



ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2019; 8(6): 1196-1199
© 2019 TPI
www.thepharmajournal.com
Received: 04-04-2019
Accepted: 06-05-2019

B Sarah Fazeeha
Department of Pharmacy,
Annamalai University,
Chidambaram, Tamil Nadu,
India

P Nivetha
Department of Pharmacy,
Annamalai University,
Chidambaram, Tamil Nadu,
India

Albin Eldhose
Department of Pharmacy,
Annamalai University,
Chidambaram, Tamil Nadu,
India

Dr. G Veeramani
Department of Pharmacy,
Annamalai University,
Chidambaram, Tamil Nadu,
India

Dr. J Kabalimurthy
Department of Surgery, Rajah
Muthiah Medical College and
Hospital, Chidambaram, Tamil
Nadu, India

Correspondence
B Sarah Fazeeha
Department of Pharmacy,
Annamalai University,
Chidambaram, Tamil Nadu,
India

Dosing pattern of insulin in diabetic foot ulcer patients

B Sarah Fazeeha, P Nivetha, Albin Eldhose, Dr. G Veeramani and Dr. J Kabalimurthy

Abstract

Background: Among the Diabetic patients, 15% develop a foot ulcer and 12-24% of patients with diabetic foot ulcer require amputation. We compared the effectiveness of various dosing pattern of insulin statistically and planned to observe wound healing by proper glycemic control.

Methods: We compared the effectiveness of sliding and fixed scale dosing pattern of insulin and observed the wound healing by proper glycemic control. Total 50 subjects were recruited with Grade 3, 4 and 5 Diabetic foot ulcer (Wagner's classification) between 40 and 70 years of age who underwent surgery for management of Foot ulcer. The study was conducted in Tertiary care teaching hospital in Chidambaram. The study period was 6 month and it was a prospective observational study. The blood glucose level (Fasting, Random and Post prandial) of subjects were monitored on daily basis and observed.

Results: The study reports suggested that the major risk factors for Diabetic Foot Ulcer were Poor glycemic control, Male gender, left foot, Ulcer of size more than 2cm, Infection. The Statistical analysis was done using SPSS software by applying Chi-square test and Mann Whitney test. The results showed that there is no statistically significant difference between sliding and fixed scale dosing of Insulin and both methods are reliable in maintaining glycemic control.

Conclusion: Our study show that poor glycemic control is one of the major risk factor leading to chronic wound and thus proper glycemic control must be ensured by adjusting Insulin dose according to patients' Blood glucose level.

Keywords: Diabetic foot ulcer, hyperglycemia, neuropathy, insulin, sliding scale, amputation, wound debridement

Introduction

Diabetes, a metabolic disorder characterized by increased blood glucose level has now emerged pandemic. ^[1] There is an estimate that around 42 million cases of Diabetes are reported in India. The WHO has estimated that in 1995, 19.4 million individuals were affected by Diabetes in India which is expected to rise up to 57.2 million by the year 2025. ^[2] 80.9 million by the year 2030 is the revised figure. ^[3]

Diabetes is associated with many complications with peripheral neuropathy being the most distressing factor. Diabetic Foot Ulcer which is characterized by a classical triad of neuropathy, ischemia and infection affects about 15% of people with diabetes. ^[4] DFU puts a lot of mental strain on patients as it is prone to infections, chronicity and recurrence and also adds up their financial burden due to its long time follow up and treatment. ^[5] Once an ulcer has developed, there is a risk of wound progression which might eventually leads to amputation. A benign looking ulcer in a patient with diabetes often leads to amputation if not managed early.

Insulin is a peptide hormone secreted by the β cells of the pancreatic islets of Langerhans and maintains normal blood glucose levels by facilitating cellular glucose uptake, optimizing carbohydrate regulation, lipid and protein metabolism and promoting cell division and growth through its mitogenic effects. ^[6] Commercially available insulin preparations are classified as given in the following Table-1 ^[7]

