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RESEARCH ARTICLE

A COMPARATIVE STUDY OF EFFECTIVENESS BETWEEN TOPICAL INSULIN VERSUS NORMAL SALINE DRESSINGS IN MANAGEMENT OF DIABETIC FOOT ULCERS

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Abstract

Foot ulcer is a common problem in diabetic patients and are seen as a common outpatient in General Surgery department all over the country. They result in significant morbidity, with prolonged duration of hospital stay as they present late to the hospital and due to uncontrolled diabetes mellitus, ultimately requiring major amputations in some instances. A study has been attempted using topical insulin, to determine its role in wound healing.

Aims &Objectives: To compare Topical Insulin versus Normal Saline dressings in management of Diabetic foot ulcers and to know the efficacy of Topical Insulin in Diabetic foot ulcers.

Methods: An interventional study was conducted on 66 patients over 18 months (from Dec 2020 to June 2022) at JSS hospital, Mysuru. 66 patients were randomized into two subgroups of 33 patients each, the control and the experimental group. Normal saline dressings were done for the 33 patients in the control group and Topical Insulin dressings were applied for the 33 patients in the experimental group. Various parameters related to wound healing, viz. size, granulation tissue, type and presence of slough, pus etc. were studied on Day 1, 7 and 15 and data compared.

Results: In the experimental group, the presence of granulation tissue was 97% and it was 39.4% in controls with a p value of <0.001 showing a significant increase in granulation tissue formation in experimental group.The percentage reduction of surface area among controls was 8.8% and among experimental group was 50% with a statistically significant p value of <0.001, which represent the effectiveness of Topical Insulin in wound healing and at a faster rate.

Conclusion: This study has shown that using topical Insulin, the rate of promotion of granulation tissue was increased, rapid reduction in surface area of wound, rate of wound healing was improved ultimately leading to lesser morbidity, decreased amputation rates and decreased hospital stay.

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Introduction:-

Diabetes mellitus is the most leading problem in the world. This increase in prevalence is due to change in the lifestyle, physical inactivity and obesity. The lifetime risk of a diabetic patient developing foot ulcer can be about 25% [1]. These patients are also at 50% [1] risk of redeveloping the ulcers within the next 3 years.Major amputation rates are 5-10 times higher in diabetics compared to non-diabetics [2].

The diabetic patients may be unaware of the presence of infections because of peripheral neuropathy and a decreased ability to sense pain. In this population, infection can progress very rapidly with significant tissue damage from a combination of immuno-compromised state and delayed presentation.

Topical dressings comprise one of the modalities of care for diabetic foot ulcers. Various studies are being made on various types of dressings. Application of topical insulin is one among them.

Role Of Topical Insulin In Wound Healing:

Insulin has been shown to have a positive effect on wound healing. It has proved to be efficacious in promoting wound healing by activating serine-threonine kinase (AKT) & extracellular signal regulated protein kinase (ERK) pathway [3]. Insulin like growth factor which is very similar to the hormone insulin, has been shown to promote the proliferation, migration and extracellular matrix excretion by keratinocytes, endothelial cells and fibroblasts and even promote the reformation of granulation tissue [4].As many studies are not available regarding the effectiveness of topical insulin when compared to normal saline dressings, this study was done to determine the role of topical insulin in diabetic foot ulcers.

Objectives Of The Study:-

- **Primary Objectives**
  - To compare Topical Insulin versus Normal Saline dressings in the management of Diabetic foot ulcers.
- **Secondary Objectives**
  - To know the efficacy of Topical Insulin in Diabetic foot ulcers.

Materials And Methods:-

Description Of Study

A single centre, interventional study was conducted on a study population of 66 patients from Department of General Surgery, JSS Hospital, Mysuru. It was carried out over 18 months from December 2020 to June 2022.

Subject Eligibility

- **Inclusion Criteria**
  - Patients who are known diabetics or recently diagnosed as diabetic with the age group of more than 18 years.
  - Patients with the diabetic foot infections presenting for the first time.
  - Grade 1 and 2 of Wagner's classification.
- **Exclusion Criteria**
  - X-rays showing features of osteomyelitis.
  - Grade 3, 4 and 5 of Wagner's classification.
  - Doppler showing gross atherosclerotic arterial changes and venous abnormalities like varicosities of lower limbs.
  - Patients who are in septicaemia.
  - Patients with various malignancies.
  - Patients who are unable to come for regular follow ups.

Study Conduct

This was an Interventional study.

