"TO COMPARE THE EFFICACY OF TOPICAL TIMOLOL VERSUS NORMAL SALINE DRESSING IN THE TREATMENT OF DIABETIC FOOT ULCERS – A RANDOMIZED CONTROLLED TRIAL"

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This is to certify that the dissertation entitled **"TO COMPARE THE EFFICACY OF TOPICAL TIMOLOL VERSUS NORMAL SALINE DRESSING IN THE TREATMENT OF DIABETIC FOOT ULCERS – A RANDOMIZED CONTROLLED TRIAL"** is a bonafide research work done by **REGISTRATION NO. BH0115001.**

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LIST OF ABBREVIATIONS USED

IP No.	-	Inpatient Number
Sl. No.	-	Serial Number
FBS	-	Fasting Blood Sugar
RBS	-	Random Blood Sugar
PPBS	-	Post Prandial Blood Sugar
HbA_1c	-	Glycosylated Heamoglobin
β_2-AR	-	Beta 2 Adrenergic Receptor

ABSTRACT

TITLE: "TO COMPARE THE EFFICACY OF TOPICAL TIMOLOL VERSUS NORMAL SALINE DRESSING IN THE TREATMENT OF DIABETIC FOOT ULCERS – A RANDOMIZED CONTROLLED TRIAL"

Background

The incidence of diabetes and its complications are on a steady rise. The risk of lower extremity amputations is 15 fold higher in diabetics as compared to non-diabetics. Chronic diabetic foot ulcer is the leading cause of amputations in these patients. These diabetic ulcers are known to be refractory to conventional treatment and may herald severe complications if not treated wisely. Topical Timolol acts by improving keratinocyte migration and accelerates epithelialization.

Objective of the study

"To compare the efficacy of topical Timolol versus normal saline dressing in the treatment of diabetic foot ulcers – a randomized controlled trial"

Methodology

The present study was a randomized controlled trial conducted at KLES Dr. Prabhakar Kore Hospital and MRC Belagavi. Total of 60 patients were enrolled. They were divided into two groups through computerized randomization . Control group patients were treated with conventional dressing and study group patients were treated with topical Timolol(0.5%) dressing and observed for reduction in the ulcer size over a span of 15 days.

Results

The study group patients showed reduction in ulcer size of about 26.71% as against 12.39 % of the control group which is statistically significant(P value at 0.0001.)

Conclusion

Topical Timolol dressing showed faster and better healing rates as compared to normal saline dressing .

Key words

Topical Timolol , Diabetic foot ulcer, Diabetes mellitus.

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INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia due to alteration in metabolism of carbohydrate, fat and protein secondary to defects in insulin secretion, insulin action or both.[1]

Over past few decades, the incidence of diabetes mellitus and its complications are on a steady rise. There is a fifteen times higher incidence of lower extremity amputations in diabetics as compared to non-diabetics.[2]

Chronic diabetic foot ulcer is the leading cause of amputations in diabetic patients and up to 25% of all diabetics develop diabetic foot ulcers.[2]

The diabetic ulcers get arrested in the inflammatory stage of healing due to neuropathy, angiopathy and infection.

The management of diabetic foot poses a challenge to the treating surgeon as the ulcers are known to be refractory to conventional treatment and may herald severe complications if not treated wisely.[3,4]

A lot of research is being done over the years in the quest for a better treatment modality for diabetic foot management.

The dressing of the wound is an important aspect of diabetic ulcer management which in most of the cases is usually neglected. Wound care involves cleaning of the ulcer, removal of exudates and rational use of dressing material.

Characteristics of ideal dressing [5] :

- Maintenance of high humidity between wound and dressing.
- Absorbant - to remove excess exudates.
- Non-adherent - allowing easy removal without trauma.
- Safe and acceptable to the patient (non-allergic).
- Permit gaseous exchange but impermeable to micro organisms
- Cost effective.

The ideal dressing does not exist and the search still continues. During the last two decades, a wide variety of innovative dressing materials have been introduced. Choosing an appropriate dressing is a challenge, as there are numerous dressing materials each one claiming to optimize the local environment for healing.

In granulating wounds, the topical application of wet saline gauze has traditionally been used and acknowledged as a standard of care. However, the use of saline soaked gauze in dressings often cause patient discomfort as these expand into hard mass on absorbing fluid. The dressings also shed fibers which may delay wound healing if not removed at the time of dressing change.[5]

Diabetic ulcers being responsible for about 50% of non-traumatic amputations, there arises a need for evaluation of newer methods for treating these ulcers which are effective and economical.[6]

The role of keratinocytes in epithelialization is integral to wound healing.[7] Keratinocytes possess several receptors, including beta-adrenergic receptors (β-AR). Beta 2-adrenergic receptors (β2-AR) is the dominant subtype expressed on keratinocyte surfaces. β2-AR play a role in keratinocyte migration.[8,9]

β2-AR agonists also distort actin cytoskeleton ,which decreases internal polarization, which ultimately reduces keratinocyte migration. In addition to decreasing migration, β2-AR agonists also impair keratinocyte proliferation.[10]

The endothelial cells also possess β2-AR. β2-AR activation has ambiguous effects on wound angiogenesis[9], but data exist showing greater wound angiogenesis in mice and rats treated with β2-AR antagonists. Through unknown mechanisms, β2-AR antagonists improve the direction of keratinocyte migration towards the negative pole of the wound center.[8]

There is no published data on the effect of topical β2-AR antagonists on skin wounds, but people with burns have been treated with systemic Propranolol to diminish the effect of excessive catecholamine response after burn injury[9]. In a randomized controlled trial of 79 people with burns, the study subjects received oral Propranolol, which attenuated the hypermetabolic response to burn injury, resulting in shorter healing time, better healing, shorter hospital stays, and smaller wound surface area that required skin graft.[11,12]

Some studies on topical Timolol have shown increased healing rate in chronic foot ulcers compared to the conventional dressings.[13,14] We used topical Timolol as a novel treatment for Diabetic foot ulcers.