Table 1 [7]: Types of Insulin preparations and Insulin analogues

Type	Appearance	Onset (hr)	Peak (hr)	Duration (hr)	Can be mixed with
Rapid Acting					
• Insulin lispro	Clear	0.2-0.3	1-1.5	3-5	Regular, NPH
• Insulin aspart	Clear	0.2-0.3	1-1.5	3-5	Regular, NPH
• Insulin glulisine	Clear	0.2-0.4	1-2	3-5	Regular, NPH
Short acting					
• Regular (soluble) insulin	Clear	0.5-1	0.5-1	6-8	All preparations(except insulin glargine/detemir)
Intermediate acting					
• Insulin zinc suspension	Cloudy	1-2	1-2	20-24	Regular
• Neutral protamine hagedorn	Cloudy	1-2	1-2	20-24	Regular
Long acting					
• Insulin glargine	Clear	2-4	-	24	None
• Insulin detemir	Clear	1-4	-	20-24	None

With obesity and diabetes reaching epidemic proportions in the developed world [8], the role of insulin resistance and its sequelae is gaining prominence. Understanding the role of insulin across a wide range of physiological processes and the influences on its synthesis and secretion, alongside its actions from the molecular to the whole body level, has significant implications for much chronic disease seen in a westernized populations today.

Lack of patient education which often leads to late diagnosis of the disease characterized by poor foot care, poor glycemic control and infection are the major risk factors contributing to poor wound healing of Diabetic Foot ulcer. “The human foot is a masterpiece of engineering and a work of art” quoted by Leonardo Da Vinci is so true. Hence taking care of God’s artwork is essential so as to avoid stigma, discrimination and other mental strains of people. This painful complication of Diabetes if often preventable by appropriate diet, foot care, Proper glycemic control, alcohol and smoking cessation and regular checkups.

Hyperglycemia interrupts the stages of normal wound healing by impeding blood flow and tissue oxygenation, causing endothelial dysfunction and prolonging a inflammatory state. Hyperglycemia also impairs neutrophil phagocytic function, which limits bacterial clearance and increase the risk of infection. Glycemic control has a significant impact on the risk of post-operative infection across a variety of surgical specialities. Post-operative glycemic control significantly influences the healing of deep sternal wound infection after open heart surgery and has been shown to have a similar on impact on healing in other forms of surgery.

Major surgery often leads to metabolic stress with an increase in catabolic hormone secretion and inhibition of anabolic hormones, particularly insulin which can lead to Transient hyperglycemia in patients with Diabetes. Since most of the

Diabetic Foot ulcer cases require surgical intervention such as wound debridement, wound closure, revascularization surgery and amputation, it is imperative to ensure proper glycemic control through insulin before and after surgical interventions. Our study aimed to focus on the glycemic part of the Diabetic foot ulcer by comparing the effectiveness of Insulin used for management of Hyperglycemia in patients undergoing surgery for Diabetic Foot ulcer.

Materials and Methods

This is a prospective observational study conducted in Department of Medicine , Rajah Muthiah Medical College Hospital, Annamalai University, Chidambaram, Tamil Nadu which is a 1400 bedded multi- specialty tertiary care teaching hospital located in rural South India. Study duration was 6 months, from November 2017 to April 2018. The study was approved by Institutional Human Ethics Committee (IHEC). All the subjects recruited were provided with written informed consent prior to the recruitment. The sample size was 50. Patient Data Collection form was used to collect demographic details, Duration of Disease, Initial Ulcer size, Disease history, Medication history, glycemic levels from the day of admission till the day of discharge, type of surgery done, insulin dose received, and outcome of the management. SPSS software was used to do statistical analysis. Chi-Square test was used to determine if there was any significant difference of baseline data between patients receiving fixed dose and Sliding scale dose. U-Mann whitney test was used to compare differences in the glycemic levels between the patients receiving Fixed Dosing and Sliding scale dose of Insulin. The collected data were and analyzed and interpreted.