66 individuals selected according to inclusion and exclusion criteria

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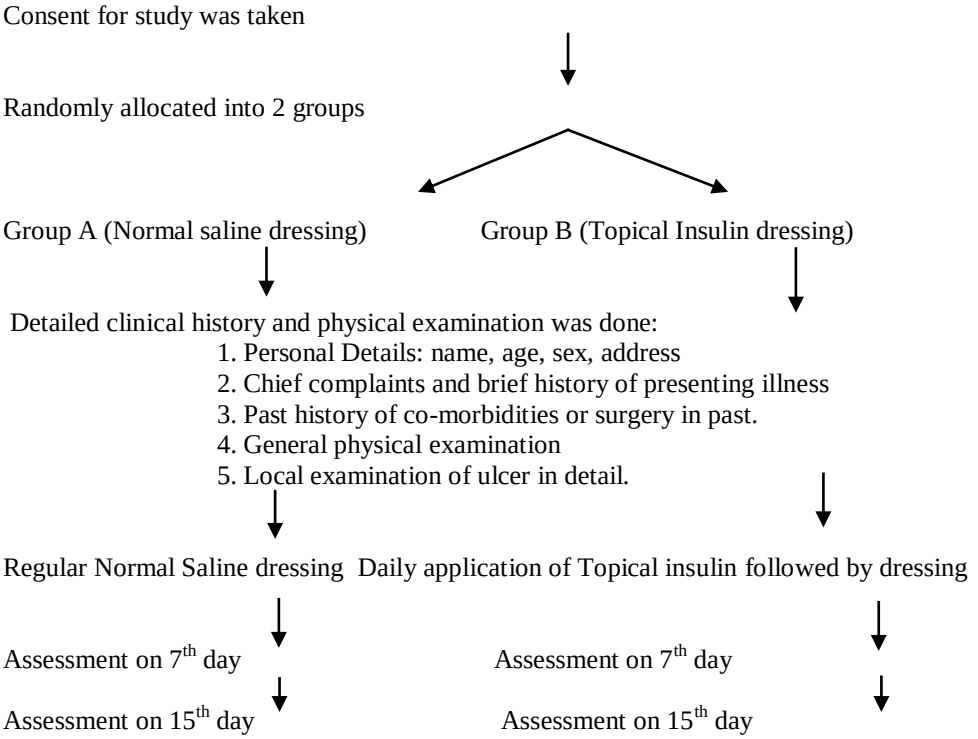


Method of performing the dressing:
Under aseptic precautions, after inspecting the wound, a culture was sent from the wound area. A thorough betadine and hydrogen peroxide wash was given and the wound was debrided until fresh bleeding occurs from the wound surface area.

In the control group, the wound was packed with normal saline dressings.

In the experimental group, wound bed was sprayed with insulin (Human Actrapid 1U/cm^2 of wound area) once daily and dressing was done. The blood glucose levels were measured using a glucometer 10 minutes before and 1 hour after the application of topical insulin to ascertain that there are no episodes of hypoglycemia. Daily dressings were done.

Wound was assessed in terms of size, granulation tissue formation and presence of discharge and slough on 1st, 7th and 15th day.

Results:-

Demographic Data Of Study Population:

a) Age (in years):

Table 1:- Age (in years) in study population.

	Dressing Method			
	Normal Saline Dressing		Topical Insulin Dressing	
	Mean	Standard Deviation	Mean	Standard Deviation
Age (years)	58.6	12.6	58.8	12.1