AIM & OBJECTIVE OF THE STUDY:

To compare efficacy of topical Timolol dressing versus normal saline dressing in reducing the size of the diabetic foot ulcers, admitted in KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi**.**

REVIEW OF LITERATURE

DIABETES MELLITUS

Definition

"Diabetes mellitus (DM) is characterized by chronic hyperglycemia with disturbances of carbohydrates, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both".[15-21]

The incidence of diabetes and its complications are on the rise. In well-studied town of Framingham the prevalence of diabetes has increased from 0.9% in 1958 to 3% in 1993. India has dubious distinction of having highest number of diabetics in the world, in the year 1995 there were 19.4 million diabetics which is expected to rise to 57.2 million by 2025.[22]

Foot ulceration, sepsis and amputation are the dreaded complications feared by almost every diabetic person, which are potentially preventable complications.[23]In diabetics, life time risk of foot ulcers is 15%. Every 2% rise in glycosylated hemoglobin increases the risk of lower extremity ulcers by 1.6 times and lower extremity amputation by 1.5 times. Neuropathy and distorted pedal architecture predispose to foot ulcerations. 20% of admissions in diabetics are for foot problems.[24]

WOUND HEALING

HISTORICAL BACKGROUND:

Wound healing and its treatment are some of the oldest subjects discussed in the medical literature and probably earliest challenges of human race.[25]

Early surgeons like Ambroise, Pare, John Hunter & Sir James Paget have given some scientific insight to the healing of wounds, particularly the war wounds . Halsted was interested in wound healing process.

In the early 1900's Carrel & his associates made investigations with the scientific approach to wound healing. Later Carrel (1916), Harvey & Howe's (1930), studied incised wounds & contributed to the knowledge of wound healing.[26]

There is a saying; "If there were no regeneration, there would be no life; if everything regenerated, then there would be no death".

Definition:"Body replacement of destroyed tissue by the living tissue" or"Integrated series of cellular and biochemical events which restores the functional integrity and regains the strength of injured tissue".

Phases of healing:

Wound healing and repair are complex processes that involve dynamic series of events.

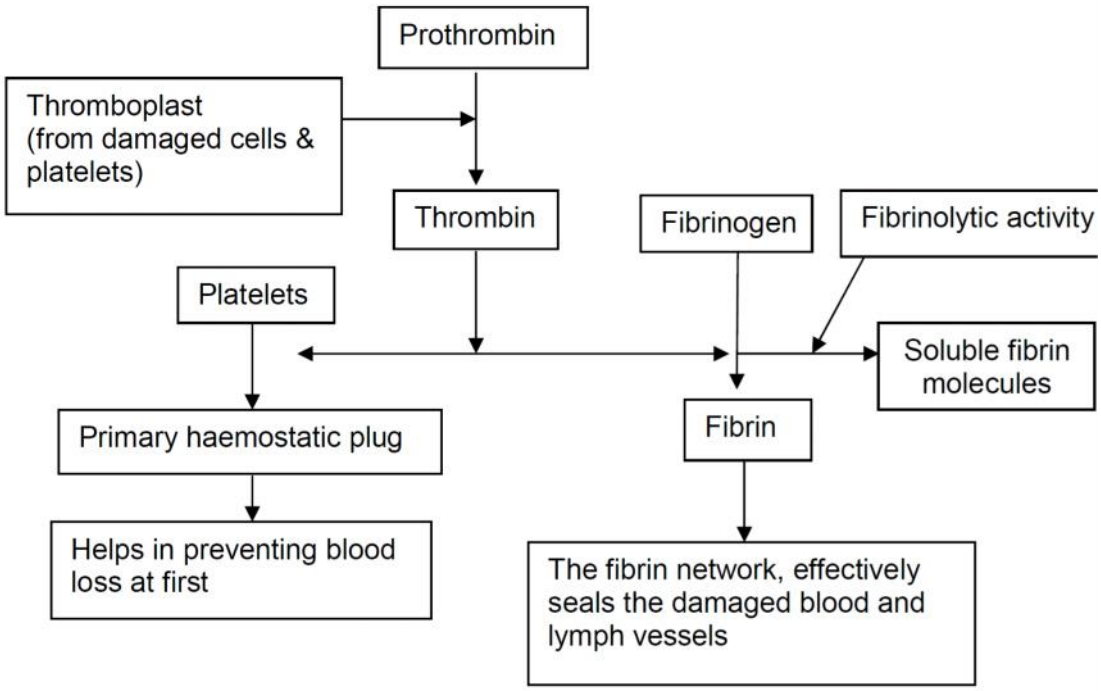
1. Coagulation
2. Inflammation
3. Fibroplasia, Angiogenesis, Proliferation & Granulation tissue formation.

4. Epithelization
5. Collagen Synthesis
6. Wound contraction / Tissue Remodelling / Scar Maturation

COAGULATION :

- Helps in preventing blood loss, covering wound surface, & holding the wound edges together & thus contributing to the healing process.
- Knighton et al (1982) & Ross (1980) have shown unequivocally that fibrin & platelets play an important role in initiating the wound healing.

MECHANISM OF COAGULATION



Granulation phase of wound healing

Granulation tissue-[27]

"This is a highly vascular tissue, contains largely of;

1. Fibroblast.
2. Endothelial cells lining capillaries of newly spouting blood vessels.
3. Macrophages.
4. Pleuripotentpericytes.

Above all are embedded in a matrix consisting of

1. Fibronectin
2. Proteoglycans rich in Hyaluronicacid and collagen [This collagen is at first mainly of Type-III, changing later to Type I].

The term granulation tissue derived from its pink, soft, granular appearance on the surface of wounds.[27]

Functions

- Fill the gap of the wound
- Supports the growing and migrating epithelial cells – The connective tissue matrix of granulation tissue forms nutritive substrate, over which regenerating epidermis can migrate and is gradually replaced by scar tissue.

Imporant factors for granulation tissue formation

- Chemotactic factor.
- Growth factor.
- Structural molecules.
- Proteases [Digests connective tissue matrix].

ANGIOGENESIS OR NEO-VASCULARISATION:[28]

It is the vital part of proliferative phase of wound healing & repair.

It is seen in

- Embryonic development phase
- During repair process (throughout life span of an organism)
- Under certain pathological conditions

Without Angiogenesis, invasion of the wound bed by macrophages & fibroblasts would cease due to lack of oxygen & nutrients.

In the initial stages, these vessels lack the basement membrane & have loose cellular junction (Gullino, 1981) & are fragile in nature.This facilitates the movement of cells & macromolecules into wound site. On slightest touch, the vessels bleed profusely which is a characteristic feature of newly formed capillaries.

There are four steps in angiogenesis[27,28]

Step-I: Proteolytic degradation of basement membrane of parent vessel to allow formation of capillary sprout & subsequent cell migration

Angiogenic factors acts on capillary endothelial cells, which releases collagenase. This enzyme degrades the collagen of basement membrane.

Step-II: Migration of endothelial cells towards the angiogenic stimulus

Fragmentation of the collagen of basement membrane, permits the migration of endothelial cells into the peri-vascular spaces.

