Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE

DOI: 10.53555/jptcp.v31i1.4230

COMPARATIVE STUDY ON WOUND HEALING WITH BETADINE, SILVER SULPHADIAZINE, SOFRAMYCIN AND PHENYTOIN AS DRESSING AGENTS IN DIABETIC FOOT ULCERS

Dr. Bodagala Venkata Radha Krishna Teja[1], Dr. Budamala Sarada[2*], Dr. M Pradeep[3] , Dr. Padala Adithya[4], Dr. Aluvala Vamshi Krishna[5], Dr. Bukke Ramanjineyulu Naik[6],

[1]Resident in Department of Urology, Gandhi medical college, Secunderabad .Mobile No.7093393070 Email:radhakrishnateja25@gmail.com

[2*]Associate Professor, Department of General Surgery, S.V.Medical college, Tirupati. Mobile No. 9989781075 Email:drbsarada@gmail.com

[3]Assistant Professor of General Surgery, SVRRGGH, Tirupati. Mobile No. 9440443791 Email:mpradeep2k6@gmail.com

[4]Post graduate, Department of General Surgery, S.V.Medical college, Tirupati. Mobile No. 9550666923 Email:adityapadala25@gmail.com

[5]Post graduate, Department of General Surgery, S.V Medical College, Tirupati. Mobile No.7386682645 Email:vamshi.aluvala@gmail.com

[6]Post Graduate, Department of General Surgery, S.V.Medical college, Tirupati. Mobile No. 8790787548 Email:ramanjibukke1710@gmail.com

***Corresponding Author:-**Dr. Budamala Sarada,

*Associate Professor, Department of General Surgery, S.V.Medical college, Tirupati. Mobile No. 9989781075 Email: drbsarada@gmail.com

Abstract

Background: Diabetic foot ulcer is a major global concern accounting for huge chunk of global healthcare attention and patient suffering. Dressing agents like betadine, silver sulphadiazine, soframycin and phenytoin show promising results with reducing duration of diabetic foot ulcers and its complications. The intention of this particular study is to compare efficacy of each of the four mentioned dressings and compare their rate of granulation and epithelization in diabetic foot ulcers.

Methods: Diabetic patients presented with foot ulcers were divided into 4 groups of 50 in each group.In Group 1 , Betadine is used as Dressing agent. In Group 2, Silver sulphadiazine is used as dressing agent.In Group 3 , Soframycin is used as dressing agent. In Group 4 ,Phenytoin is used as dressing agent.

Study design – A Prospective interventional study in a Tertiary care hospital

Duration of the study – 12 months from institutional scientific committee and institutional ethical committee approval

The wound surface areas are measured using Graph paper – Tracing method. The wound surface areas were measured initially at the beginning of the study and one again at the 21st day.

Results: The reduction in ulcer surface area is expressed as percentage points in comparision to ulcer surface area at the start of the study to the ulcer surface area at the end of 21 days . Group *1* (Betadine) showed a reduction in ulcer surface area at 57.59±14.456% , Group 2 (silver sulphadiazine) showed a reduction in ulcer surface area at 56.74 ± 12.710 % , Group 3 (Soframycin)

showed a reduction in ulcer surface area at 54.16 ± 15.512% with and Group 4(Phenytoin) showed a reduction of ulcer surface area at 61.46 ± 8.938%

Conclusion: The diabetic foot ulcers in Topical phenytoin dressing group contracted more than those in patients with Betadine, Silver sulphadiazine and Soframycin groups (61.46% as compared to 57.59%, 56.74% and 54.16% with statistical significance), which indicates that the Topical Phenytoin dressing therapy is one of the effective modality to aid the reduction of wound surface area in patients suffering from diabetic ulcer.

INTRODUCTION

Diabetic foot ulcer is a major global concern accounting for huge chunk of global healthcare attention and patient suffering. Its prevalence is gaining momentum particularly in subcontinent which has now become world capital of diabetes mellitus. Among huge variety of potential complications that could develop with diabetes mellitus, diabetic foot ulcers hold a very high position. Among those who develop diabetic foot problems, 15% underwent some type of toe to foot amputations. Such a huge number could be ascertained to improper to insufficient control of diabetes mellitus and delayed seeking of medical care particularly among
lower socio-economic status population.

Diabetes mellitus is a modern world disease, with major reason for hospitalization being diabetic foot complications. Diabetes mellitus patients have upto 25% risk of developing diabetic foot ulcers among which 15% undergo various forms of toe to foot amputations. Management of diabetic foot mainly depends on diabetic foot ulcer grading, its vascularity and presence of infection. Among Indian population, lack of knowledge regarding foot complications of diabetes mellitus, habits like barefoot walking, hot climate, poor hygiene etc. increase the chance of diabetic foot complications.

Diabetes mellitus being a metabolic disorder is caused by increased insulin resistance and/or decreased of insulin production. The deficiency of insulin in diabetic patients could be due to excessive glucose in blood or decreased insulin production or Anti-insulin antibodies. Diabetes mellitus with its estimated incidence rate at 150 million by 2030 is a global health burden.[2]

Uncontrolled blood sugar levels in patients with chronic diabetes cause irreversible damage in multiple organs leading to severe life-threatening complications, most important of which micro-vascular complications like diabetic retinopathy, nephropathy, macrovascular complications, and diabetic neuropathy are the forerunners,
that predispose to a 3 times increased risk of cardiovascular and cerebrovascular disease.[3]

Diabetic foot ulcers are the most visible, prevalent external manifestations in patients who have uncontrolled diabetes mellitus. Poor glycemic control, associated peripheral vascular diseases, with underlying neuropathy and lack of proper foot care and foot hygiene makes diabetic foot ulcers, a part and parcel of disease progression. It is also one of the most common causes for osteomyelitis of the lower limb bones leading to inevitable surgical intervention like amputations. Ulcers situated on the plantar aspect of the foot, bears a constant pressure of body weight through loading and causing repetitive trauma and delay in wound healing. The prevalence rate of chronic diabetic foot ulcer worldwide is around 10 to 25 millions.[4]

About 20% of diabetic patients carry risk of developing foot ulcers during their entire lifetime.[5] Based on the etiology diabetic foot ulcers can be classified into neuropathic ulcers ,neuro ischemic ulcers ,vascular ischemic ulcers.[6,7]

Diabetic foot ulcers are more prevalent or aggravated with infection, elder age, smoking, alcohol consumption, uncontrolled blood glycemic status, previous foot ulcerations, surgical procedures, peripheral vascular diseases and diabetic neuropathy.[8]

Wound care has a prominent role in diabetic foot ulcer management. Such a wound care involves cleaning the wound surface with strict aseptic precautions and the use of novel wound management modalities like vacuum assisted dressings which will provide environment that is near ideal and better suitable for wound healing.[9]

Healing ulcers represent a much important health predicament and strain on health resources worldwide. Contemporary studies, augmented our understanding of chronic wound healing physiology and have driven for the development of newer treatments with their major focus of promoting a moist environment in the wound to assist accelerated natural healing process.
Scientists introduced recently the concept of interactive dressings, that can completely change the local micro-environment of the wound. Such interactive dressings with huge range of various useful properties are under intense research currently.
Phenytoin, a Hydantoin derivative, that is being used primarily as an anticonvulsant is now increasingly used in wound care due to its property of fibroblast stimulation.
Soframycin (framycetin) is an aminoglycoside antibiotic used to treat bacterial skin infections and eye or ear infections.
Silver sulphadiazine, being a sulfonamide based topical antibiotic that has both antibacterial and antifungal properties. It is commonly used in partial and full thickness burns to avoid infections.
Betadine (povidone iodine) is an iodine releasing broad spectrum antiseptic used as topical agent in wounds, burns and ulcers.
Dressing agents like betadine, silver sulphadiazine, soframycin and phenytoin
show promising results with reducing duration of diabetic foot ulcers and its complications. Though the above stated dressing agents are in use for diabetic foot ulcers for quiet a long period, proper comparative studies on which kind of dressing agents bring about faster and better outcomes along with good patient compliance have not been conducted, which all when combined could aim to reduce the prevalence of diabetic foot ulcers and its complications.
The intention of this particular study is to compare efficacy of each of the four mentioned dressings and compare their rate of granulation and epithelization in diabetic foot ulcers.

AIMS AND OBJECTIVES

To assess the efficiency of topical betadine, silver sulphadiazine, soframycin, topical phenytoin on diabetic foot ulcers.
To compare the results of above efficiency assessments and identifying the agent with best healing property in diabetic foot ulcers of grade 1 and 2.