P=0.96

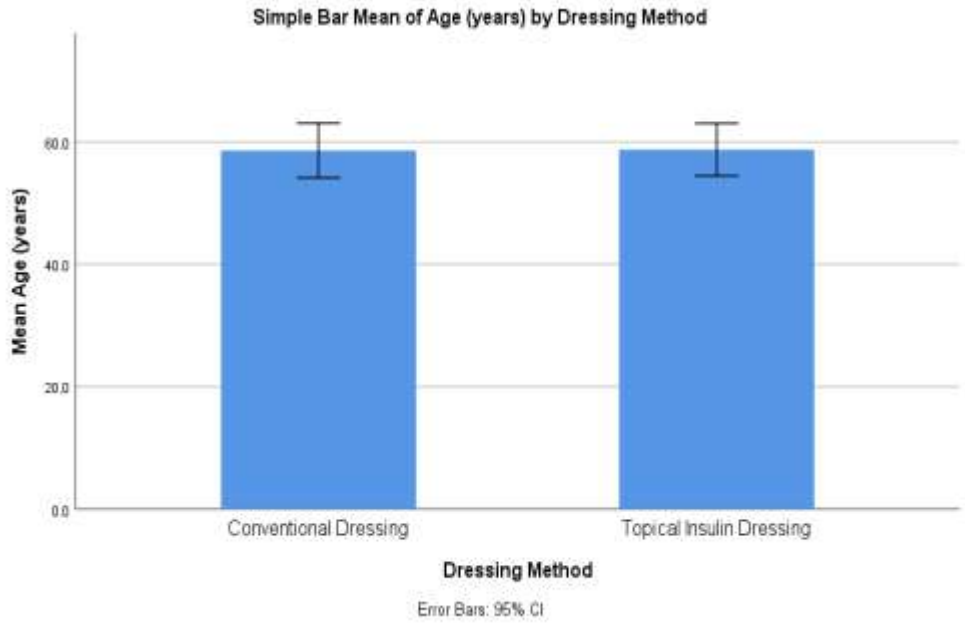


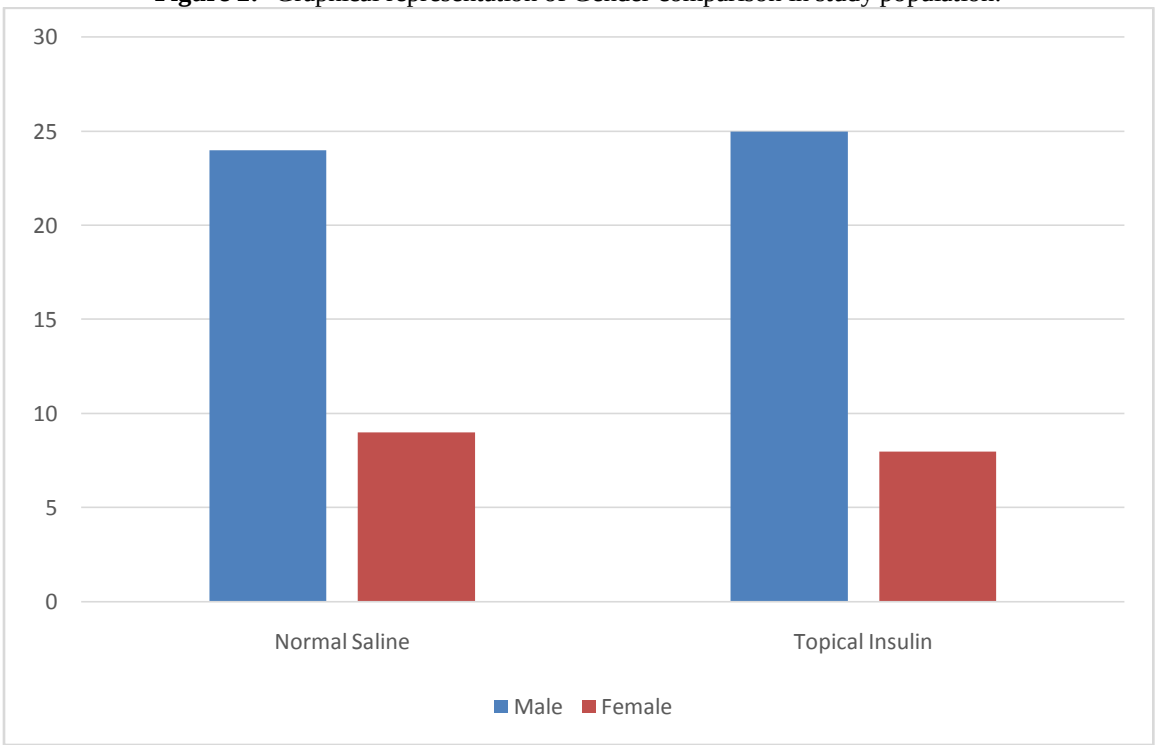
Figure 1:-Graphical representation of age comparision in study population.

Gender :

Table 2:- Gender Distribution in study population P=0.8;

		Dressing Method			
		Normal Saline Dressing		Topical Insulin Dressing	
		Count	Column N %	Count	Column N %
Gender	Female	9	27.3%	8	24.2%
	Male	24	72.7%	25	75.8%

Figure 2:- Graphical representation of Gender comparison in study population.

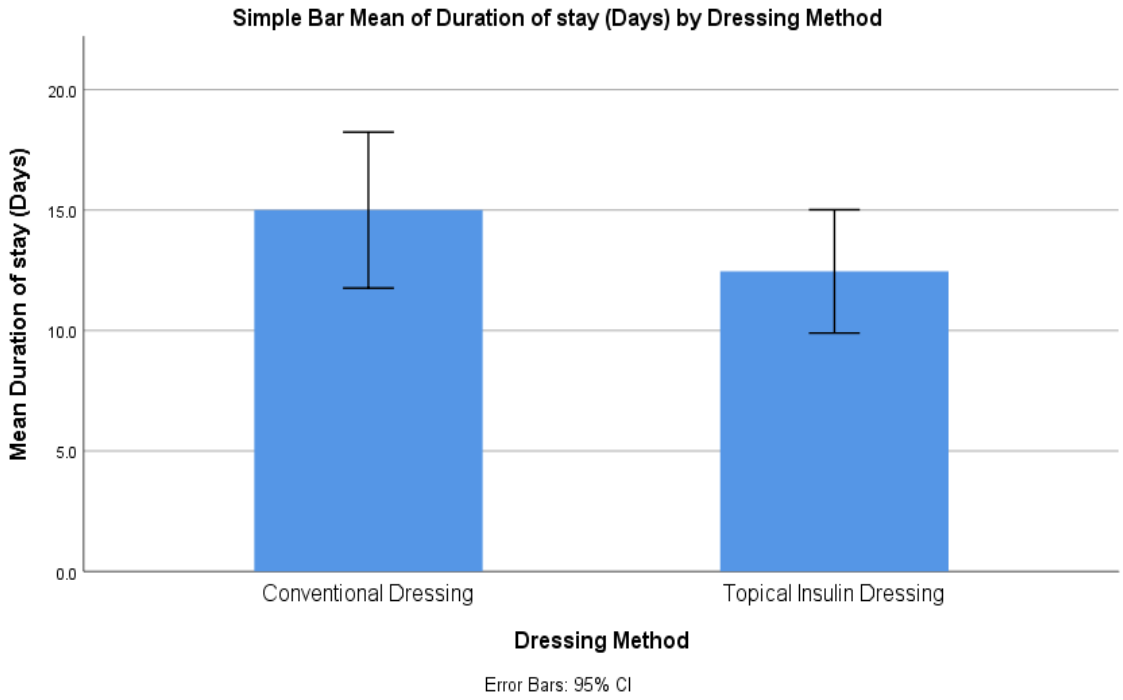


Duration Of Hospital Stay (IN DAYS):

Table 3:- Comparison of duration of hospital stayComparison of hospital stay duration.

	Dressing Method			
	Normal Saline Dressing		Topical Insulin Dressing	
	Mean	Standard Deviation	Mean	Standard Deviation
Duration of stay (Days)	15.0	9.1	12.5	7.2

Figure 3:-Graphical representation of P=0.2



Details of the patients in study population:

Table 4:- Details of the patients in study population.