Step-III: Proliferation of endothelial cells, just behind the leading front of migratory cells

Endothelial cells migrate into the peri-vascular spaces where they form buds, which are added by the proliferation of cells with in & near parent vessel (Kalebie et al, 1983).

Step-IV: Maturation of endothelial cells &organisation into capillary loops

- Functional Capillary Loops: During dermal repair, these buds grow rapidly towards the free surface, where they branch at their tips & unite to form functional capillary loops.
- Superficial Capillary Plexus: On these loops, new buds develop, so that, a superficial capillary plexus rapidly forms in the granulation tissue.
- Canalization: Proliferation & branching of cords of endothelial cells later become canalized to form growing capillary buds of healing wound.

- Fusion: Capillaries originating from opposite sides of the wound fuse & establish a complete circulation within the wound.

REMODELLING OF THE VASCULATURE:[28]

There is constant remodelling of the vasculature, which involves obliteration of many of the capillaries (Marchesi, 1985).

As each capillary loop becomes functional, it brings nutrients & oxygen to nearby cells, enabling the fibroblasts to secrete materials for the matrix, through which macrophages & other cells can migrate further. The above proliferative & migratory processes are repeated sequentially, until wound bed is filled with granulation tissue.

As the scar maturation proceeds, capillaries gradually regress & the red vascular wound tissue transforms into a white, relatively avascular cell poor scar (Zitelli, 1987)

MACROPHAGIA[28]

It is a point at which protecting & clearing functions of inflammatory response are linked to starting of reparatory process.

What is Macrophagia?

Macrophagia is

1. Migration of Monocytes [from blood] to tissue injury site
2. Conversion of monocyte to Macrophage after migration to tissue injury site. These are key cells in dermal repair.

Wound macrophages play pivotal role in healing by liberating various factors.

Functions of macrophages[29]

- Take over the function of phagocytes that is debridement.
- Release matrix metalloproteinases (MMP).
- Macrophages secrete numerous cytokines.
- Macrophages also release growth factors that stimulate fibroblast, endothelial cells and keratinocyte proliferation.
- Promote angiogenesis by liberating endothelial growth factor [EGF].

Macrophage-secreted platelet derived growth factor (PDGF) stimulatecollagen and proteoglycan synthesis.

Fibroplasia[29]

After injury, the normally and sparse fibroblasts are chemoattracted to the inflammatory site, where they divide and produce the components of the extra cellular matrix (ECM). After stimulation by macrophage- and platelet-derived cytokines and growth factors, the fibroblast which is normally arrested in G0 phase, undergoes replication and proliferation.

The primary function of fibroblasts is to synthesize collagen. The rate ofcollagen synthesis declines after 4 weeks and eventually balances the rate of collagen destruction by collagenase (MMP-1). At this point the wound enters a phase of collagen maturation. The maturation phase continues for months or even years.

Collagen[29]

Structure

The proline- and glycine- rich collagen molecule is a long, stiff, triplestranded helical structure that consists of three collagen polypeptide α chains twist around one another in a ropelike superhelix. With its ringlike structure, proline provides stability to the helical conformation in each α chain, whereas glycine, because of its small size, allows tight packing of the three α chains to form the final superhelix. There are at least 20 types of collagen, the main constituents of connective tissue being types I, II, III,V, IX. In early wound healing there is increased expression of type III collagen.

Collagen synthesis:[29]

Collagen polypeptide chains are synthesized on membrane-bound ribosomes and enter the endoplasmic reticulum (ER) lumen as pro-α chains. Within the lumen of the ER, some of the prolines and lysines undergo hydroxylation to form hydroxyproline and hydroxylysine.

Hydroxylation results in the stable triple-stranded helix through the formation of interchain hydrogen bonds. The pro-α chain then combines with two others to form procollagen, a hydrogen-bonded, triple-stranded helical molecule. After secretion into the ECM, specific proteases cleave the propeptides of procollagen molecule to form collagen monomer. These monomers assemble to form collagen fibrils in the ECM.

Functions

a) Collagen is essentially a product of fibroblast.
b) Collagen is the most abundant proteins of the connective tissue.
c) Supports to the tissues

d) Provides structural framework to other types of tissues.

e) Acts as a medium where blood vessels and nerves are passing.

f) Brings and keeps the wound edges together and provides tensile strength for holding together – this holding strength prevents the breakdown of tissue (organ) at the healed site.

g) Fill the gap caused by the tissue loss.

***Ground substance in healing wound*[29]**

- Connective tissue consists of cellular and non cellular elements (matrix). Matrix is again composed of fibres and ground substance.
- Ground substance is non-fibrous part of the matrix in which cells and fibres are embedded.
- Consistency: Except in mineralized connective tissue, the ground substance is viscous gel.

Constituents

- Water (High proportion).
- Mucopolysaccharides.
- Fibronectin.
- Chondronectin.
- Mucoproteins.
- Glycoproteins.
- Lamenin.
- Entactin.

***Wound contraction*[29]**

- *Definition*: "Wound contraction may be defined as a process by which the size of full thickness open wound is diminished by centripetal movement of the surrounding skin".
- The feature that most clearly differentiates primary from secondary healing is the phenomenon of wound contraction, which occurs in large surface wounds.
- Wound contraction is one function of granulation tissue which is critical for repair.
- The events of wound healing from injury to fibroplasia, occur in all wounds. But certain events like wound contraction occurs characteristically in dermal wound.
- In humans, the wound contraction is less because in most part of the body the skin is somewhat firmly attached to subcutaneous tissue but it can occur in areas like back of neck and buttocks.

Timing

Wound contraction starts from about third or fourth day of healing and continues upto 15th or 16th day and stops thereafter, irrespective of whether the wound is totally closed or not.

Rate

- The rate of wound contraction is about 0.60 - 0.75 mm /day.
- Wound contraction is not materially affected by size or shape of the wound but perhaps by the length of the wound perimeter.

Mechanism

- The mechanism of wound contraction is debated. Many theory like Pull theory, Push theory / Picture Frame theory etc. have been proposed but none of them appears to be satisfactory.
- Modified fibroblasts rich in actin filaments are responsible for wound contraction.
- Myofibroblasts are situated just under the advancing edges of the wound.
- In early phases of wound contraction, contractile epidermal cells in wound edges are suggested as a source of force.
- Wound contraction can be both beneficial or detrimental. Wound contraction can lead to distortion, disfigurement and impairment of function.

Epithelization

Definition

- Epithelization is a process of wound healing involving body surface.[7]
- Unlike healing by fibroplasia where lost parenchymal cells are replaced by non-specific connective tissue, in epithelialization lost epithelial cells are replaced by epithelial cells only. It is an example of healing by regeneration.