Results and Discussion

Table 2: Background Variables among Patients receiving Fixed and Sliding scale doses

		SS		FS		Chi Square Test Value	P-Value
		N	%	N	%		
Duration of DFU (in month)	<1	13	65	23	76.6	0.810	0.368
	1-3	7	75	7	23.3		
Duration of DM (in years)	<10	11	55	22	73.3	1.79	0.180
	>10	9	45	8	26.6		
Duration of Hospital Stay (Days)	0-15	9	45	16	53.3	0.375	0.829
	>15	11	55	14	46.7		
Foot Involvement	Left	15	75	17	56.6	1.75	0.186
	Right	5	25	13	43.4		
Type of Surgery	Minor	8	40	19	63.3	2.63	0.15
	Major	12	60	11	36.7		
Condition at Discharge	Relieved	17	85	26	86.7	0.028	0.868

	Chronic Wound	3	15	4		
--	---------------	---	----	---	--	--

SS= Sliding Scale, FS= Fixed scale

From the period of Nov 2017- April 2018, 67 patients of Diabetic foot ulcer cases were reported in RMMCH. Among them 50 subjects met our inclusion and exclusion criteria.

From the reports we collected, it was seen that Diabetic foot ulcer was more common in the age group of above 50 years and in male gender. The study reports also suggested that 46% of patients were on irregular medications for Diabetes Mellitus which led them to have a poor glycemic control. Our reports also suggested that about 28% of patients consulted the doctor only after 1-3 month of ulcer formation which led to late diagnosis and worsening of condition. This led to increased number of hospital stay (Table -2) (40% required 1 month stay , 10% required more than 1 month of hospital stay). Our reports also showed that about 84% of patients had ulcer of size more than 2cm (Table – 2) which falls under Wagner classification of 3, 4 or 5. From the baseline data, it was found that the 15% of patients who required below knee amputation, had a poor glycemic control. Also the 14% of patients who were discharged at request due to chronic wound also had poor glycemic control. This suggests that *glycemic control* proves to be one of the major risk factors in diabetic foot ulcer patients. There was no significant difference among the patients receiving Fixed and Sliding scale doses when Chi- square test was applied as shown in Table – 2.

The common types of insulin used to manage Hyperglycemia were H. Actrapid, H. Monotard, H. Mixtard. The distribution of Insulin preparations used is given in Figure 1. For statistical analysis chi –square test and Mann-Whitney test were used by applying SPSS software. Among the background data, initial ulcer size (Table – 3) shows a

statistical significance (p- value 0.015) between both methods, which reveals that sliding scale method is given to those with larger initial ulcer size with poor glycemic control. From Mann- whitney test as shown in Table - 4, it reveals that there is no statistically significant difference between sliding and fixed scale dosing of insulin. Hence, both the methods are reliable in management of hyperglycemia. However, from descriptive analysis as shown in Table- 5 hypoglycemia incidence is higher in patients receiving fixed dose s of insulin but there is no statistically significant difference.

It is also found that almost all of the patients admitted in RMMCH had a poor social background and poor education about Diabetes as well as Diabetic foot ulcer. Proper education about Diabetic diet, Foot care and hygiene and medications can reduce the worsening of condition and lead to early diagnosis of the disease progress which in turn can reduce the risk of amputation.

Our study showed that poor glycemic control is one of the major risk factor leading to chronic wound and thus proper glycemic control must be ensured. The use of Insulin pumps can tackle this issue. However the high cost of the pumps can be a drawback.

Also, various studies which are in its preliminary stage such as topical Insulin therapy in wound healing [9], Ozone therapy for treating Diabetic foot ulcers [10], Hyperbaric Oxygen therapy [11] and the use of granulocyte colony stimulating factor [12] gives us hope that Diabetic Foot Ulcer can further be managed effectively. For the time being, appropriate patient counseling regarding foot hygiene, glycemic control, exercise and diet can help to prevent the worsening of the condition.

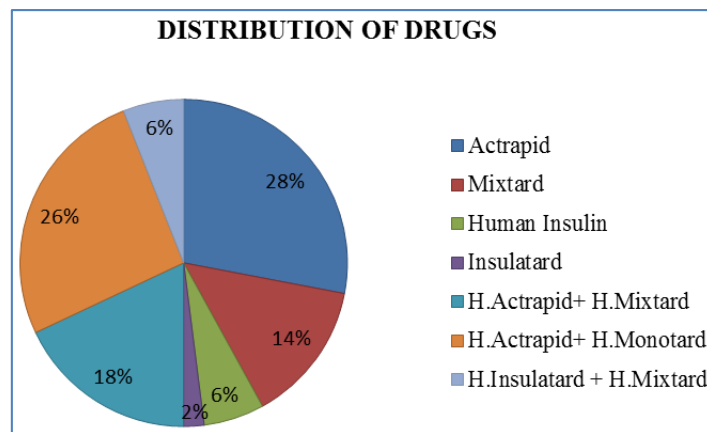


Fig 1: Distribution of Insulin

Table 3: Initial Ulcer size among patients receiving Fixed and Sliding scale doses