		Dressing Method				
		Normal Saline Dressing		Topical Insulin Dressing		
		Count	Column N %	Count	Column N %	P
Mode of Onset	Spontaneous	21	63.6%	22	66.7%	0.8
	Trauma	12	36.4%	11	33.3%	
Associated Symptoms (Fever)	No	21	63.6%	21	63.6%	1
	Yes	12	36.4%	12	36.4%	
Associated symptoms (Pain)	No	9	27.3%	6	18.2%	0.4
	Yes	24	72.7%	27	81.8%	
Associated symptoms (Discharge)	No	4	12.1%	18	54.5%	<0.001
	Yes	29	87.9%	15	45.5%	
Treatment for Diabetes	Insulin	5	15.2%	0	0.0%	0.02
	OHA	28	84.8%	33	100.0%	

HTN	No	14	42.4%	16	48.5%	0.6
	Yes	19	57.6%	17	51.5%	
IHD	No	25	75.8%	25	75.8%	1
	Yes	8	24.2%	8	24.2%	
Personal History (Smoking)	No	21	63.6%	25	75.8%	0.3
	Yes	12	36.4%	8	24.2%	
Personal History (Alcoholic)	No	25	75.8%	28	84.8%	0.3
	Yes	8	24.2%	5	15.2%	

Characteristics Of Patients In Study Population:

Table 5:- Characteristics of patients in study population.

		Dressing Method				
		Normal Saline Dressing		Topical Insulin Dressing		
		Count	Column N %	Count	Column N %	P
Build	Moderate	33	100.0%	32	97.0%	0.3
	Poor	0	0.0%	1	3.0%	
Anemia	No	19	57.6%	21	63.6%	0.6
	Yes	14	42.4%	12	36.4%	
Jaundice	No	31	93.9%	33	100.0%	0.2
	Yes	2	6.1%	0	0.0%	
Lower Limb - Side	Left	17	51.5%	18	54.5%	0.8
	Right	16	48.5%	15	45.5%	

Ulcer Details In Study Population:

Table 6:- Details of Ulcer in study population.

	Dressing Method										
	Normal Saline Dressing					Topical Insulin Dressing					
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Length (cm)	5.1	2.5	4.0	3.0	6.0	4.3	1.9	4.0	3.0	5.0	0.2
Breadth (cm)	4.4	1.8	4.0	3.0	5.0	3.8	1.6	3.0	3.0	5.0	0.2
Area (sq.cm)	24.8	20.9	15.0	12.0	35.0	17.9	15.7	12.0	9.0	20.0	0.2
Duration of Ulcer (Days)	26.5	28.1	20.0	7.0	30.0	11.1	8.4	7.0	4.0	20.0	0.006

Laboratory Investigations (HB, TC, RBS, HBA1C, UREA, CREATININE) :

Table 7:- Laboratory investigations of patients in study population.

	Dressing Method				
	Normal Saline Dressing		Topical Insulin Dressing		
	Mean	Standard Deviation	Mean	Standard Deviation	P
Hb (g/dL)	10.6	1.9	11.3	1.4	0.1
PCV	32.0	5.4	34.0	3.7	0.1

TC (cells/cu.mm)	12904	4714	14022	4231	0.3
Neutrophils (%)	78.33	7.06	77.86	8.04	0.8
RBS (mg/dL)	221	82	232	78	0.8
HbA1C	9.9	2.3	9.7	1.8	0.6
Urea (mg/dL)	30	15	32	15	0.5
Creatinine (mg/dL)	0.96	0.38	1.00	0.74	0.8

Other Characteristics:

Table 8:- Other characteristics in study population.

		Dressing Method				
		Normal Saline Dressing		Topical Insulin Dressing		
		Count	Column N %	Count	Column N %	P
Number	1	29	87.9%	26	78.8%	0.3
	2	2	6.1%	6	18.2%	
	3	2	6.1%	1	3.0%	
Peripheral Pulses	Not Palpable	8	24.2%	2	6.1%	0.04
	Palpable	25	75.8%	31	93.9%	
Joint Movement	Not Affected	32	97.0%	33	100.0%	0.3
	Restricted	1	3.0%	0	0.0%	
Deformity	No	33	100.0%	33	100.0%	NA
Foot X-ray Taken	No	19	57.6%	16	48.5%	0.5
	Yes	14	42.4%	17	51.5%	
Arterial Doppler Done	No	15	45.5%	22	69.7%	0.1
	Yes	18	54.5%	10	30.3%	
Amputation Done	No	29	87.9%	33	100.0%	0.04
	Yes	4	12.1%	0	0.0%	
Glycemic Control	No	5	15.2%	8	24.2%	0.3
	Yes	28	84.8%	25	75.8%	

A) Assessment Of Ulcer On Day 1,7 And 15 (Discharge, Slough, Granulation) :

Table 9:- Assessment of Ulcer on day 1, 7 and 15.