Stages

a) Mobilization and loosening of basal cells from their dermal attachment.
b) Migration or movement of cells to a position of cell deficit.
c) Proliferation or replacement of cells to a position of cell deficit
d) Differentiation or restoration of cellular function.

Epithelization which depends on several factors:[30]

- Size of wound.
- Location of wound.
- Shape of wound.
- Impairment of blood supply.
- Pathological modification of wound

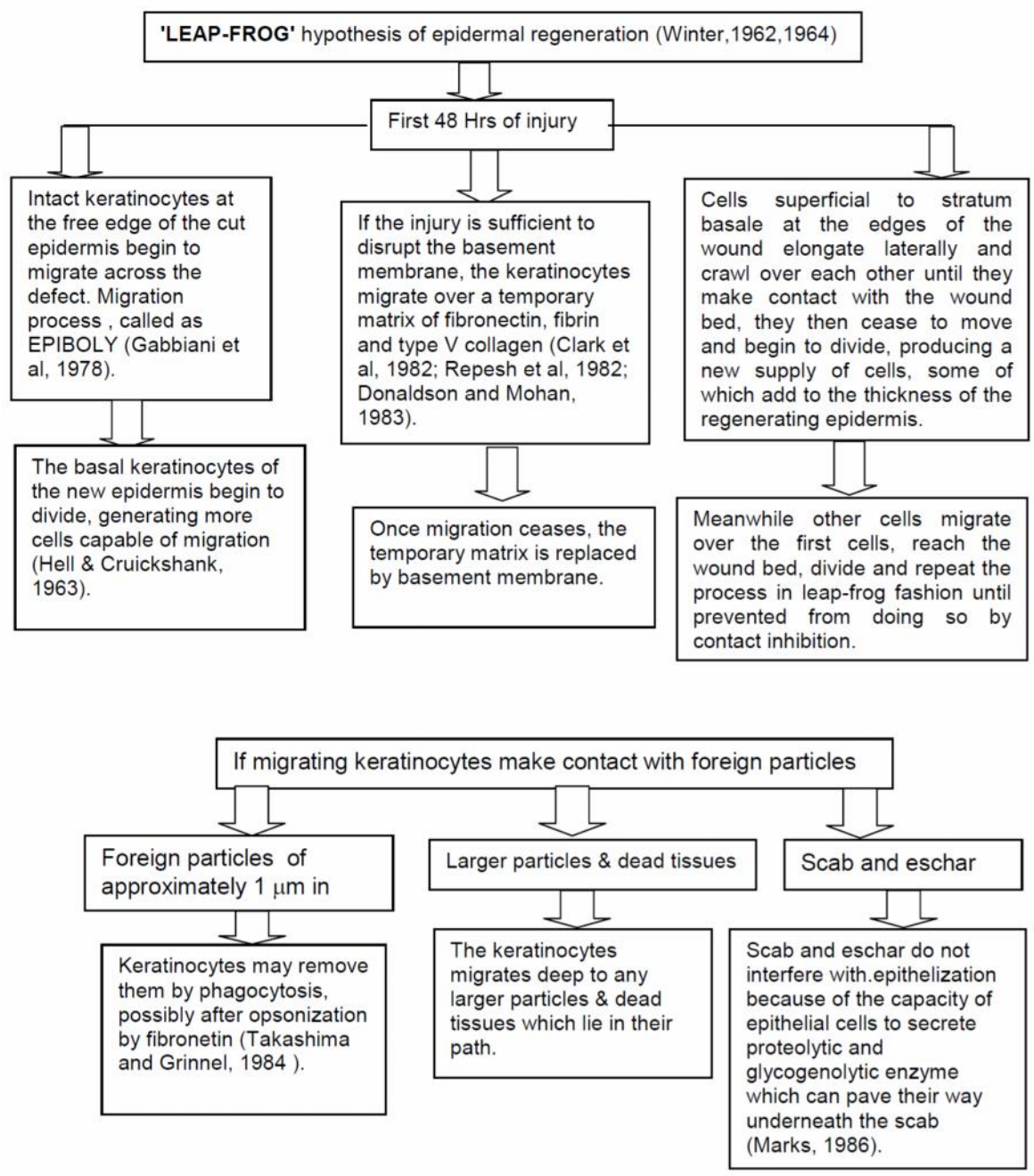
Healing by epithelization occurs in-

- ✓ Dermal wounds
- ✓ Wounds of tracheobronchial surface
- ✓ Surface wounds in gut, urinary bladder, uterus etc

Timing

First 24 hrs of injury: Changes in epidermis leading to re-epithelization begin within 24 hours of the formation of a cutaneous wound.

MECHANISM OF EPITHELISATION



Types of wound healing[29]

Healing by primary intention

The wounds are sealed immediately with simple suturing, skin grafting or flap closure, such as closure of the wound at the end of surgical procedure.

Healing by secondary intention

No active intent to seal the wound. Generally, this type of repair is associated with a highly contaminated wound and will close by re-epithelialization, which results in contraction of the wound.

Healing by tertiary intention

It is also referred to as delayed primary closure. A contaminated wound is initially treated by repeated debridement, systemic or topical antibiotics, or negative pressure wound therapy for several days to control infection. Once the wound is assessed as being ready for closure, surgical intervention, such as suturing skin grafting or flap is performed.

MANAGEMENT OF CHRONIC WOUNDS

Wound dressings have been used since antiquity to facilitate the healing process. A dressing material which when applied to the surface of a wound, should provide and maintain an environment in which healing can take place at maximum rate; Thomas (1986).[31] The first antiseptic dressing was introduced by Lister in1867 , who soaked the lint and gauze in carbolic acid.[32]

Dressings used in chronic diabetic ulcer

Conventional dressings, such as gauze, impregnated gauze, gauze and cotton, packing strips have been in use for over fifty years.

Action of saline dressing

Normal saline dressing keeps the environment moist for proper healing.

Normal saline dressing acts as an osmotic dressing, with time the concentration of the saline increases due to evaporation altering it from isotonic to hypertonic dressing which in turn decreases evaporation of fluid from the wound, keeping it moist.[33] Moist wound environment is good for regeneration and repair and for increasing the rate of healing. Effective wound management aims to strike a balance between a moist environment which promotes healing and an excessively wet environment which causes maceration.

Two factors are important for natural wound healing. One is wound exudates which is generic term given to liquid produced from wounds. Exudate keeps the wound moist, supplies nutrients, and provides the medium for migration and mitosis of epithelial cells. This in turn, keeps the wound supplied with leucocytes, to control micro organism.