MATERIALS AND METHODS

Study design – A Prospective interventional study in a Tertiary care hospital
Duration of the study – 12 months from institutional scientific committee and institutional ethical committee approval.
Sample size – 200
Source of the date – patients presenting with diabetic foot ulcers to Department of general surgery.
Inclusion criteria –
• Patients presenting with diabetic foot ulcers with controlled and uncomplicated diabetes mellitus to the Department of General surgery.
• patients above age of 18 years who will give informed and written consent.
• Ulcer size ranging between 1 -5% of the total body surface area.
Exclusion criteria –
• Diabetic foot ulcers of Meggit Wagner classification with grades 3,4 and 5.
• Ulcers due to other chronic etiology like arteriosclerosis, venous insufficiency, clotting disorders, hypertension, lymphedema, vasculitis, scleroderma, lupus,
Rheumatological conditions, hypercholesterolemia, sickle cell anemia, habit of smoking, pressure sores, malignancy, other infections and certain medications.
• Other co-morbid conditions like renal failure, generalized debility that adversely affect wound healing.
• Patients with allergy to phenytoin, silver ointments, soframycin or betadine.
Data collection -

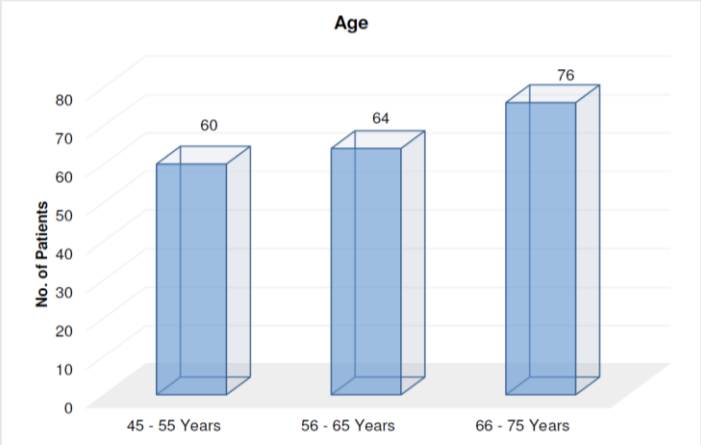
The wound surface areas are measured using Graph paper – Tracing method. The wound surface areas were measured initially at the beginning of the study and one again at the 21st day. The differences in the wound surface areas were expressed in percentage point reductions in wound surface areas over the course of the study. Tracings of the wound surface is made by placing a sterilized transparency film over the wound and the wound's perimeter is traced. The border between the wound floor and the peripheral epithelium is considered as the wound perimeter. A fine tipped transparency marker is used for tracing the wound perimeter on the film. The tracings from the transparency film is carefully cut and is placed over a standard graph paper and the measurement of the surface area is done. The measurement is done in cm2 and complete 1*1 squares are considered as 1 cm2 and any 1*1 squares with more than half under the tracings is considered as 1 cm2. Any 1*1 squares with less than half of it's area under the tracings is omitted.[13]

OBSERVATIONS & RESULTS

Table No.1 : Age wise distribution

Age	**No. of Patients**	**%**
45 – 55 Years	60	30.0
55 – 65 Years	64	32.0
65 – 75 Years	76	38.0
Total	200	100.0
Mean Age	**61.045 ± 8.656**	

Graph No.1 : Age Wise Distribution

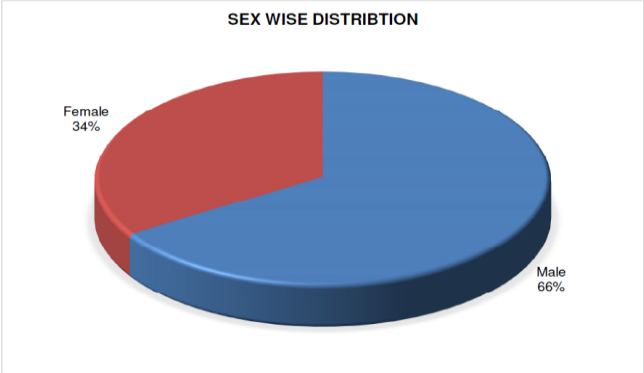


The mean age of study group was 61.045 years with standard deviation of 8.656 years, with 60 patients (30%) in age bracket of 45- 55 years and with 64 patients (32%) in age bracket 55-65 years and with remaining 76 patients (38%) in age bracket of 66-75 years.

Table No.2 : Sex distribution

Sex	**No. of Patients**	**%**
Male	132	66.0
Female	68	34.0
Total	200	100.0

Graph No.2 : Sex Distribution

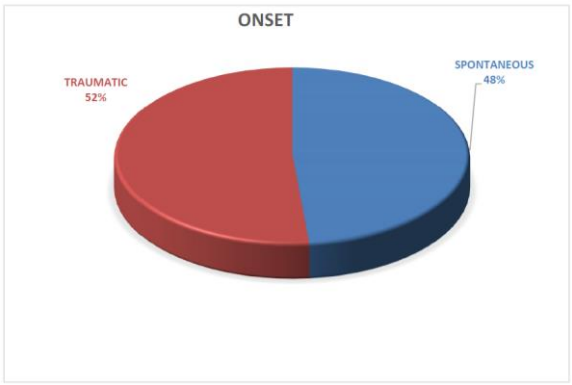


In the entire study population, 132 (66%) were male and the remaining 68(34%) were females and it is observed that there is no significant relation or association between sex of the patient and group to which they were randomized to.

Table No.3 : Onset of the ulceration

Onset	**No. of Patients**	**%**
SPONTANEOUS	97	48.5
TRAUMATIC	103	51.5
Total	200	100.0

Graph No.3 : Oncet of the ulceration

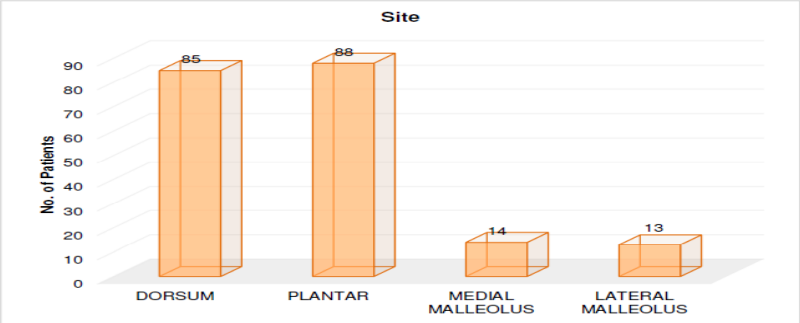


In the entire study population, 97 patients (48.5%) acquired their ulcerations as spontaneous eruptions or rupture of bullae and the remaining 103 (51.5%) acquired their ulcerations as a consequence of a trauma.

Table No.4 : Site of the ulceration

Site	**No. of Patients**	**%**
Dorsal aspect of the foot	85	42.5
Plantar aspect of the foot	88	44.0
Medial Malleolus	14	7.0
Lateral Malleolus	13	6.5
Total	200	100.0

Graph No.4 : Site of the ulceration

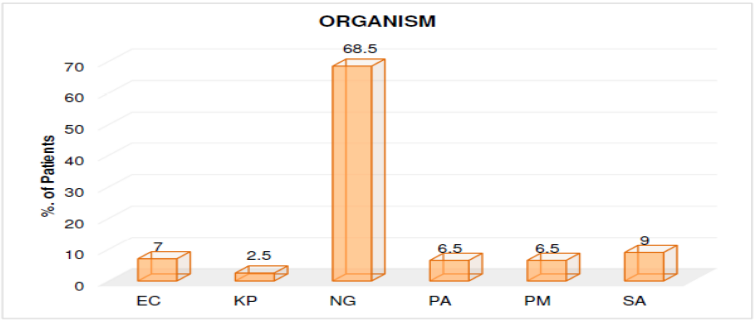


In the entire study population, 85 patients (42.5%) had their ulcer over the dorsal aspect of the foot where as other majority group with 88 patients (44%) had their ulcerations over the plantar aspect of the foot. In the rest of the study population, 14 patients (7%) had ulcers over medial malleolus of the foot and the rest 13 patients (6.5%) had their ulcers over the lateral malleolus.

Table No.5 : Organism isolated from ulcer culture

Organism	**No. of Patients**	**%**
EC	14	7.0
KP	5	2.5
NG	137	68.5
PA	13	6.5
PM	13	6.5
SA	18	9.0
Total	200	100.0

Graph No.5 : Organism isolated from ulcer culture

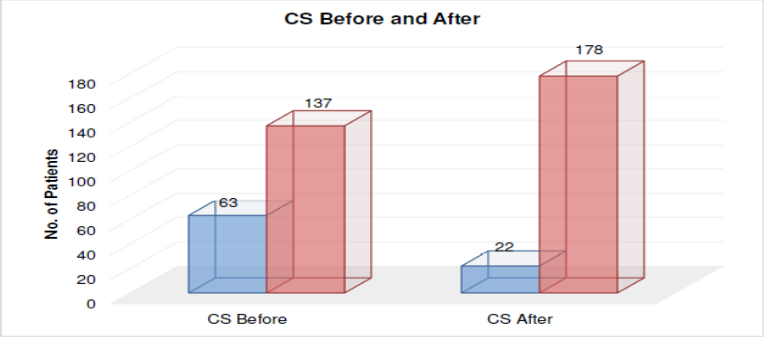


Out of all the instances of culture and sensitivity done with secretions from the ulcers, in majority of the instances i.e. 137 (68.5%) have no organism found. In the rest of the instances 18 (9%) had Staphylococcus aureus, 14 (7%) had Escherichia coli , 13(6.5%) had Pseudomonas aeruginosa, 13 (6.5%) had Proteus mirabilis and 5 (2.5%) had Klebsiella pneumonia.

Table No.6 : Culture and Sensitivity before and after dressings

		No. of Patients	**%**
CS Before	Positive	63	31.5
	Negative	137	68.5
	Total	200	100.0
CS After	Positive	22	11.0
	Negative	178	89.0
	Total	200	100.0

Graph No.6 : Culture and Sensitivity before and after dressings

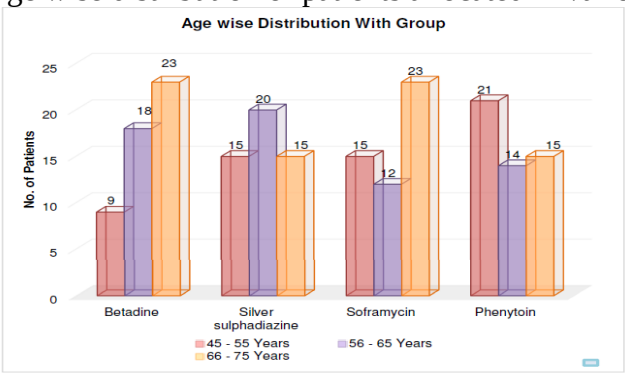


In the entire study, through its course, culture and sensitivity is done for the discharge from the ulcer once at the recruitment of the patients into the study and once at the end of the study. In the initial assessment of the ulcer microbiomes, 63 (31.5%) showed positive growth and the rest 137 (68.5%) showed no growth. In the final assessment of the ulcer microbiomes, only 22 (11%) showed positive growth and the remaining majority of 178 (89%) showed no growth. A shear reduction of 21.5% points noted in the culture positivity rates.