		Dressing Method				
		Normal Saline Dressing		Topical Insulin Dressing		
		Count	Column N %	Count	Column N %	P
$Discharge	Day 1 - Discharge	33	100.0	26	78.8	0.005
	Day 7 - Discharge	18	54.5	1	3	<0.001
	Day 15 - Discharge	5	15.2	0	0.0	0.02
$Granulation	Day 1- Granulation	1	3.3	1	3.0	1
	Day 7 - Granulation	13	39.4	32	97.0	<0.001
	Day 15 - Granulation	30	90.9	33	100.0	0.07
$Slough	Day 1 - Slough	33	100.0	31	93.9.0	0.2
	Day 7 - Slough	33	100.0	10	30.3	<0.001
	Day 15 - Slough	29	87.9	1	3	<0.001

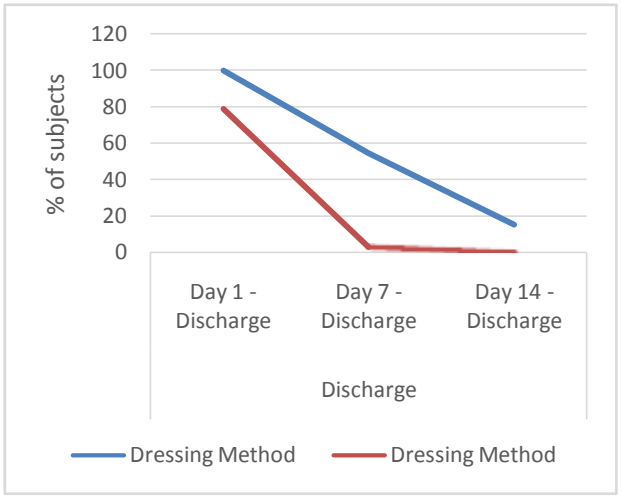


Figure 4:- % of subjects with Discharge.

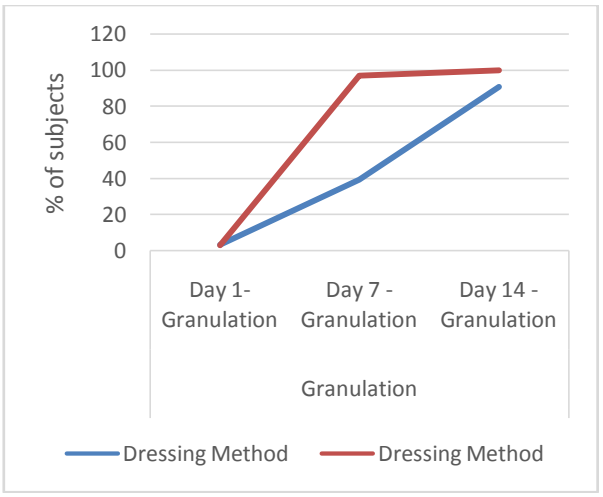


Figure 5:- % of subjects with Granulation.

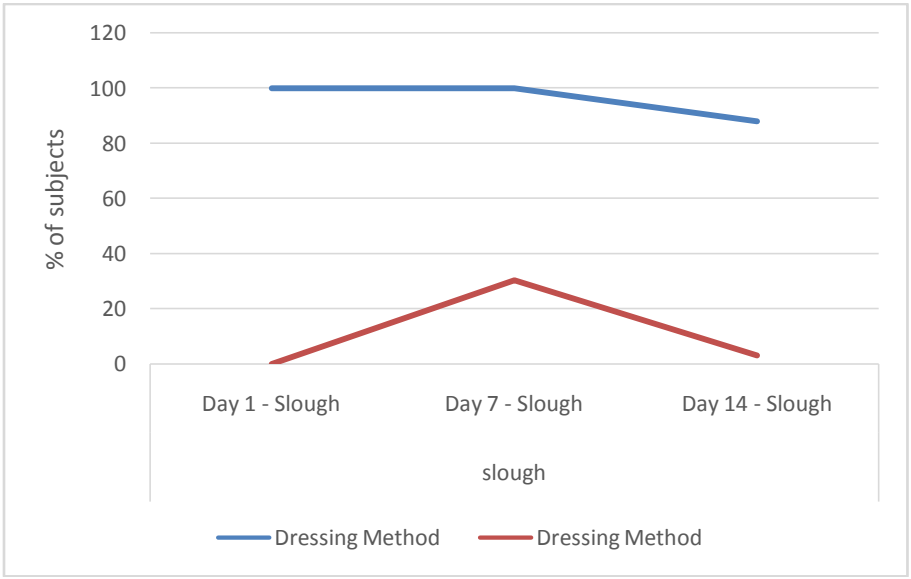


Figure 6:- % of subjects with Slough.