Second factor is the presence of white cells in the wound. White cells play a major role in wound healing by cleaning the wound, removing potentially pathogenic micro organisms and producing collagen, the building block of new tissue. Excessive exudates can cause maceration and hence the dressing should be able to absorb excessive exudates from the wound.[34]

Basic requirements of the ideal ulcer dressing[5]

- Maintain high humidity between wound and dressing
- Absorbent, removes excess exudates
- Non-adherent, allowing easy removal without trauma
- Safe and acceptable to patient(non-allergic)
- Permit gaseous exchange but impermeable to micro-organism
- Cost-effective

Newer dressings available for diabetic ulcer

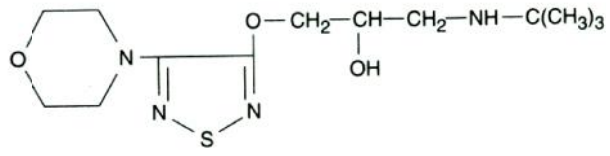
A wide variety of new dressing materials have been developed. However none of the newer dressing materials fulfill all the characteristics of an ideal dressings.

- Film dressing.
- Foam dressing
- Nonadherent dressing (Paraffin-impregnated tulle dressing).
- Hydrogels.
- Hydrocolloids.
- Alginates.

Newer therapies available for diabetic ulcer

- Platelet derived growth factor
- Epidermal growth factor
- Demagraft.
- Apligraft.
- Granulocyte-colony stimulating factor.
- Hyaff.(Hyaluronan-based biodegradable polymer)

TIMOLOL:



Timolol

Timolol is a potent non –subtype –selective beta receptor antagonist with molecular formula $C_{13}H_{24}N_4O_3S$ with chemical name 2-propanol ,1-[(1,1-dimetyletyl) amino]-3-[[4-(4-morpholinyl)-1,2,5-tiadiazol-3-yl]oxy]-,(S)-. Molecular weight 316. It is available in tablet formulation and ophthalmic formulation (0.25% and 0.5%).Timolol is generally used for hypertension,congestive heart failure, migraine prophylaxis, open angle glaucoma , and intra ocular hypertension. Timolol is well absorbed from the GI tract and is metabolized extensively by CYP2D6 in the liver.The ophthalmic formulation of Timololused for the treatment of glaucoma may be extensively absorbed systemically, causing adverse effects in susceptible patients. But systemic absorption of Timolol from topical application on wounds, is unclear.[35] In our study we have used commercially available 0.5% Timolol maleate ophthalmic solution.

ROLE OF TOPICAL TIMOLOL IN ULCER TREATMENT:

Skin is our primary defense against noxious environmental agents.

Upon injury, keratinocytes migrate into the wound bed to initiate re-epithelialization and restoration of barrier integrity. Keratinocytes express a high level of beta 2 adrenergic receptors (β_2AR)and synthesize AR agonists. Aberrations in

either keratinocyte β2AR function or density are associated with various skin diseases.[8].

AR antagonists are found to promote wound re-epitheliazation in a "chronic" human skin wound healing model. β2AR antagonists increase ERK phosphorylation, rate of keratinocyte migration , electric field directed migration and accelerate epithelialization.[8] The β2AR antagonist prevent the binding of endogenously synthesized epinephrine

β2AR –blockade appears to enhance angiogenesis in the wound which helps in early healing of ulcers.Beta receptor -Agonists have the opposite effect via a phosphatase 2A-dependent mechanism.[14]

All the effects of β2AR blockage support the usage of Topical Timolol as a novel treatment of chronic refractory wounds.However it is important to consider the possibility of its systemic absorption on topical usage.

Timolol has the potential to be an inexpensive, noninvasive and non-labour intensive means to achieve rapid healing of ulcers.

MATERIALS AND METHODS

The present study was carried out at Department of Surgery, Jawaharlal Nehru Medical College and KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi for a period of one year (from January 2016 to December 2016).

Study Design: The Randomised controlled trial was conducted on patients with diabetic foot ulcers .

Source of Data : Patients with diabetic foot ulcers admitted at KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi over a period of one year from January 2016 to December 2016.

Sample Size :

The present study comprised of 60 patients

30patients -in the study group

30-patients -in the control group

Sampling procedure: since there is no evidence of previous randomized controlled trial on this subject as a thumb rule, total of 60 patients are divided into 2 groups .

Duration :one year between January 2016 to December 2016

Inclusion criteria

1. Both Type I and II Diabetes mellitus.
2. Diabetics between 18 to 65 years of age.
3. Ulcer on the foot
4. Size of ulcer more than 2 x2cm and less than 10x10cm, depth less than 1cm
5. Fasting blood glucose level measured on two occasions 24 hours apart between 140mg/dl to 200mg/dl
6. Patients with grade 1 and grade 2 ulcers of wagner's classification

Exclusion criteria:

1. Ischemic limb
2. Immunocompromised patients
3. Associated osteomyelitis.
4. Cellulitis
5. Diabetic Ketoacidosis
6. Have exposed tendon or bone or presence of charcot joint.
7. patients with grade 3, 4and 5 ulcers of wagner's classification
8. Hb level less than 10mg

Procedure

The study was approved by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belagavi. As per inclusion and exclusion criteria patients were selected for the study and briefed about the nature of the study, the interventions used and written informed consent was obtained.

Further patients were randomized with the help of a computer generated randomization chart into two groups namely study group and control group.

Out of the 60 participants, 30 were (Control group) treated with conventional wet saline dressings and the remaining 30 were (study group) treated with topical Timolol (0.5%)dressings.

The descriptive data of the participants like name, age, sex, detailed history, were obtained by interviewing the participants. Clinical examination was done and necessary investigations like complete blood count, blood urea and serum creatinine and culture of the ulcer were recorded on predesigned and pretested proforma.

Both groups received slough excision ,betadine and H_2O_2 wash prior to application of dressing .

Empirical antibiotics (ciprofloxacin and metronidazole are started) and changed to sensitive antibiotics after sensitivity reports .

Initial wound area measurement

The ulcer were examined and photographed by the investigator at the beginning of the study and at the end of the study. Ulcer area measurement was recorded on a transparent sheet on day one and on day 15.The dressing was changed every day. Ulcer were observed over period of 15 days.

Demographic variables include age, ethnic background, gender ,principal diagnosis.

Confounding factors :

Age of the patient .