Table No.7 : Age wise distribution of patients allocated in various study groups

Age	GROUP					Chi-square
	Betadine	Silver sulphadiazine	Soframycin	Phenytoin	Total	
45 - 55 Years	9 (18.0)	15 (30.0)	15 (30.0)	21 (42.0)	60 (30.0)	$x2 = 10.668^{@}$; (p = 0.099) ; df= 6; Not Significant
56 - 65 Years	18 (36.0)	20 (40.0)	12 (24.0)	14 (28.0)	64 (32.0)	
66 - 75 Years	23 (46.0)	15 (30.0)	23 (46.0)	15 (30.0)	76 (38.0)	
Total	50 (100.0)	50 (100.0)	50 (100.0)	50 (100.0)	200 (100.0)	
Mean Age	63.06±7.86	60.54±8.37	61.98±9.02	58.60±8.92	61.04±8.66	

Graph No.7 : Age wise distribution of patients allocated in various study groups



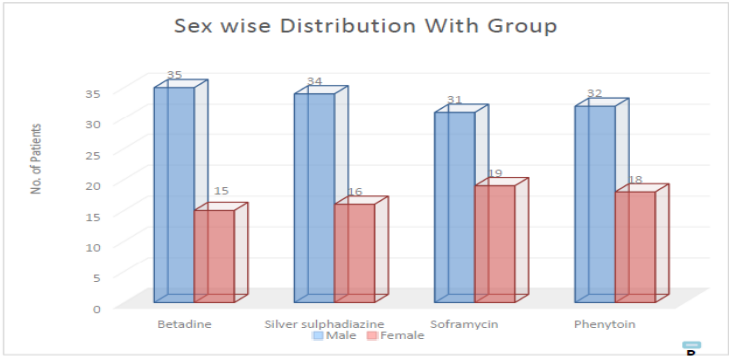
Of all the 50 patients allotted in Group 1 (Betadine), 9 belong to 45-55 years group, 18 belong to 55-65 years group and 23 belong to 65-75 years age group. Of all the 50 patients allotted in Group 2 (silver sulphadiazine), 15 belong to 45-55 years group, 20 belong to 55-65 years group and 15 belong to 65-75 years age group. Of all the 50 patients allotted in Group 3 (Soframycin), 15 belong

to 45-55 years group, 12 belong to 55-65 years group and 23 belong to 65-75 years age group. Of all the 50 patients allotted in Group 4 (phenytoin), 21 belong to 45-55 years group, 14 belong to 55-65 years group and 15 belong to 65-75 years age group . No significant association is noted between the age distribution in relation to the group allotment.

Table No.8 : Sex wise distribution as allotted to various study groups

Sex	GROUP					Chi-square
	Betadine	Silver Sulphadiazine	Soframycin	Phenytoin	Total	
Male	35 (70.0)	34 (68.0)	31 (62.0)	32 (64.0)	132 (66.0)	$\chi2 = 0.891^{@}$; (p = 0.828); df= 3; Not Significant
Female	15 (30.0)	16 (32.0)	19 (38.0)	18 (36.0)	68 (34.0)	
Total	50 (100.0)	50 (100.0)	50 (100.0)	50 (100.0)	200 (100.0)	

Graph No.8 : Sex wise distribution as allotted to various study groups

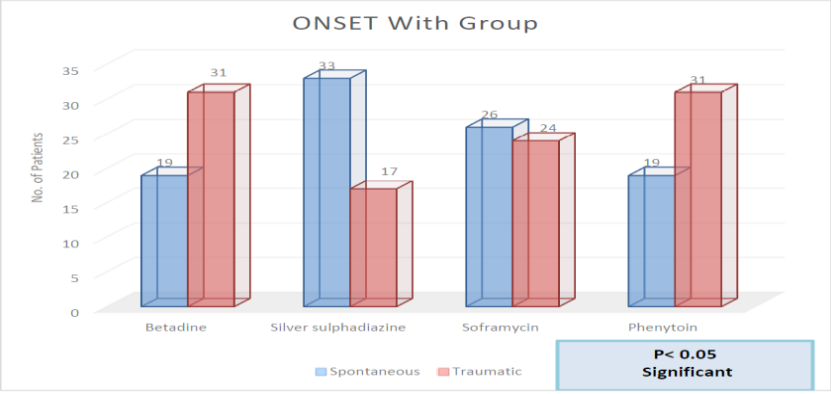


Of all the 50 patients allotted in Group 1 (Betadine), 35 (70%) were male and remaining 15 (30%) were female. Of all the 50 patients allotted in Group 2 (silver sulphadiazine), 34 (68%) were male and remaining 16 (32%) were female. Of all the 50 patients allotted in Group 3 (soframycin), 31 (62%) were male and remaining 19 (38%) were female. Of all the 50 patients allotted in Group 4 (phenytoin), 32 (64%) were male and remaining 18 (36%) were female. No significant association is noted between the sex wise distribution in relation to the group allotment.

Table No.9 : Onset of the ulcer wise distribution as allotted to various study

ONSET	GROUP					Chi-square
	Betadine	Silver sulphadiazine	Soframycin	Phenytoin	Total	
Spontaneous	19 (38.0)	33 (66.0)	26 (52.0)	19 (38.0)	97 (48.5)	$\chi2 = 10.790^{*}$; (p =0.013); df= 3; Significant P<0.05
Traumatic	31 (62.0)	17 (34.0)	24 (48.0)	31 (62.0)	103 (51.5)	
Total	50 (100.0)	50 (100.0)	50 (100.0)	50 (100.0)	200 (100.0)	

Graph No.9 : Onset of the ulcer wise distribution as allotted to various study groups

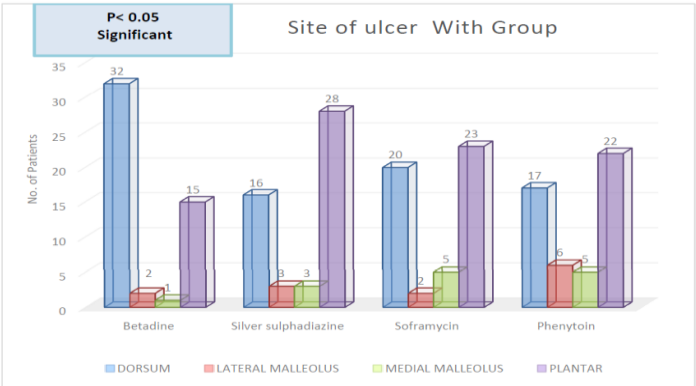


Of all the 50 patients allotted in Group 1 (Betadine), 19 had their ulcers spontaneously and 31 got their ulcers due to various types of trauma. Of all the 50 patients allotted in Group 2 (silver sulphadiazine), 33 had their ulcers spontaneously and 17 got their ulcers due to various types of trauma. Of all the 50 patients allotted in Group 3 (soframycin), 26 had their ulcers spontaneously and 24 got their ulcers due to various types of trauma. Of all the 50 patients allotted in Group 4 (phenytoin), 19 had their ulcers spontaneously and 31 got their ulcers due to various types of trauma.

Table No.10 : Ulcer wise distribution as allotted to various study groups

SITE	GROUP					Chi-square
	Betadine	Silver sulphadiazine	Soframycin	Phenytoin	Total	
Dorsal aspect of the foot	32 (64.0)	16 (32.0)	20 (40.0)	17 (34.0)	85 (42.5)	
Lateral malleolus	2 (4.0)	3 (6.0)	2 (4.0)	6 (12.0)	13 (6.5)	χ^2 = 18.018*; (p=0.035); df= 9; Significant P<0.05
Medial malleolus	1 (2.0)	3 (6.0)	5 (10.0)	5 (10.0)	14 (7.0)	
Plantar aspect of the foot	15 (30.0)	28 (56.0)	23 (46.0)	22 (44.0)	88 (44.0)	
Total	50 (100.0)	50 (100.0)	50 (100.0)	50 (100.0)	200 (100.0)	

Graph No.10: Ulcer wise distribution as allotted to various study groups



Of all the 50 patients allotted in Group 1 (Betadine), 32 had ulcer in dorsum of the foot, 2 had ulcer in lateral malleolus of the foot, 1 had ulcer in medial aspect of the of the foot and 15 had ulcer in plantar aspect of the foot. Of all the 50 patients allotted in Group 2 (silver sulphadiazine), 16 had ulcer in dorsum of the foot, 3 had ulcer in lateral malleolus of the foot, 3 had ulcer in medial aspect

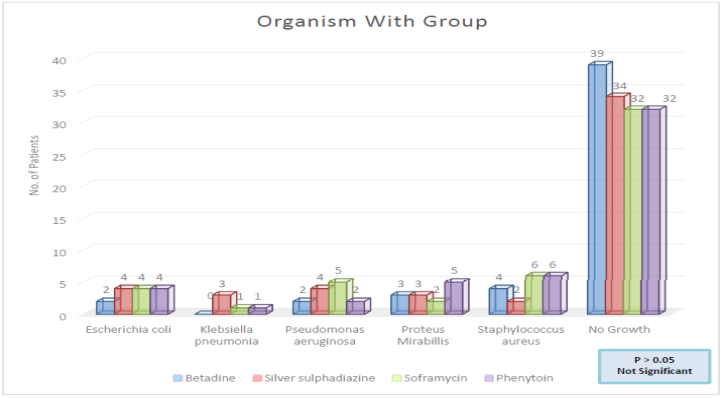
of the of the foot and 28 had ulcer in plantar aspect of the foot. Of all the 50 patients allotted in Group 3 (soframycin), 20 had ulcer in dorsum of the foot, 2 had ulcer in lateral malleolus of the foot, 5 had ulcer in medial aspect of the of the foot and 23 had ulcer in plantar aspect of the foot. Of all the 50 patients allotted in Group 4 (Phenytoin), 17 had ulcer in dorsum of the foot, 6 had ulcer in lateral malleolus of the foot, 5 had ulcer in medial aspect of the of the foot and 22 had ulcer in plantar aspect of the foot. A significant association is noted between the site of the ulcer and the patients allotted to various study groups.