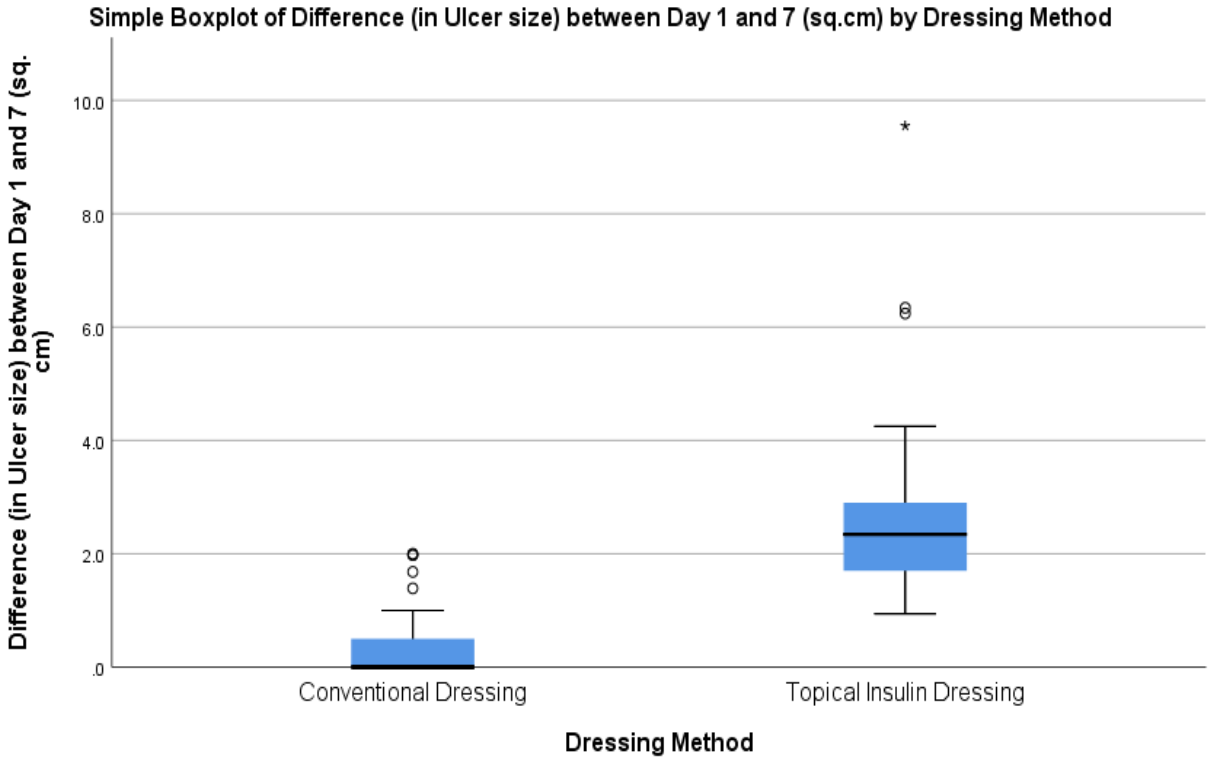
B) Measurements Of Ulcer On Day 1, 7 AND 15:

Table 10:- Measurements of Ulcer on Day 1, 7 and 15 in length and breadth.

	Dressing Method			
	Normal Saline Dressing		Topical Insulin Dressing	
	Mean	Standard Deviation	Mean	Standard Deviation
Ulcer Size Day 1 Length (cm)	5	2	5	2
Ulcer Size Day 7 Length (cm)	5.1	2.4	4.2	1.7
Ulcer Size Day 15 Length (cm)	4.9	2.4	3.3	1.6
Ulcer Size Day 1 Breadth (cm)	4	2	4	2
Ulcer Size Day 7 Breadth (cm)	4.4	1.7	3.5	1.6
Ulcer Size Day 15 Breadth (cm)	4.3	1.7	2.8	1.4

Table 11:- Measurements of Ulcer on Day 1, 7 and 15 in Area and percentage reduction.

	Dressing Method						
	Normal Saline Dressing			Topical Insulin Dressing			
	Median	Q1	Q3	Median	Q1	Q3	
Ulcer Area Day 1 (sq.cm)	16	12	35	15	12	20	0.2
Ulcer Area Day 7 (sq.cm)	15.6	12.0	35.0	11.7	9.1	16.9	0.2
Ulcer Area Day 15 (sq.cm)	13.9	10.6	33.3	7.3	4.3	11.2	0.03
Difference (in Ulcer size) between Day 1 and 7 (sq.cm)	.0	.0	.5	2.3	1.7	2.9	<0.001
Difference (in Ulcer size) between Day 7 and 15 (sq.cm)	1.2	1.0	1.9	4.7	3.5	6.6	<0.001
Area Reduction on Day 15 compared to Day 1	1.3	1.0	2.9	7.4	6.0	9.3	<0.001
Percentage Reduction (from Day 1 to 15)	8.8	6.0	11.3	50.0	38.7	58.0	<0.001



