.8

Considering the oral hypoglycemic drugs, 18 (32.2%) patients were treated with Metformin, 27 (48.2%) patients were treated with Metformin and Glimepiride, 05 (8.9 %) treated with Metformin and Glibenclamide, 02 (3.5%) patients were treated with Pioglitazone + Metformin + Glimepiride, 03 (5.4%) patients were treated with Voglibose + Metformin + Glimepiride, 01 (1.8%) patients were treated with Dapagliflozin + Sildagliptin.

DISCUSSION

In our study, the prevalence of diabetic foot ulcer found to be 28% more in male patients than in female patients which was also found by Nasibeh vantankhah at Portland⁽⁵⁾.

Higher prevalence of diabetic foot ulcer was reported in patients among the age group of 50-59 years i.e., 35 (41.2%) patients, followed by 60-70 years 26 (30.6%) patients. This is similar to the study conducted by Balakrishnan⁽⁷⁾.

Wagner's scale was used to grade the 85 patients who were enrolled in this study and had been diagnosed with diabetic foot ulcer. Most of the ulcer was predominantly grade 2 to 3. This suggests decreased awareness of foot care among the study population.

The study results shows, 29 (34.1%) patients were treated with insulin, 18 (21.2%) patients were treated with oral hypoglycemic agents and 38 (44.7%) patients were treated with both insulin and oral hypoglycemic agents.

Insulin was used to treat 67 patients. Out of 67 patients, 29 (43.2%) patients treated with Human Actrapid and 18 (26.9%) patients treated with Human Monotard and 20 (29.9%) patients were treated with Human Mixtard.

Considering the oral hypoglycemic drugs, 18 (32.2%) patients were treated with Metformin, 27 (48.2%) patients were treated with Metformin and Glimepiride. In this study, dual therapy is most commonly used than monotherapy, which is similar to research carried out by Nithin baby at Karnataka⁽⁸⁾.

According to this study, administering insulin improves the reduction of wound size in diabetic ulcers. Even though OHA might boost insulin release, administering insulin directly promotes wound healing. Therefore, combined therapy had

better wound healing effect.

CONCLUSION

Data from this study have been used to inform the use of oral hypoglycemic medications and insulin in the management of diabetic wound healing. Diabetic foot ulcer were treated by oral hypoglycemic agents, insulin and combination of both were prescribed to treat severe glycemic condition. We concluded that, in the treatment of type 2 diabetic wound healing insulin with oral hypoglycemic agents have better wound healing compared with monotherapy.

REFERENCES

1. Akyol AD. Reliability and validity of Turkish version of Quality of life index in stroke patients. *Annals of nursing and practice* 2015; 2(2): 1-6.
2. Centers for Disease Control and Prevention. "National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2014." Retrieved 1 July 2022, from <http://www.cdc.gov/diabetes/pubs/statsreport14/nationaldiabetes-report-web.pdf>.
3. Del Castillo, T.R.A.; Fernández, L.J.A.; Del Castillo, T.F.J. Diabetic foot clinical practice guide. *Med Pub J*. 2014, 10, 1–17.
4. Echeverria, G. V; Sotomayor, L.C.; Norambuena, G.M.; Vidal, VP; Campos, G.A. Diabetic foot. *Rev. Hosp. Clin. Univ. Chile* 2016, 27, 207-219. Available online <https://www.redclinica.cl/Portals/0/Users/014/14/14/999.pdf> (accessed on 10 Feb 2022).
5. Nasibeh Vatankhah, M.D.,¹ Younes Jahangiri, M.D.,² Gregory J Landry, M.D.,¹ Gregory L Moneta M.D.,¹ Amir F Azarbal, M.D. Effect of Systemic Insulin Treatment on Diabetic Wound Healing *Wound Repair Regen.* 2017 Apr; 25(2): 288–291.
6. Nithin Baby, Cyril Tom, Asha Ann Joseph, Ann Abraham, Basavaraj K. Nanjwade Prescribing Pattern of Antidiabetic Drugs for Type 2 Diabetic in Tertiary Care Teaching Hospital March 2017, *World Journal of Pharmacy and Pharmaceutical Sciences* 6(3):1302-1315.
7. R. Balakrishnan, v. nagarajan comparative study of insulin with oral anti diabetic drug in type 2 diabetic wound healing. *Int j acad med pharm* 2023; 5(2); 394-396.
8. Tripathi, K. D. (2019). *Essential of medical pharmacology* (Eighth edition). Jaypee Brothers Medical publishers.