Table No.11 : Culture sensitivity wise distribution as allotted to various study groups

Organism	GROUP					Chi-square
	Betadine	Silver sulphadiazine	Soframycin	Phenytoin	Total	
EC	2 (4.0)	4 (8.0)	4 (8.0)	4 (8.0)	14 (7.0)	$x2 = 11.596^{@}$; (p = 0.709) ; df= 15; Not Significant P>0.05
KP	0 (.0)	3 (6.0)	1 (2.0)	1 (2.0)	5 (2.5)	
NG	39 (78.0)	34 (68.0)	32 (64.0)	32 (64.0)	137 (68.5)	
PA	2 (4.0)	4 (8.0)	5 (10.0)	2 (4.0)	13 (6.5)	
PM	3 (6.0)	3 (6.0)	2 (4.0)	5 (10.0)	13 (6.5)	
SA	4 (8.0)	2 (4.0)	6 (12.0)	6 (12.0)	18 (9.0)	
Total	50 (100.0)	50 (100.0)	50 (100.0)	50 (100.0)	200 (100.0)	

Of all the 50 patients allotted to group 1 (Betadine), before initiation of dressings, 2 showed positive growth for Escherichia coli, 0 showed positive growth for Klebsiella pneumonia , 2 showed positive growth for Pseudomonas aeruginosa, 3 showed positive growth for Proteus mirabilis, 4 showed positive growth for Staphylococcus aureus and 39 showed no growth upon culture. Of all the 50 patients allotted to group 2 (Silver sulphadiazine), before initiation of dressings, 4 showed positive growth for Escherichia coli, 3 showed positive growth for Klebsiella pneumonia, 4 showed positive growth for Pseudomonas aeruginosa, 3 showed positive growth for Proteus mirabilis, 4 showed positive growth for Staphylococcus aureus and 34 showed no growth upon culture.

Graph No.11 : Culture sensitivity wise distribution as allotted to various study



Of all the 50 patients allotted to group 3 (Soframycin), before initiation of dressings, 4 showed positive growth for Escherichia coli, 1 showed positive growth for Klebsiella pneumonia, 5 showed positive growth for Pseudomonas aeruginosa, 2 showed positive growth for Proteus mirabilis, 6 showed positive growth for Staphylococcus aureus and 32 showed no growth upon culture. Of all the 50 patients allotted to group 4 (Phenytoin), before initiation of dressings, 4 showed positive growth for Escherichia coli, 1 showed positive growth for Klebsiella pneumonia, 2 showed positive

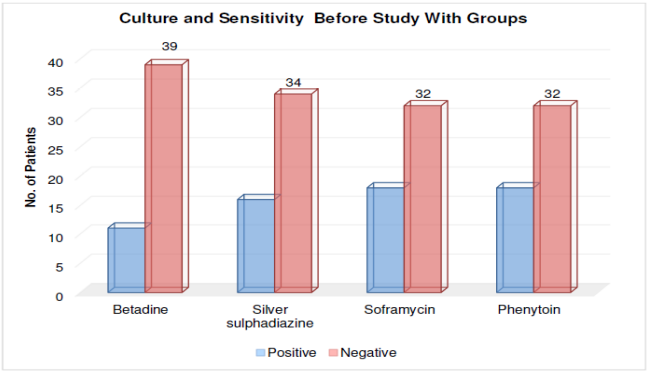
growth for Pseudomonas aeruginosa, 5 showed positive growth for Proteus mirabilis, 6 showed positive growth for Staphylococcus aureus and 32 showed no growth upon culture.

Table No.12 : Culture and sensitivity wise distribution as allotted into various study groups

		GROUP					Chi-square
		Betadine	Silver sulphadiazine	Soframycin	Phenytoin	Total	
Culture and Sensitivity Before	Positive	11 (22.0)	16 (32.0)	18 (36.0)	18 (36.0)	63 (31.5)	x2 = 3.036@; (p =0.386); df= 3;
	Negative	39 (78.0)	34 (68.0)	32 (64.0)	32 (64.0)	137 (68.5)	
	Total	50 (100.0)	50 (100.0)	50 (100.0)	50 (100.0)	200 (100.0)	
Culture and Sensitivity After	Positive	4 (8.0)	6 (12.0)	4 (8.0)	8 (16.0)	22 (11.0)	x2 = 2.247@; (p =0.523); df= 3; @ - Not Significant
	Negative	46 (92.0)	44 (88.0)	46 (92.0)	42 (84.0)	178 (89.0)	
	Total	50 (100.0)	50 (100.0)	50 (100.0)	50 (100.0)	200 (100.0)	

Out of all 50 patients allotted into Group 1 (Betadine), 11 showed positive growth before dressings and 4 showed positive growth after 21 days of dressings and 39 showed no growth before dressings and 46 showed no growth after 21 days of dressings, showing a reduction of 14% points in culture positivity. Out of all 50 patients allotted into Group 2 (Silver sulphadiazine), 16 showed positive growth before dressings and 6 showed positive growth after 21 days of dressings and 34 showed no growth before dressings and 44 showed no growth after 21 days of dressings, showing a reduction of 20% points in culture positivity.

Graph No.12 : Culture and Sensitivity Before Study With Groups



Graph No.13 : Culture and Sensitivity After Study With Groups

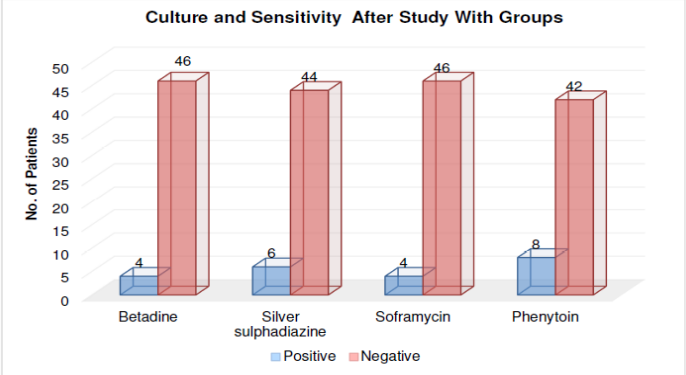


Table No.13 : CS Before Study and CS After Study

Paired Samples Statistics				t-value (p-value)	Sig.
	N	Mean ± S.D	S.E		
CS Before	200	0.32 ± 0.466	0.033	4.938** (0.000)	**P< 0.001
CS After	200	0.11 ± 0.314	0.022		

Data showing significant association @ p< 0.001 between culture positivity before and after frequent and regular dressings .

Table No.14 : Mean scores of ulcer surface area at the initiation of the study as in various study groups

Initial Area	N	Mean±S.D in cm^2	S.E	F-value	Sig.
Betadine	50	427.32 ± 107.240	15.166	0.170@ (0.917)	@P>0.05 Not significant
Silver sulphadiazine	50	433.80 ± 98.551	13.937		
Soframycin	50	424.44 ± 91.079	12.880		
Phenytoin	50	419.50 ± 111.801	15.811		
Total	200	426.27 ± 101.835	7.201		

The mean ulcer surface area at the beginning of the study in group 1 (Betadine) with it's 50 patients is 427.32 ± 107.24 cm2 with standard error at 15.166. The mean ulcer surface area at the beginning of the study in group 2 (Silver sulphadiazine) with it's 50 patients is 433.80 ± 98.551 with standard error at 13.937. The mean ulcer surface area at the beginning of the study in group 3 (Soframycin) with it's 50 patients is 424.44 ± 91.079 with standard error at 12.880. The mean ulcer surface area at the beginning of the study in group 4 (Phenytoin) with it's 50 patients is 419.50 ± 111.801 with standard error at 7.201.

Table No.15 : Mean scores of ulcer surface area at the end of the 21 day checkpoint as in various study groups

Final Area	N	Mean ± S.D	S.E	F-value	Sig.
Betadine	50	171.50 ± 45.764	6.472	4.702** (0.003)	**P<0.001 Highly Significant
Silver sulphadiazine	50	178.86 ± 37.288	5.273		
Soframycin	50	184.26 ± 38.684	5.471		
Phenytoin	50	155.84 ± 38.756	5.481		
Total	200	172.62 ± 41.368	2.925		

The mean ulcer surface area at 21 day check point in the study in group 1 (Betadine) with it's 50 patients is 171.50 ± 45.764 cm2 with standard error at 6.472. The mean ulcer surface area at 21 day check point in the study in group 2 (Silver sulphadiazine) with it's 50 patients is 178.86 ±37.288 cm2 with standard error at 5.273. The mean ulcer surface area at 21 day check point in the study in group 3 (soframycin) with it's 50 patients is 184.26 ± 38.684 cm2 with standard error at 5.471. The mean ulcer surface area at 21 day check point in the study in group 4 (Phenytoin) with it's 50 patients is 155.84 ± 38.756 cm2 with standard error at 5.481. A significant association is noted @ p<0.001 with respective to ulcer area at 21 day checkpoint in the course of the study.