Nutritional status of the patient as reflected by serum albumin level

Renal function test as reflected by serum creatinine level

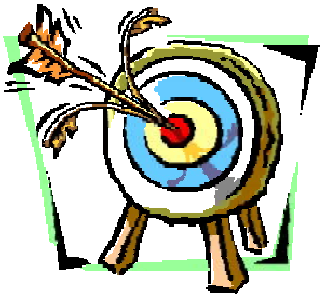
Duration and control of diabetes

Outcome was measured in terms of ulcer size reduction in the two groups. Data was tabulated and the two groups were compared with reference to area and percentage of reduction.

Statistical analysis

The data obtained was tabulated and analysed. Differences in the mean reduction in ulcer size between two groups compared using independent ‘t’ test, dependent ‘t’ test and chi square test whichever is appropriate .

Introduction



Objectives

Review of Literature

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Results

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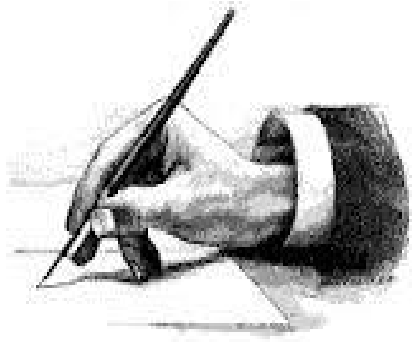
Summary

Bibliography



Annexure-I

Annexure-II

Annexure-III

Annexure-IV

Annexure-V

RESULTS

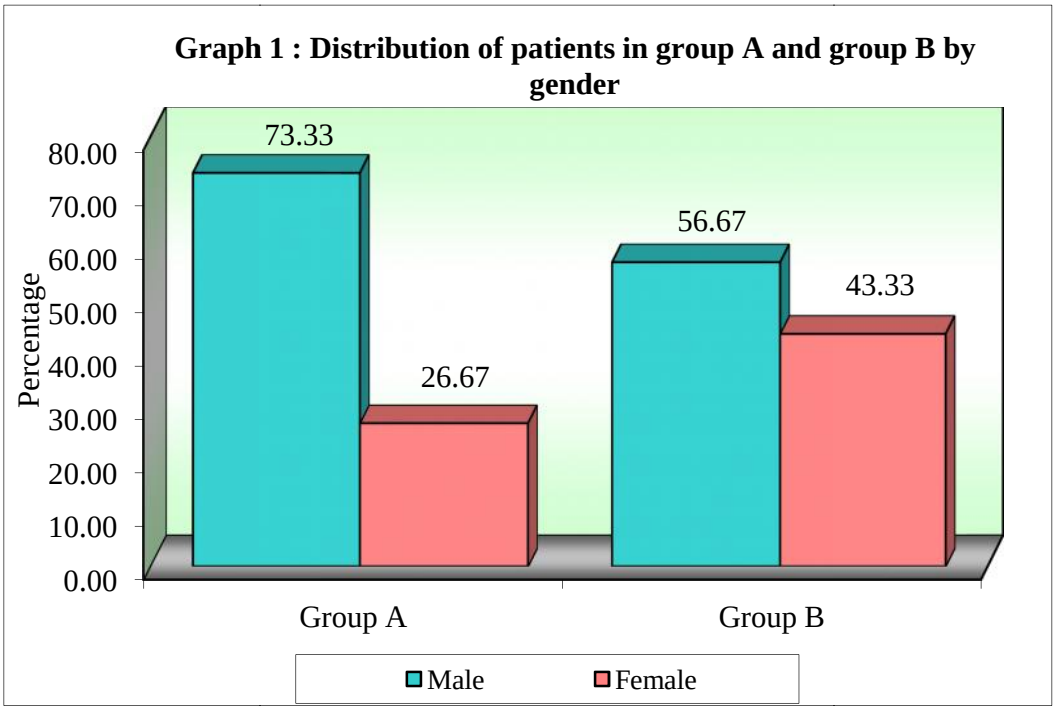
The present study is conducted in KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi and the findings are tabulated as below.

During the study year from January 2016 to December 2016, 60 patients with diabetic foot ulcers are randomized into study (Topical TIMOLOL 0.5% dressings) and control (Normal saline dressings) groups. These groups were studied for the effect of conventional saline dressings versus Topical Timolol dressing on reduction in size of the ulcer.

A total of 60 patients satisfied the selection criteria, analysis was done by using independent ‘t’ test, dependent ‘t’ and chi square test.

Table1 1: Distribution of patients in group A and group B by gender

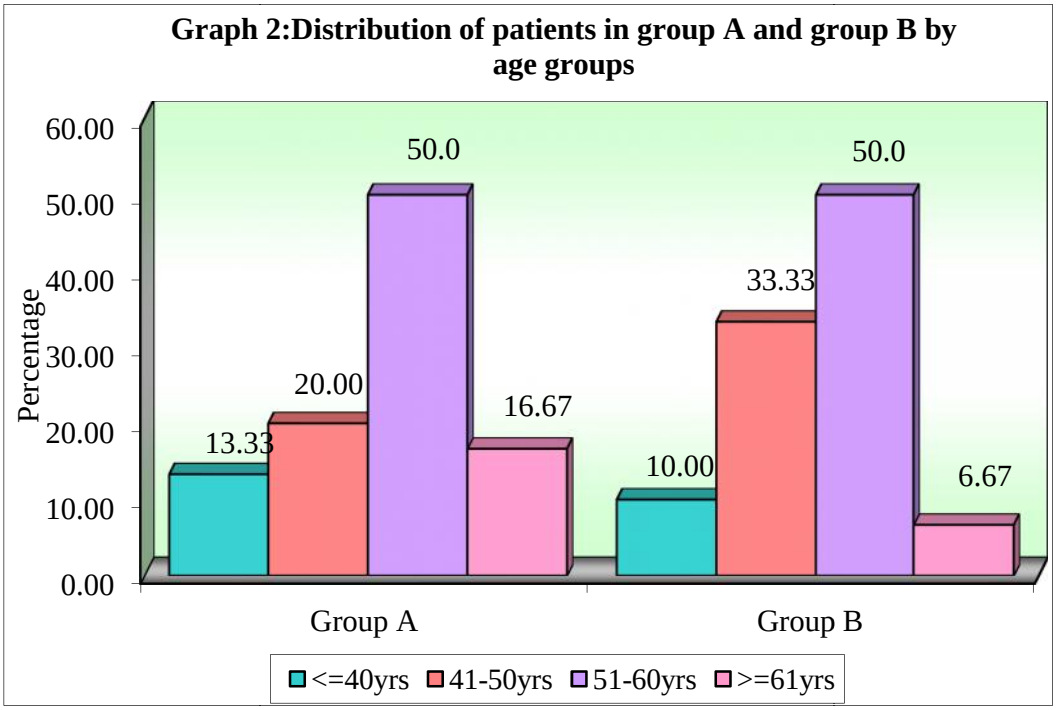
Sex	Group A	%	Group B	%	Total	%
Male	22	73.33	17	56.67	39	65.00
Female	8	26.67	13	43.33	21	35.00
Total	30	100.00	30	100.00	60	100.00
Chi-square=1.8321 P = 0.1762						



In the study group (group A), total number of males and females are 22 (73.33%) and 8(26.67%) respectively. The male: female ratio is 2.75:1. In control group (Group B), total number of male and females are 17 (56.67%) and 13 (43.33%) respectively. The male: female ratio is 1.30:1. Statistically in this study, there is no significant difference in sex distribution between interventional and control group.