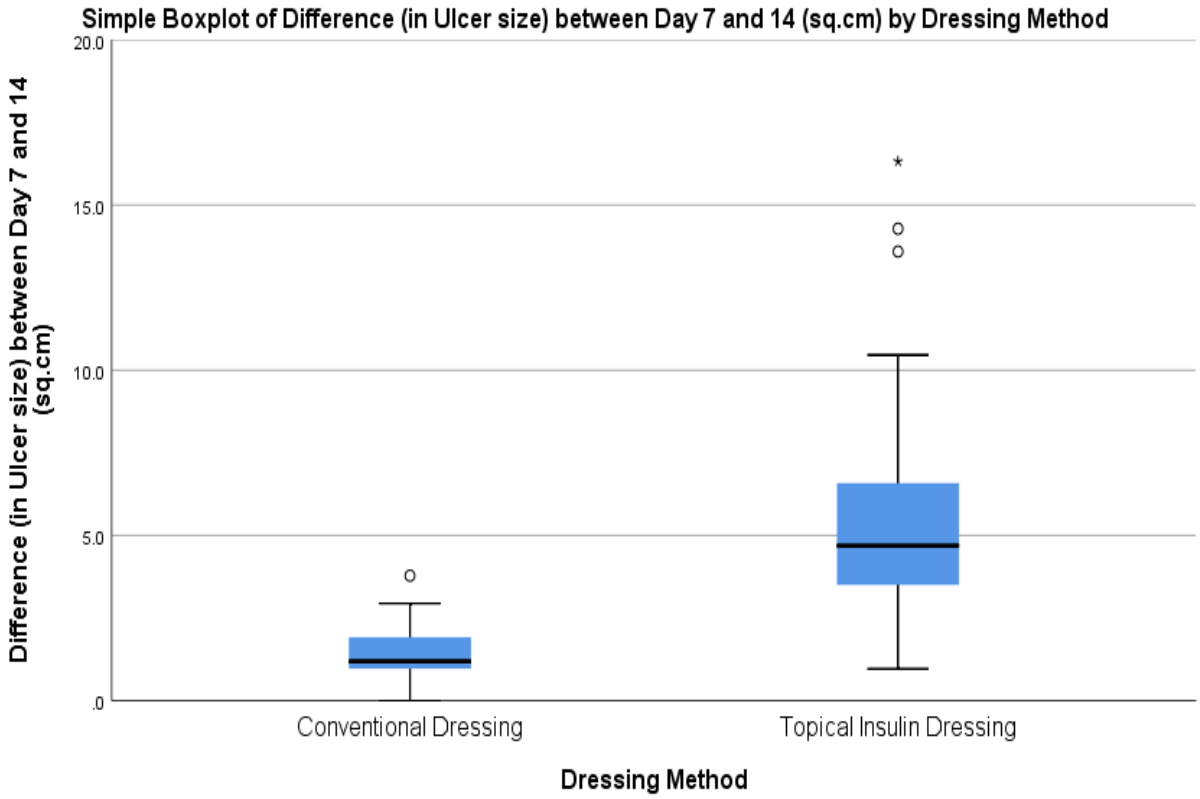


Figure 8:- Simple Boxplot of Difference in ulcer between Day 1 & 7 size between Day 7 & 14.

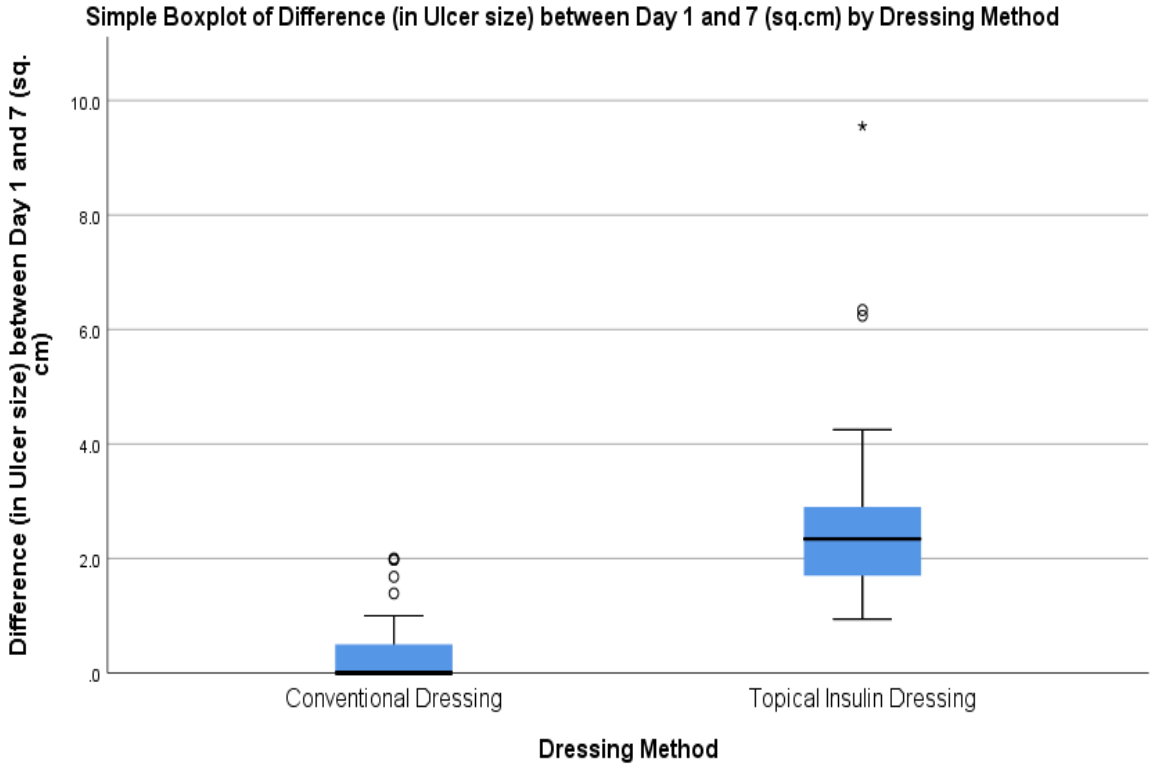


Figure 7:- Simple Boxplot of Difference in ulcer size.