Graph No.14 : Mean scores of ulcer surface area at the end of the 21 day

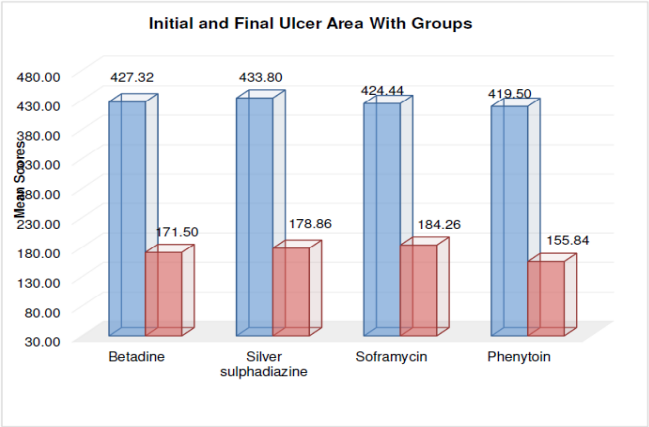


Table No.16 : Mean scores of percentage point reduction in ulcer surface area as a distribution as allotted to various study groups

Area Reduction	N	Mean ± S.D	S.E	F-value	Sig.
Betadine	50	57.59 ± 14.456	2.044	2.651* (0.050)	*P<0.05 Significant
Silver sulphadiazine	50	56.74 ± 12.710	1.797		
Soframycin	50	54.16 ± 15.512	2.194		
Phenytoin	50	61.46 ± 8.938	1.264		
Total	200	57.49 ± 13.306	0.941		

The reduction in ulcer surface area is expressed as percentage points in comparision to ulcer surface area at the start of the study to the ulcer surface area at the end of 21 days . Group 1 (Betadine) showed a reduction in ulcer surface area at 57.59±14.456% with standard error at 2.04, Group 2 (silver sulphadiazine) showed a reduction in ulcer surface area at 56.74 ± 12.710 % with standard error at 1.8, Group 3 (Soframycin) showed a reduction in ulcer surface area at 54.16 ± 15.512% with standard error at 2.2 and Group 4 (Phenytoin) showed a reduction of ulcer surface area at 61.46 ± 8.938% with standard error at 0.94. The study acquired a statistical significance of F value of 2.651 @p< 0.05.

Graph No.15 : Mean scores of percentage point reduction in ulcer surface area as a distribution as allotted to various study groups

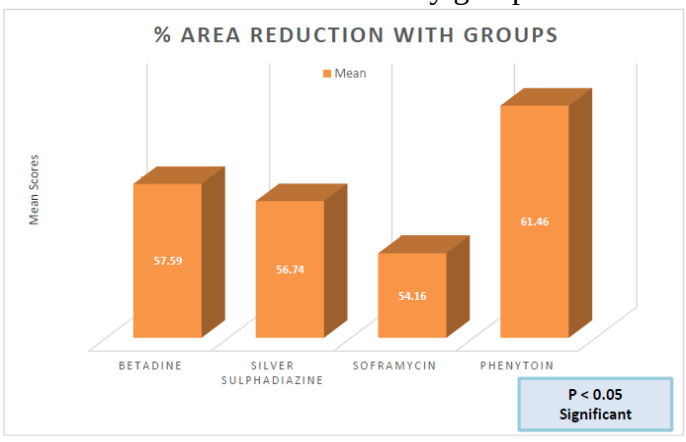


Table No.17 : Paired statistical analysis between initial and final ulcer areas

Paired Samples Statistics				t-value	Sig.
	N	Mean ± S.D	S.E	(p-value)	
Initial Area	200	426.27 ± 101.84	7.201	34.931**	**P< 0.001
Final Area	200	172.62 ± 41.37	2.925	(0.000)	

The ulcer surface area of all the 200 patients that participated in the study when compared and levied against the ulcer surface area at the beginning of the study acquired a statistically significant association @p<0.001 with mean of initial surface area being at 426.27±101.84 and mean of final surface area at 172.62±41.37.

Table No.18 : Paired statistical analysis between initial ulcer area and percentage area reduction

Paired Samples Statistics				t-value	Sig.
	N	Mean ± S.D	S.E	(p-value)	
Initial Area	200	426.27 ± 101.84	7.201	55.534**	**P< 0.001
Area Reduction	200	57.49 ± 13.306	0.941	(0.000)	

The mean ulcer surface area of all the 200 patients (426.27±101.84) acquired a statistically significant association @p<0.001 when levied against percentage point reduction in surface area of the ulcer at the end of 21 day study duration (57.49 ±15.533).

Table No.19 : Paired statistical analysis between final ulcer area and percentage area reduction

Paired Samples Statistics				t-value	Sig.
	N	Mean ± S.D	S.E	(p-value)	
Final Area	200	172.62 ± 41.37	2.965	32.188**	**P< 0.001
Area Reduction	200	57.49 ± 15.533	1.098	(0.000)	

The mean ulcer surface area of all the 200 patients at the end of 21 days of dressings (172.62±41.37) acquired a statistically significant association @p<0.001 when levied against percentage point reduction in surface area of the ulcer at the end of 21 day study duration(57.49 ±15.533).

DISCUSSION

Crude methods, such as the application of topical herbal remedies or traditional medications, may fail to achieve better outcomes in the treatment of diabetic ulcers. This is because these methods may not effectively address the underlying cause of the ulcer, which is often a lack of adequate blood flow to the area due to diabetes-related vascular damage. In addition, these methods may not be able to adequately address the infection or inflammation that can accompany diabetic ulcers, both of which can lead to further tissue damage. As a result, the healing process is often not effective, and the ulcer may remain open and prone to complications.

The best treatment modality for diabetic foot ulcers depends on the severity and cause of the ulcer. Generally, treatment includes cleaning and debriding the wound, offloading pressure, using dressings to manage the wound, providing antibiotics and medications if needed, and managing factors contributing to the ulcer (such as poor glycemic control and neuropathy). In some cases, advanced treatments such as hyperbaric oxygen therapy and skin grafting may be recommended. Therefore, testing these strategies in the new world is essential to improve outcomes for diabetic foot ulcer patients.

The need for testing different treatment methods for treatment of diabetic foot ulcers in the new world is of paramount importance. Diabetes is one of the leading causes of disability and death in

the India and other countries, and diabetic foot ulcers are one of the most common and serious complications of diabetes. Without proper treatment, diabetic foot ulcers can lead to serious infections, amputations, and even death. Therefore, it is essential that new treatment methods are tested to see if they are effective in improving outcomes and reducing complications.

The main goal of the treating surgeon in case of a diabetic foot ulcers is to avoid further increase in the size of the ulceration and avoid its complications and at the same time strive for the early healing of the ulcer with frequent and regular dressings. Ulcers in diabetic foot ulcers are chronic, arrested in inflammatory phase and shows arrest of epidermal growth. Persistent raw surface of the wound makes them more susceptible for infections and due to persistent high blood sugars and micro vascular angiopathy , more susceptible for ischemia.

An ideal dressing is one that heals the chronic foot ulcers without any complications and maintains a persistent healthy moist micro environment at the level of wound, promoting quicker wound healing by granulation and re epithelization and being non reactive, non allergy eliciting, inhibiting infections, avoiding skin macerations and wound breaching.

This study is conducted in S.V.R.R Government General Hospital, Tirupathi, to compare the four readily available dressing agents in a Public health care setup as a viable, effective and economical alternative to plain saline dressings.

It is observed that in the entire study population, 132 (66%) were male and the remaining 68(34%) were females and it is observed that there is no significant relation or association between sex of the patient and group to which they were randomized to. Of all the 50 patients allotted in Group 1 (Betadine), 35 (70%) were male and remaining 15 (30%) were female. Of all the 50 patients allotted in Group 2 (silver sulphadiazine), 34 (68%) were male and remaining 16 (32%) were female. Of all the 50 patients allotted in Group 3 (soframycin), 31 (62%) were male and remaining 19 (38%) were female. Of all the 50 patients allotted in Group 4 (phenytoin), 32 (64%) were male and remaining 18 (36%) were female .The National Health Data Source (NHDS) documented a similar higher rate of admission in male population country-wide. In similar studies, B Naik et al[14] showed 74% male dominance in hospitalization as compared to 26% in female population and J Shaw et al[15] showed 72% male domination and Leo F Tauro et al[16] showed 61% male dominance and Anis Ahmed et al showed 60% male domination in hospitalization rates as compared to female hospitalization rates.

Study	B naik et al	J shaw et al	Leo F Tauro et al	Current study
Male %	74%	72%	61%	66%
Female %	26%	28%	39%	34%

The mean age of study group was 61.045 years with standard deviation of 8.656 years, with 60 patients (30%) in age bracket of 45- 55 years and with 64 patients (32%) in age bracket 55-65 years and with remaining 76 patients (38%) in age bracket of 66-75 years. The mean age in patients with Betadine dressings group is 63.06 years, mean age in patients with Silver sulphadiazine dressing group is 60.54 years, mean age of patients in Soframycin group is 61.58 years and the mean age of patients in Phenytoin dressing group is 58.60 years. In similar study, conducted by B Naik et al[14], mean age group is around 44 years and in study conducted by Singh B et al[12], the mean age of the patients undergoing the study is around 56 years. In study by J Shaw et al[15], mean age of the study population is 61.7 years and in study conducted by Leo F Tauro et al[16], the mean age of the study population is around 51 years.