Table 2: Distribution of patients in group A and group B by age groups

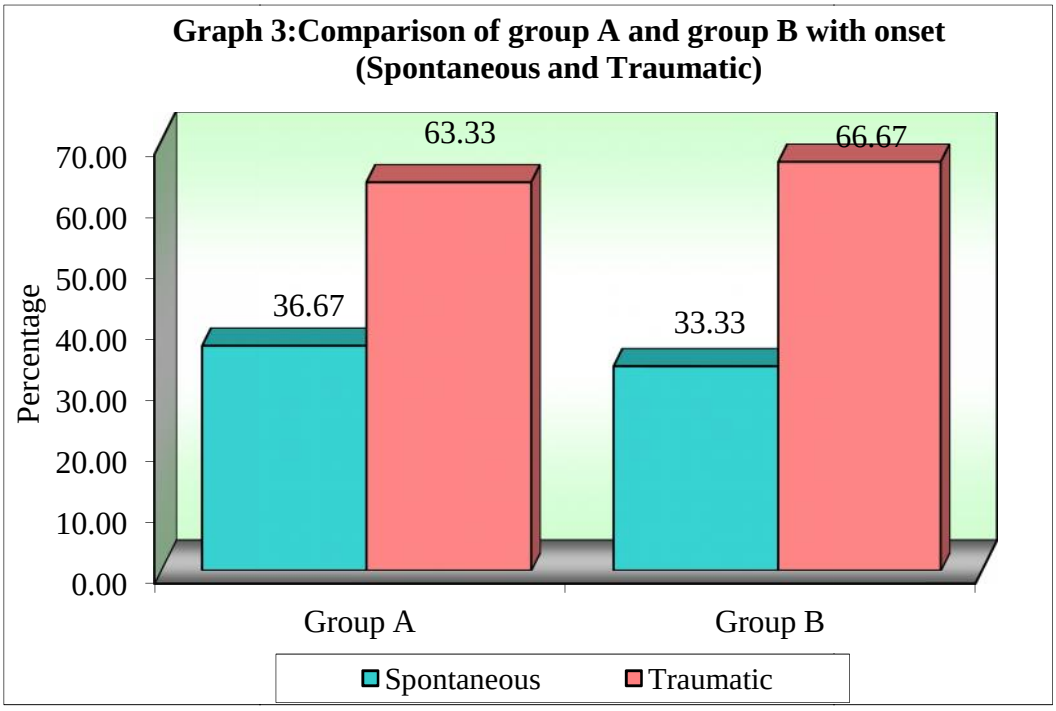
Age groups	Group A	%	Group B	%	Total	%
<=40yrs	4	13.33	3	10.00	7	11.67
41-50yrs	6	20.00	10	33.33	16	26.67
51-60yrs	15	50.00	15	50.00	30	50.00
>=61yrs	5	16.67	2	6.67	7	11.67
Chi-square=2.4291 P = 0.4883						
Total	30	100.00	30	100.00	60	100.00
Mean age	52.10		51.10		51.60	
SD age	7.87		8.71		8.24	



In this study, the mean age in study group and control group are 52.10 ±7.87 and 51.1 ± 8.71 respectively. Statistically there is no significant difference in mean age between study and control groups.

Table 3: Comparison of group A and group B with onset (Spontaneous and Traumatic)

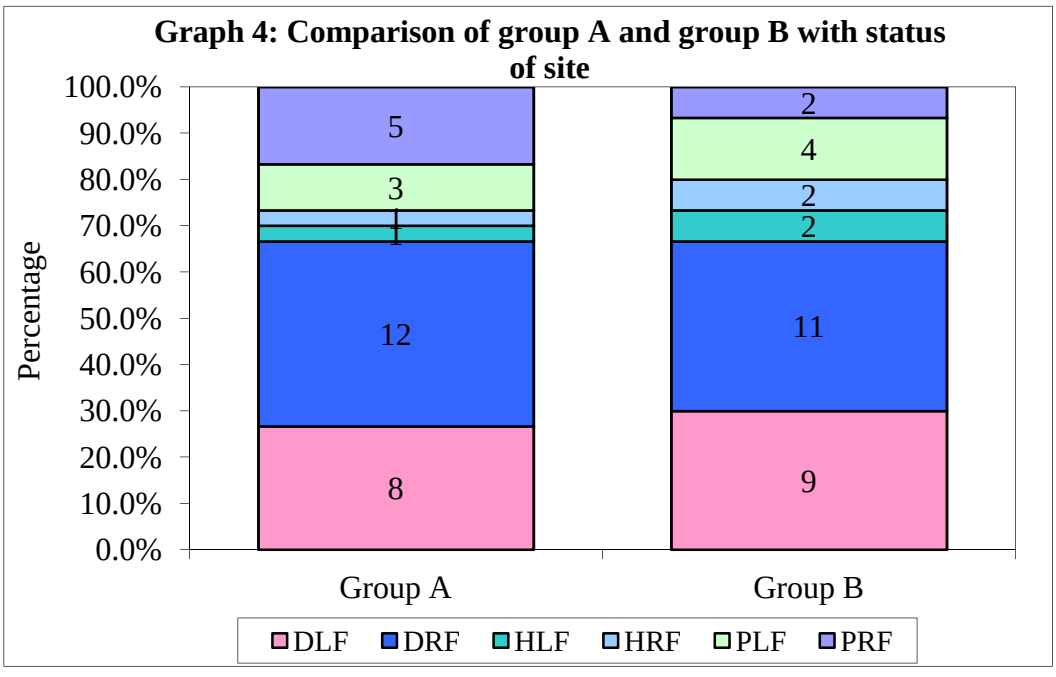
Onset	Group A	%	Group B	%	Total	%
Spontaneous	11	36.67	10	33.33	21	35.00
Traumatic	19	63.33	20	66.67	39	65.00
Total	30	100.00	30	100.00	60	100.00
Chi-square=0.0733 P = 0.7871						



Trauma is the most common cause of diabetic foot ulcer (65%) while only (35%) are spontaneous in origin.