Initial Ulcer Size	Sliding Scale		Fixed Scale		Chi Square Test Value	P- Value
	N	%	N	%		
<2cm	3	15	3	10	8.40	0.015
2-5 cm	7	35	21	70		
>5cm	10	50	6	20		

Table 4: Glycemic levels among patients receiving Fixed and Sliding scale doses

Variables	Sliding Scale		Fixed		Mann Whitney Value	p-value
	Mean	S.D	Mean	S.D		
FBS 0	230.1	111.6	187.0	107.2	202.00	0.052
FBS1	136.5	40.6	129.6	50.7	236.50	0.276
PPBS0	307.9	85.3	258.8	104.3	199.00	0.450
PPBS1	180.75	54.94	168.55	60.49	664.00	0.371

RBS0	368.60	396.23	204.2	97.85	144.50	0.002
RBS1	155.60	43.83	138.86	59.82	194.50	0.052
DIFFFBS	93.65	85.55	58.62	116.79	206.00	0.870
DIFPPBS	127.20	87.33	92.34	96.53	222.50	0.170
DIFFRBS	213	394.55	66.48	84.26	145.00	0.030

FBS0= Fasting blood glucose at the day of admission, FBS1= Fasting Blood Glucose at the day of Discharge

RBS0= Random Blood Glucose at the day of admission, RBS1= Random Blood Glucose at the day of Discharge

PPBS0= Post prandial Blood Glucose at the day of admission, PPBS1= Post prandial Blood Glucose at the day of Discharge

DIFFRBS = Difference in Random Blood Glucose, DIFFFBS = Difference in Fasting Blood Glucose, DIFPPBS = Diff in Post prandial Blood Glucose.

Table 5: Hypoglycemia Incidence among patients receiving Fixed and Sliding scale Doses

Hypoglycemia	Sliding Scale		Fixed Scale		Chi Square Test Value	P-Value
	N	%	N	%		
Negative	19	95%	20	74.1%	3.56	0.059
Positive	1	5%	7	25.9%		

References

- Mohan V. Why are Indians more prone to Diabetes? JAPI, 2004, 52.
- King H, Aubert.RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projection. Diabetes care. 1998; 21:1414-1131
- Bjork S, Kapur A, King H *et al.* Global Policy: aspects of diabetes in India. Health policy. 2003; 66:61-72
- Pendsey SP. Understanding diabetic foot. Int J Diabetes Dev Ctries. 2010; 30:75-79
- Carrington AL, Mawdsley SK, Morley M, Kinsey J, Boulton AJ. Psychological status of diabetic people with or without lower limb disability. Diabetes Res Clin Pract. 1996; 32:19-25.
- Wilcox G. Insulin and insulin resistance. Clin Bio chem Rev. 2005; 26(2):19-39.
- Tripathi KD. Essentials of Medical Pharmacology, 8th Edition, Jaypee Brothers Medical Publishers(P) Ltd, New Delhi, 2019.
- World Health Organization. Obesity: Preventing and Managing the Global Epidemic Report of a WHO Consultation Technical Report Series. World Health Organization, Geneva, 2000.
- Shridharan K *et al.* Wound Repair Regen, 2017.
- Zhang P, Yang K, Tian J, Ma B, Liu Y, Li J *et al.* Ozone therapy for treating diabetic foot ulcers. Cochrane Database of Systematic Reviews. 2010, 4. Art. No.: CD008474. DOI: 10.1002/14651858.CD008474.
- Barnes RC. Point: hyperbaric oxygen is beneficial for diabetic foot wounds. Clin Infect Dis. 2006; 43:188-192.
- Cruciani M, Lipsky BA, Mengoli C, de Lalla F. Are granulocyte-colony stimulating factors beneficial in treating diabetic foot infections? A meta-analysis. Diabetes Care. 2005; 28:454-460.