Study	B Naik et al	Singh B et al	J Shaw et al	Leo F Tauro	Current study
Mean age	44	56	61.7	51	61

Of all the 50 patients allotted in Group 1 (Betadine),32 had ulcer in dorsum of the foot, 2 had ulcer in lateral malleolus of the foot, 1 had ulcer in medial aspect of the of the foot and 15 had ulcer in plantar aspect of the foot. Of all the 50 patients allotted in Group 2 (silver sulphadiazine), 16 had ulcer in dorsum of the foot, 3 had ulcer in lateral malleolus of the foot, 3 had ulcer in medial aspect of theof the foot and 28 had ulcer in plantar aspect of the foot. Of all the 50 patients allotted in Group 3 (soframycin), 20 had ulcer in dorsum of the foot, 2 had ulcer in lateral malleolus of the foot, 5 had ulcer in medial aspect of the of the foot and 23 had ulcer in plantar aspect of the foot. Of all the 50 patients allotted in Group 4 (Phenytoin), 17 had ulcer in dorsum of the foot, 6 had ulcer in lateral malleolus of the foot, 5 had ulcer in medial aspect of the of the foot and 22 had ulcer in plantar aspect of the foot. In this study, 88 patients (44%) had their ulcers over the plantar aspect of the foot and 85 patients (42.5%) had their ulcers over the dorsum of the foot and in the rest 14 patients (7%) over medial malleolus and rest 13 patients (6.5%) had their ulcers over lateral malleolus. A study by Edmonds at al[17] showed that majority of ulcers in diabetics are located in fore foot plantar surface and most were related to inappropriate foot wear and associated with abnormal gait. A study by B Naik et al[14] showed 40 % of their study population had their ulcers over the lateral malleolus of the foot.

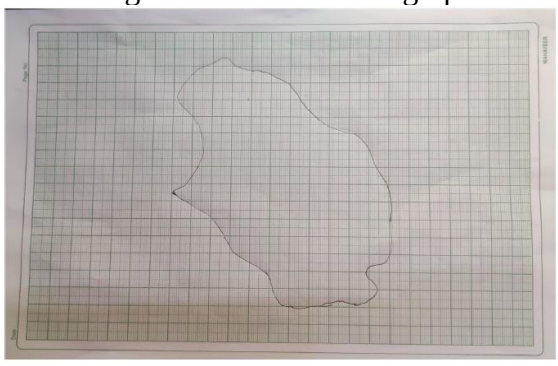
Of all the 50 patients allotted to group 1 (Betadine), before initiation of dressings, 2 showed positive growth for Escherichia coli, 0 showed positive growth for Klebsiella pneumonia , 2 showed positive growth for Pseudomonas aeruginosa, 3 showed positive growth for Proteus mirabilis, 4 showed positive growth for Staphylococcus aureus and 39 showed no growth upon culture. Of all the 50 patients allotted to group 2 (Silver sulphadiazine), before initiation of dressings, 4 showed positive growth for Escherichia coli, 3 showed positive growth for Klebsiella pneumonia, 4 showed positive growth for Pseudomonas aeruginosa, 3 showed positive growth for Proteus mirabilis, 4 showed positive growth for Staphylococcus aureus and 34 showed no growth upon culture. Of all the 50 patients allotted to group 3 (Soframycin), before initiation of dressings, 4 showed positive growth for Escherichia coli, 1 showed positive growth for Klebsiella pneumonia, 5 showed positive growth for Pseudomonas aeruginosa, 2 showed positive growth for Proteus mirabilis, 6 showed positive growth for Staphylococcus aureus and 32 showed no growth upon culture. Of all the 50 patients allotted to group 4 (Phenytoin), before initiation of dressings, 4 showed positive growth for Escherichia coli, 1 showed positive growth for Klebsiella pneumonia, 2 showed positive growth for Pseudomonas aeruginosa, 5 showed positive growth for Proteus mirabilis, 6 showed positive growth for Staphylococcus aureus and 32 showed no growth upon culture.

Out of all 50 patients allotted into Group 1 (Betadine), 11 showed positive growth before dressings and 4 showed positive growth after 21 days of dressings and 39 showed no growth before dressings and 46 showed no growth after 21 days of dressings, showing a reduction of 14% points in culture positivity. Out of all 50 patients allotted into Group 2 (Silver sulphadiazine), 16 showed positive growth before dressings and 6 showed positive growth after 21 days of dressings and 34 showed no growth before dressings and 44 showed no growth after 21 days of dressings, showing a reduction of 20% points in culture positivity. Out of all 50 patients allotted into Group 3 (Soframycin), 18 showed positive growth before dressings and 4 showed positive growth after 21 days of dressings and 32 showed no growth before dressings and 46 showed no growth after 21 days of dressings, showing a reduction of 28% points in culture positivity. Out of all 50 patients allotted into Group 4 (Phenytoin), 18 showed positive growth before dressings and 8 showed positive growth after 21 days of dressings and 32 showed no growth before dressings and 42 showed no growth after 21 days of dressings, showing a reduction of 20% points in culture positivity. In similar study conducted by B Naik et al, 4 showed positive growth for Escherichia coli, 10 for Klebsiella pneumonia, 6 for Pseudomonas aeruginosa, 5 for Proteus mirabilis, 21 for Staphylococcus aureus and 14 showed no growth.

Figure 1 : Ulcer to be measured

Figure 2 : Ulcer markings over a tracer sheet

Figure 3 : Ulcer markings transferred on to a graph sheet from the tracer



The mean ulcer surface area at the beginning of the study in group 1 (Betadine) with it's 50 patients is 427.32±107.24 cm2 with standard error at 15.166. The mean ulcer surface area at the beginning of the study in group 2 (Silver sulphadiazine) with it's 50 patients is 433.80±98.551 with standard error at 13.937. The mean ulcer surface area at the beginning of the study in group 3 (Soframycin) with it's 50 patients is 424.44±91.079 with standard error at 12.880. The mean ulcer surface area at the beginning of the study in group 4 (Phenytoin) with it's 50 patients is 419.50±111.801 with standard error at 7.201.

The mean ulcer surface area at 21 day check point in the study in group 1 (Betadine) with it's 50 patients is 171.50 ± 45.764 cm2 with standard error at 6.472. The mean ulcer surface area at 21 day

check point in the study in group 2 (Silver sulphadiazine) with it's 50 patients is 178.86±37.288 cm2 with standard error at 5.273. The mean ulcer surface area at 21 day check point in the study in group 3 (soframycin) with it's 50 patients is 184.26± 8.684 cm2 with standard error at 5.471. The mean ulcer surface area at 21 day check point in the study in group 4 (Phenytoin) with it's 50 patients is 155.84±38.756 cm2 with standard error at 5.481. A significant association is noted @ $p<0.001$ with respective to ulcer area at 21 day checkpoint in the course of the study. The reduction in ulcer surface area is expressed as percentage points in comparision to ulcer surface area at the start of the study to the ulcer surface area at the end of 21 days. Group 1 (Betadine) showed a reduction in ulcer surface area at 57.59 ± 14.456% with standard error at 2.04, Group 2 (silver sulphadiazine) showed a reduction in ulcer surface area at 56.74±12.710% with standard error at 1.8, Group 3 (Soframycin) showed a reduction in ulcer surface area at 54.16±15.512% with standard error at 2.2 and Group 4 (Phenytoin) showed a reduction of ulcer surface area at 61.46±8.938% with standard error at 0.94.

In the present study, the participants of phenytoin group showed a better reduction in ulcer surface area in percentage points of 61.46% as compared to 57.59% with Betadine group, 56.74% with Silver sulphadiazine group and 54.16% with Soframycin group with a strong statistical significance @ $p< 0.05$. In similar study, by B Naik et al[14], mean percentage reduction in ulcer surface area is around 90 % for povidone iodine group and in study by Singh B et al[12], a mean percentage area reduction of 83% is noted. Such high figures can be attributed for rather smaller population sizes and longer study courses.

Phenytoin is an proven anti-convulsant therapeutic agent used in prophylaxis and management of different types of seizures. (J Shaw et al 2007)[15]. Phenytoin promotes wound healing by stimulating proliferation of fibroblasts and deposition of collagen and enhances granulation tissue formation and decrease the activity of collagenases and also leads to neo-vascularization and inhibits glucocorticoid activity. (Inchingolo F et al 2017)[18]. Topical Phenytoin shows anti microbial activity against Staphylococcus aureus, Escherichia coli, Klebsiella pneumonia species via direct or indirect anti bacterial activity by affecting inflammatory cells and promoting neovascularization (Muthukumaraswamy et al, 1991[19]; Anstead et al.1996[20]; Talas et al ,1999[21]; Genever et al , 1996[22]) and leads to platelet derived growth factor gene expression in macrophages (Dill et al,1993[23])

Many other studies were conducted and being conducted to identify the best dressing materials for ever growing diabetic ulcer disease.

In a related study conducted in 2015 by Agarwal et al[10], 60 patients were divided into groups of 30 participants. According to the study, only 10 (33.34%) of the patients who had wounds dressed with povidone iodine-based dressing had 100% granulation tissue, compared to 19 (63.34%) patients whose wounds had been dressed with honey-impregnated dressing.

In order to examine the benefits of alginate dressings vs traditional saline dressings in patients with chronic foot ulcers, Chitrambalam et al[11] carried out a cohort study in 2020. In the study, 88 individuals with diabetic foot ulcers were randomly divided into two groups, each of which had 44 patients. All study participants' wounds had full debridement initially, and the Pressure Ulcer Scale for Healing (PUSH) grading method was used for the initial evaluation. According to a study, Alginates dressing outperforms saline dressings in terms of reducing ulcer size and microbial activity control in diabetic foot ulcers. Alginate is excellent for treating cavity wounds in diabetic foot syndrome because it absorbs significant amounts of exudates and fills in irregularly shaped cavities.