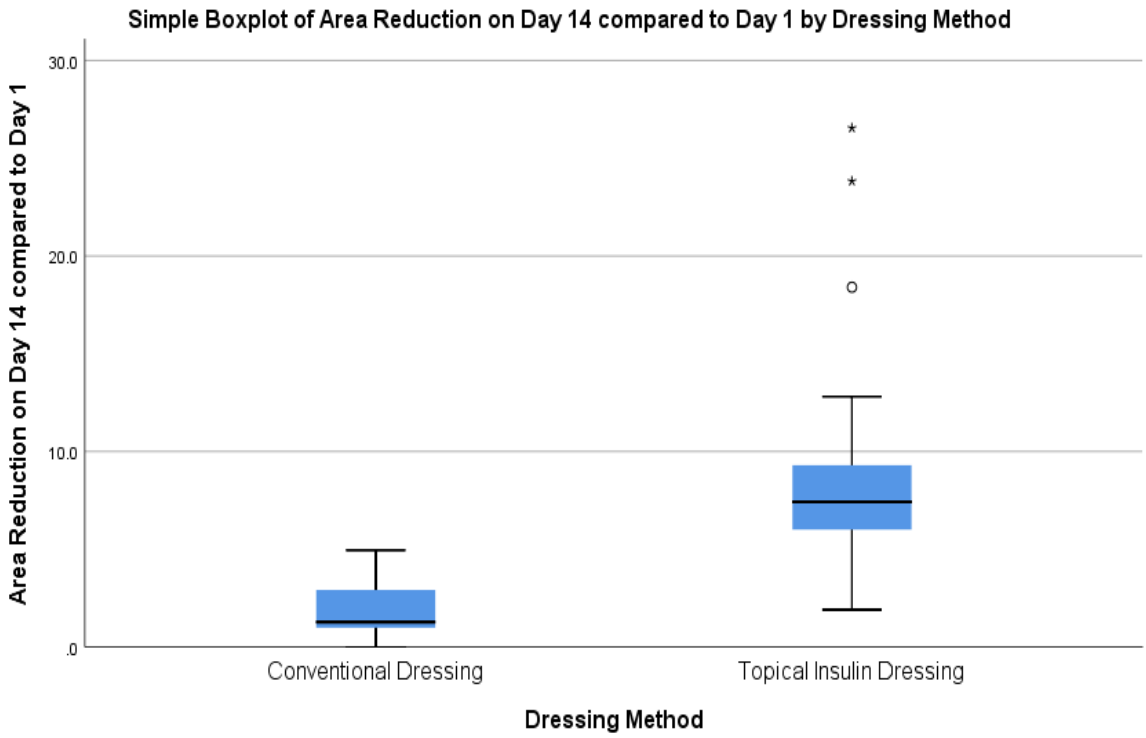


Figure 9:- Simple Boxplot of Area Reduction on Day 14 compared to Day 1.

Figure 10:- Wound over left foot treated with Topical Insulin – Day 15

Figure 11: Wound over left foot s/p fore foot theamputation treated with Topical Insulin – Day 15.

Discussion:-

Diabetic foot ulcers present as a serious complication of diabetes which are very common. Foot ulcers are a leading cause of hospitalization for people with diabetes. They are also a major cause of amputations. This occurs in the patients where they neglect and present late to the hospital with uncontrolled diabetes and extensive spread of infection. Another risk factor is smoking, which results is Peripheral Arterial Occlusive Disease which ultimately leads to decrease blood supply to the wound and becomes non-healing.

For Diabetic foot ulcers, along with antibiotics, local wound care takes a major role in managing it. Dressings with Betadine, Normal saline, application of antibiotics to the wound such as metronidazole, mupirocin, amikacin, gentamicin, rifampicin are being used.

This study dealt with use of application of Topical Insulin over the ulcer bed and assessing the ulcer on 1st, 7th and 15th day. In this study which was implemented over a period of 18 months, 66 subjects were randomly divided equally into experimental group with Topical Insulin dressing and control group with Normal Saline dressing.

This study concluded that Diabetic foot ulcers are more common in middle age group with mean age of 58.6 years (control group) and 58.8 years (experimental group) and predominantly affecting males in both groups.

The average duration of hospital stay was comparatively lesser in experimental group (12.5 days vs 15 days, p= 0.2)

In this study, among experimental group 8 (36.4%) were smokers and among control group, 12 (24.2%) were smokers.

In this study, among control group 4 patients (12.1%) had subsequently underwent amputation while no patient in experimental group underwent amputation, thus showing the effectiveness of Topical Insulin in wound healing.

The presence of slough on day 7 among controls was 100% (33) where as in experimental group it was 30.3% (10) with a p value of <0.001 and on day 15 among controls it was 87.9% (29) whereas 3% (1) in experimental group with a p value of <0.001 with a significant reduction rate of slough in experimental group.

The presence of discharge in control group on day 7 was 54.5% (18) and among experimental group was 3% (1) with a p value of <0.001 with a significant reduction rate of discharge in experimental group and on day 15 it was 15.2% (5) among controls and 0% among experimental group with a p value of 0.02.

The presence of granulation tissue on day 7 among controls was 39.4% (13) where as 97% (32) in experimental group with a p value of <0.001 with a significant increase in granulation tissue formation in experimental group and on day 15 it was 90.9% (30) in controls and 100% (33) among experimental group with a p value of 0.02.

The percentage reduction of surface area among controls was 8.8% and among experimental group was 50% with a statistically significant p value of <0.001, which represent the effectiveness of Topical Insulin in wound healing and at a faster rate.

Conclusion:-

Diabetic foot ulcers are the leading problem in diabetics and has to be managed appropriately. Local aggressive management with use of systemic antibotics is helpful. This study concludes use of Topical Insulin in diabetic foot ulcers promotes wound healing by promoting granulation tissue faster and rapidly reducing the surface area of ulcer when compared to Normal Saline dressings thus preventing amputations. Insulin (Human Actrapid) which was used in this study is easily available all over the country and usage of Topical Insulin doesn't show any systemic side effects and is easier to use.

Limitations

This study was associated with few limitations, viz.:

1. The sample size of 66 patients with 33 each in control and experimental group is a smaller sample size and may not be able to represent the total population.
2. Inclusion criteria doesn't include Peripheral vascular diseases and Osteomyleitis conditions which requires further study in those fields.
3. Various factors including Anaemia, Immuno suppression, comorbidities and nutritional status, also play a role in wound healing like granulation tissue formation and the spread of infection, and may have been hampering the wound healing.
4. Microbial growth like type of organism was not mentioned in the study.

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