Similar research was done by Singh B et al[12] in 2020, dividing 100 instances of diabetic foot ulcers into two groups of 50 each and comparing the healing responses to nano silver dressing and betadine dressing. Evaluation was based on a number of factors, including decrease in size of the ulcer and good granulation tissue, among others. According to the study, the nano silver group experienced a greater percentage reduction in size than the betadine group. In the nano silver group, wounds were successfully treated early on, and wound healing was superior to that of the betadine group. Nano silver also had superior antibacterial properties.

The beneficial effect of phenytoin is demonstrated in decubitus ulcers (el Zayat, 1989[24], Rhodes et al, 2001[25]), in venous stasis ulcers (Simpson et al, 1965[26]), in traumatic wounds (Modaghegh et al 1989[27], Pendse et al, 1993[28]), burns (Lodha, 1991[29]) and leprosy trophic ulcers (Bansal and Mukul, 1993[30]). Xiang yong hao et al conducted a review analysis considering over three randomized controlled trials and concluded that there is uncertain evidence of topical phenytoin in improvement of ulcer healing in patients with grade 1 and grade 2 pressure ulcers.

Leo F Tauro et al[16], 2013., concluded that topical phenytoin by decreasing bacterial load , forming healthy granulation tissue helps in better graft uptake when compared to conventional dressings . M El- Nahas et al, 2009[31], concluded that Topical Phenytoin is a safe drug that could enhance wound healing in recalcitrant diabetic foot ulcerations.

Manoj V V et al 2021[32], concluded that Topical Phenytoin based dressings are more efficient strategy for management and treatment of chronic non healing diabetic ulcers as compared to conventional saline based dressing regimens. He also stated that topical phenytoin not only significantly reduces the hospital stay but additional application of phenytoin also prevented microbial infection or colonization in chronic non healing ulcers.

Jayaraman Selvaraj et al, 2016[33], stated that topical phenytoin moist wound dressings can be considered as a superior option in the management of diabetic foot ulcers.

Vijaya patil et al conducted a randomized control study in 2013 to evaluate the effect of topical phenytoin over healing in diabetic foot ulcers. 100 patients with grade I and II diabetic foot ulcers were randomly divided into two groups. Patients then subjected to topical phenytoin dressing were classified under study and others who underwent normal saline wound dressings classified as control. Both groups were compared in terms of discharge, slough, wound area reduction and duration of hospital stay. They found that in the phenytoin group, discharge and slough from the wound dramatically decreased by day 14 while it took 21 days in the control group. The average hospital stay in the phenytoin group was 20 days, compared to 26 days in the control group. This difference was statistically significant (p value< 0.005, df1).They concluded that Phenytoin proved to be useful as a topical agent in promoting healing and in controlling infections in diabetic foot ulcers.[35]

JA Jayalal conducted a study over 60 patients with diabetic foot ulcers to assess the efficiency of topical application of phenytoin as powder on healing in diabetic foot ulcer Category I and II. 60 patients with diabetic foot ulcers were randomized into two groups, assigned regular saline and betadine dressing for the control group and phenytoin powder application for the study group. Patient with vascular impairment and uncontrolled diabetes are excluded. Both the control and study group are compared in the reduction in slough, granulating tissue formation, pain, duration of hospital stay, mean surface area reduction of ulcer to assess the healing process. The development of granulation tissue, a reduction in slough, and a wound's size were measured every week to determine how well the wound was healing. At the end of 14 days, just 10% of the control group had healthy granulation tissue present, compared to 60% of the phenytoin study group. Additionally, wound reduction in the study group was 66%, compared to 44% in the control group. The average length of stay in the hospital is dramatically shortened in the phenytoin group. The study group likewise had an excellent pain score. Based on the study, they concluded that phenytoin sodium powder topical application on diabetic foot ulcer promotes early wound healing.[36]

M El-Nahas conducted a prospective trial to study the impact of topical phenytoin on the healing of recalcitrant neuropathic diabetic foot ulcers in patients with no clinical evidence of ischaemia or infection, and to evaluate its antibacterial effect. In the study, 32 patients were included. For eight weeks, in addition to the patient's regular treatment (weekly sharp debridement, offloading, and use of a gauze dressing), topical phenytoin in the form of 2% aerosol powder was administered once daily. The main result was the grid-traced change in ulcer area over time. The effectiveness of topical phenytoin to eliminate bacterial isolates and the occurrence of adverse effects were secondary outcomes. Topical phenytoin significantly improved healing of recalcitrant neuropathic diabetic foot ulcers. Baseline wound area was 319.3±340.4mm2, reducing to 286.1±341.1mm2 and

269.1±341.2mm2 after four and eight weeks respectively. However, only 18.3%, 27.5%, and 25.7%, 38.6% of the total ulcer size were reduced, respectively. None of the bacterial wound isolates were eliminated by topical phenytoin therapy throughout an eight-week period (Staphylococcus spp., Proteus spp. or Pseudomonas spp.). Only eight (25%) of the 32 individuals tested showed a more than 50% reduction in ulcer size after the eight-week therapy period. Although only 25% of patients saw a more than 50% reduction in ulcer size after eight weeks of therapy, topical phenytoin can improve wound healing in resistant neuropathic diabetic foot ulcers. To identify patients who will respond to such therapy satisfactorily, more research is required.[37]

Fatemeh shakeri et al conducted a study over 76 rats to assess the role of topical phenytoin powder in the enhancement of wound healing in 2017. These 76 rats were separated into two groups and given either phenytoin treatment or regular saline treatment. Both groups' incised open wounds received phenytoin and saline treatments. During a 4-week period, the effectiveness of phenytoin and normal saline administrations was evaluated using morphological and histological analysis. In comparison to the control group, the phenytoin-treated group underwent significant epithelization reduction over the course of the study. Additionally, rats given phenytoin had much higher levels of neovascularization and tensile strength. The change in wound contraction speed was negligible. They concluded that Phenytoin application promoted wound healing. The healing properties of topical phenytoin powder were better in wounds.

In their investigation, DaCosta et al. came to the conclusion that phenytoin modifies the normal course of wound healing and might be useful in instances in which deficient wound collagen deposition may result in subpar wound healing and subsequent morbidity and mortality. In comparison to controls, fibroblast proliferation and neovascularization were observed in the wounds treated with phenytoin at 3 days. On day 6, the treated wounds' inflammatory infiltrate had nearly entirely disappeared, although fibroblast infiltration and angiogenesis remained visibly evident.[38]

PB Mohan et al published a case report on a 34 year old gentleman with a two week old diabetic foot ulcer of traumatic etiology and concluded that although diabetic foot ulcers can significantly increase a patient's risk of morbidity, they can be efficiently treated with the right management. We strongly advocate the use of phenytoin as a treatment for diabetic ulcers due to its demonstrable effectiveness in promoting wound healing as well as its accessibility, low cost, simplicity of use, and safety. To validate the same, a prospective study including a larger sample size is needed.[39]

In the integrative literature review conducted by Flavia firmino et al, Topical phenytoin has been shown to have substantial evidence of therapeutic benefits on the healing process in venous, pressure, diabetic foot, leprosy, pyoderma gangrenosum ulcers, and bed preparation for grafting. According to the quality of the studies, however, ranges from acceptable to poor. It is important to conduct more thorough investigations that back up the use of the phenytoin protocol as a different therapeutic alternative in clinical settings. [40]

Figure 4 : Ulcer on Day 1

Figure 5 : Ulcer on Day 21

Figure 6 : Image a * Image b

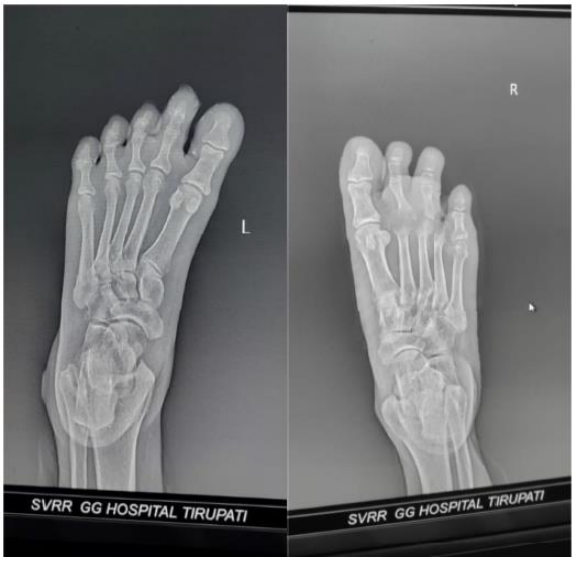


*Image a shows a roentgenogram of a left foot of a patient with diabetic foot ulcer with no involvement of the bone
**Image b shows a roentgenogram of a right foot of a patient with diabetic foot ulcer with bone involvement

LIMITATION OF THE STUDY

Sample size is the main limitation in the study. Though for statistical analysis, a sample size of 200 is sufficient, for substantiation of the findings and revelation of the variations which were not noticed in the study, a randomized controlled comparative study with much larger sample size is recommended.
A large number of factors like cost of the dressing materials, duration of hospital stay and need for recurrent dressings and constant surveillance by a medical professional as a monetary and psychological burden on the patient is not studied in the present study.

CONCLUSION

The diabetic foot ulcers in Topical phenytoin dressing group contracted more than those in patients with Betadine, Silver sulphadiazine and Soframycin groups (61.46% as compared to 57.59%, 56.74% and 54.16% with statistical significance), which indicates that the Topical Phenytoin dressing therapy is one of the effective modality to aid the reduction of wound surface area in patients suffering from diabetic ulcers and it can be used in conjunction with the conventional dressings for even faster and better healing of chronic diabetic foot ulcers.

REFERENCES

1. Delshad E, Tavakkoli-kakhki M, Motavasselian M. Successful Repair of Diabetic Foot Ulcer with Honey-Based Treatment A Case Report. Iran Red Crescent Med J. 201619
2. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018 Feb14(2)88-98.
3. Goyal R, Jialal I. Diabetes Mellitus Type 2. In StatPearls [Internet]. Treasure Island (FL) StatPearls Publishing 2021 [cited 2021 Jun 24]. Available from http//www.ncbi.nlm. nih.gov/books/NBK513253/
4. Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. N Engl J Med. 2017 Jun 15376(24)2367-2375.
5. Mutluoglu M, Uzun G, Turhan V, Gorenek L, Ay H, Lipsky BA. How reliable are cultures of specimens from superficial swabs compared with those of deep tissue in patients with diabetic foot ulcers J Diabetes Complications.2012 May- Jun26(3)225-9.
6. Oliver TI, Mutluoglu M. Diabetic Foot Ulcer. In StatPearls [Internet]. Treasure Island (FL) StatPearls Publishing 2021 [cited 2021 Jun 24]. Available from http//www.ncbi. nlm.nih.gov/books/NBK537328/
7. lavi, A. Sibbald, R.G. Mayer, D. Goodman, L. Botros, M. Armstrong, D.G. Woo, K. Boeni, T. Ayello, E.A. Kirsner, R.S. Diabetic foot ulcers Part, I. Pathophysiology and prevention. J. Am. Acad. Dermatol. 2014, 70, 1.e1–1.e18.81
8. Aumiller, W.D. Dollahite, H.A. Pathogenesis and management of diabetic foot ulcers. J. Am. Acad. PAs 2015, 28, 28–34. 10. Noor, S. Zubair, M. Ahmad, J. Diabetic foot ulcer—A review on pathophysiology, classification and microbial etiology. Diabetes Metab. Syndr. Clin. Res. Rev. 2015, 9, 192–199
9. Chantelau, E.A. Nociception at the diabetic foot, an uncharted territory. World J. Diabetes 2015, 6, 391–402
10. Agarwal, S., Bhardwaj, V., Singh, A., Goel, S., Bharat, M., & Krishna, J. A. I. (2015). a Control Clinical Trial of Honey-Impregnated and Povidone Iodine Dressings in the Treatment of Diabetic Foot Ulcers Among Northern Indian Subjects. International Wound Journal, 6(2), 7–10
11. Chitrambalam, T.G.; Christopher, P.J.; Sundaraj, J.; Paladugu, R.; Selvamuthukumaran, S. Comparison of Efficacy of Alginate Filler Dressings with Conventional Saline Dressings for Cavity Wounds in Diabetic Foot Ulcer- A Prospective Cohort Study. J.Clin. Diagn. Res. 2020, 14, PC1–PC4.
12. Singh B, Kapoor S, Gupta AK. Comparing the efficacy of nano crystalline silver dressing versus betadine dressing in management of diabetic foot ulcer. Int Surg J. 2020;7(5):1424. doi:10.18203/2349- 2902.isj20201568
13. Bohannon RW, Pfaller BA. Documentation of wound surface area from tracings of wound perimeters. Clinical report on three techniques. Phys Ther. 1983 Oct;63(10):1622-4. doi: 10.1093/ptj/63.10.1622. PMID: 6622538.
14. Naik BN, Srinivasan M, Reddy MM, Kanungo S, Sarkar S, Kar SS. Diabetes Foot Ulcer Risk - A Public Health Concern in Rural Pondicherry!!. Natl J Community Med 2018;9(10):755-759
15. J.Shaw, C.M.Hughes, K.M.Lagan, M.R.Stevenson, C.R Irwin, P.M.Bell , The effect of topical phenytoin on healing in diabetic foot ulcers : a randomized controlled trial. Wiley Online Library ,11 April 2011, https://doi.org/10.1111/j.1464-5491.2011.03309.x 87
16. Tauro et al., 2013, A Comparative Study of Efficacy of Topical Phenytoin vs Conventional Wound Care in Diabetic Ulcers, International Journal of Molecular Medical Science, Vol.3, No.8 pp.65-71 (doi: 10.5376/ijmms.2013.03.0008)
17. Edmonds ME, Foster AV (2006) Diabetic foot ulcers. BritMed J 332:407–410
18. Inchingolo, F.; Vermesan, D.; Inchingolo, A.D.; Malcangi, G.; Santacroce, L.; Scacco, S.; Benagiano, V.; Girolamo, F.; Cagiano, R.;Caprio, M.; et al. Bedsores Successfully Treated with Topical Phenytoin. Acta Biomed. 2017, 88, 45–48. [CrossRef]

19. Muthukumaraswamy MG, Sivakumar G, Manoharan G. Topical phenytoin in diabetic loot ulcers. Diabetes Care 1991;14:909-11
20. Anstead, G.M.; Hart, L.M.; Sunahara, J.F.; Liter, M.E. Phenytoin in wound healing. Ann. Pharmacother. 1996,30, 768–775. [CrossRef] [PubMed]
21. Talas G., Brown R.A., McGrouther D.A. Role of phenytoin in wound healing—a wound pharmacology perspective. Biochem. Pharmacol. 1999;57:1085–1094. [Abstract] [Google Scholar]
22. P.G. Genever, I.R. Dickson, Influence of vitamin D status on hyaluronan localization in bone, Bone, Volume 18, Issue 5,1996, Pages 429-435,ISSN 8756-3282, https://doi.org/10.1016/8756-3282(96)00046-4
23. Dill, R. E., E. K. Miller, T. Weil, S. Lesley, G. R. Farmer, and A. M. Iacopino. 1993. "Phenytoin Increases Gene Expression for Platelet-Derived Growth Factor B Chain in Macrophages and Monocytes."Journal of Periodontology 64(3): 169–173. doi:10.1902/jop.1993.64.3.169.88
24. Shafik Goda El Zayat, MB, BCh, FRCS, Preliminary Experience with Topical Phenytoin in Wound Healing in a War Zone, Military Medicine, Volume 154, Issue 4, April 1989, Pages 178–180, https://doi.org/10.1093/milmed/154.4.178
25. Rhodes RS, Heyneman CA, Culbertson VL, WilsonSE, Phatak HM. Topical phenytoin treatment of stage II decubitus ulcers in the elderly. Ann Pharmacother.2001;35(6):675-681.
26. Simpson, G M et al. "Use of Sodium Diphenylhydantoin in Treatment of Leg Ulcers." New York state journal of medicine vol. 65 (1965): 886-8.
27. Modaghegh S, Salehian B, Tavassoli M et al. Use of phenytoin in healing of war and non war wounds. A pilot study of 25 cases. Int J Dermatol 1989; 28:347–50.
28. Pendse AK, Sharma A, Sodani A, Hada S. Topical phenytoin in wound healing. Int J Dermatol 1993; 32:214–17.
29. Lodha SC, Lohiya ML, Vyas MC et al. Role of phenytoin in healing of large abscess cavities. Br J Surg 1991; 78:105–8.
30. Bansal NK, Mukul MD. Comparison of topical phenytoin with normal saline in the treatment of chronic trophic ulcers in leprosy. Int J Dermatol 1993; 32:210–13.
31. El-Nahas, M., Gawish, H., Tarshoby, M., State, O. The impact of topical phenytoin on recalcitrant neuropathic diabetic foot ulceration. J Wound Care. 2009; 18: 33–37.
32. Manoj VV, Stephen B. A study to compare the effect of topical phenytoin dressing and conventional saline dressing in chronic nonhealing ulcers. Int Surg J 2021;8:2078-84.89
33. Selvaraj, Jayaraman, and Solaiappan Jeevaraman. "Efficiency of topical phenytoin on healing in diabetic ulcer: a randomized control trial." Journal of Evolution of Medical and Dental Sciences, vol. 5, no. 23, 21 Mar. 2016, pp. 1225+. Gale OneFile: Health and Medicine.
34. Mason J, O'Keeffe C, Hutchinson A, et al. A systematic review of foot ulcer in patients with Type 2 diabetes mellitus - II: treatment. 1999. In: Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]. York (UK): Centre for Reviews and Dissemination (UK); 1995
35. V. Patil, R. Patil, P. L. Kariholu, L. S. Patil and P. Shahapur, J. Clin. Diagn. Res., 2013, 7, 2238–2240
36. J.A. Jayalal et al. Efficiency of topical phenytoin on healing in diabetic foot ulcer: a randomized controlled trial Int J Sci Stud (Jun 2015)
37. El-Nahas M, Gawish H, Tarshoby M, State O. The impact of topical phenytoin onrecalcitrant neuropathic diabetic foot ulceration. J Wound Care 2009;18:33– 7. https://doi.org/10.12968/jowc.2009.18.1.32146.
38. DaCosta ML, Regan MC, Al Sader M, Leader M, Bouchier-Hayes D. Diphenylhydantoin sodium promotes early and marked angiogenesis and results in increased collagen deposition and tensile strength in healing wounds. Surgery. 1998;123:287–93. [PubMed] [Google Scholar]

39. Bharathi Mohan P, Chapa UK, Chittoria RK, et al. Role of Phenytoin in Diabetic Foot Ulcers. J Cutan Aesthet Surg. 2020;13(3):222-225.doi:10.4103/JCAS.JCAS_48_19
40. Firmino F, de Almeida AM, e Silva RdeJ et al. Scientific production on the applicability of phenytoin in wound healing. Rev Esc Enferm USP 2014; 48:166-73. https://doi.org/ 10.1590/S0080-623420140000100021