Table 4: Comparison of group A and group B with status of site

Site	Group A	%	Group B	%	Total	%
DLF	8	26.67	9	30.00	17	28.33
DRF	12	40.00	11	36.67	23	38.33
HLF	1	3.33	2	6.67	3	5.00
HRF	1	3.33	2	6.67	3	5.00
PLF	3	10.00	4	13.33	7	11.67
PRF	5	16.67	2	6.67	7	11.67
Total	30	100.00	30	100.00	60	100.00
Chi-square=4.2612 P = 0.2351						



In our study it is observed that diabetic foot more commonly occurs on the dorsal aspect of the foot as compared to the plantar aspect and heel.

DLF-dorsum of left foot

DRF-dorsum of right foot

HLF-heel of left foot

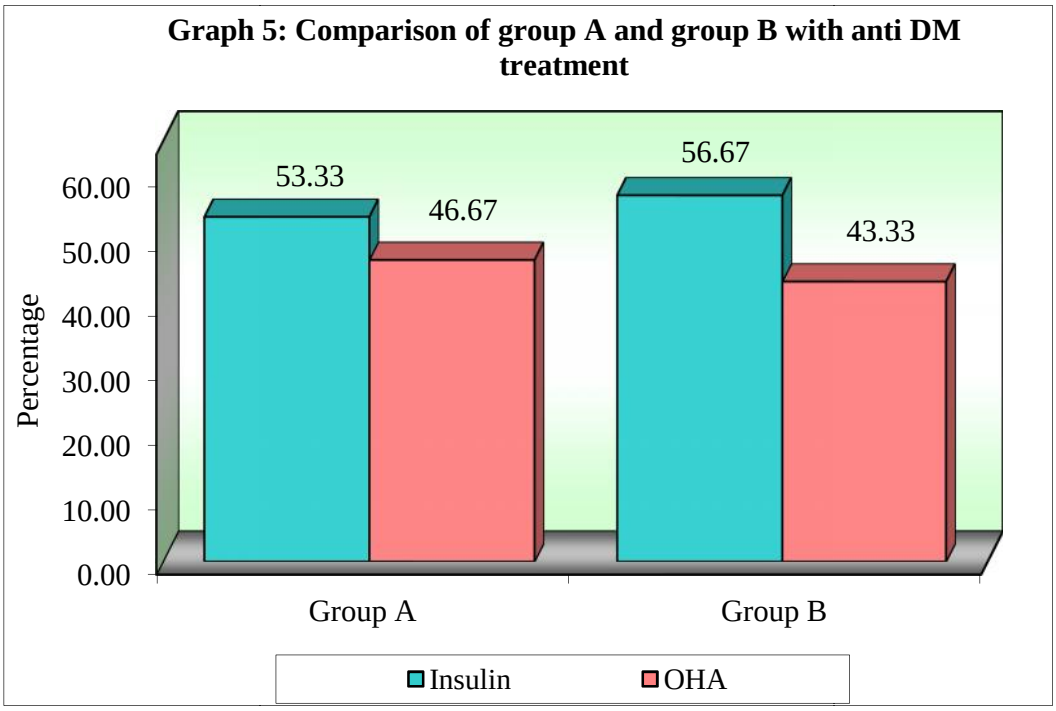
HRF-heel of right foot

PLF-plantar of left foot

PRF-plantar of right foot

Table 5: Comparison of group A and group B with anti DM treatment

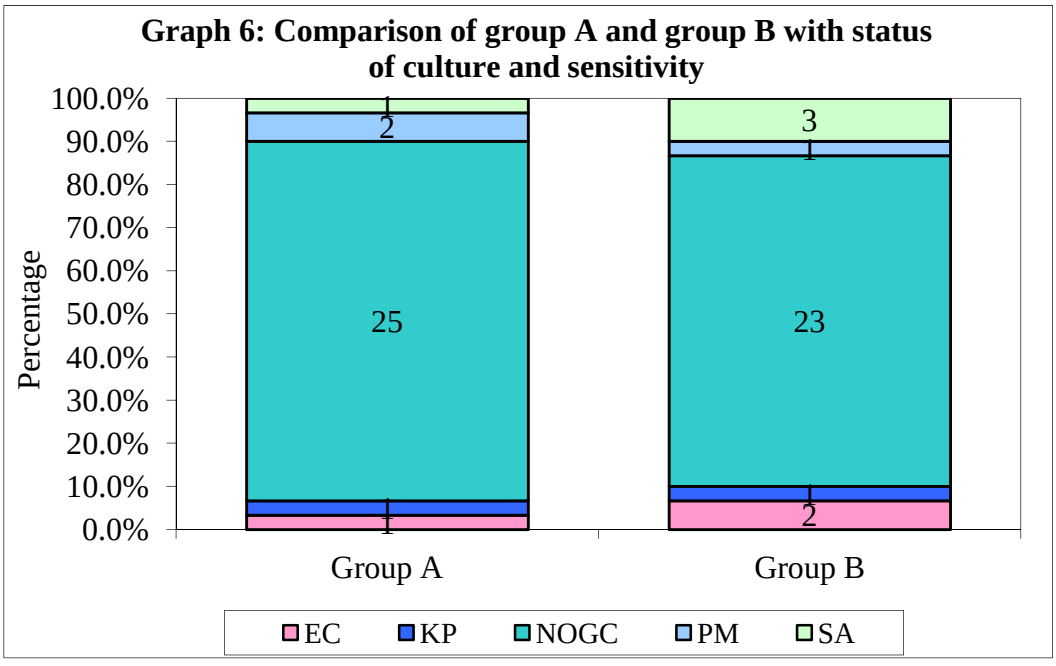
Anti DM Rx	Group A	%	Group B	%	Total	%
Insulin	16	53.33	17	56.67	33	55.00
OHA	14	46.67	13	43.33	27	45.00
Total	30	100.00	30	100.00	60	100.00
Chi-square=0.0676 P = 0.7955						



In our study most of the participants were taking Insulin (55%) for glycaemic control.

Table 6: Comparison of group A and group B with status of culture and sensitivity

C/S	Group A	%	Group B	%	Total	%
EC	1	3.33	2	6.67	3	5.00
KP	1	3.33	1	3.33	2	3.33
NOGC	25	83.33	23	76.67	48	80.00
PM	2	6.67	1	3.33	3	5.00
SA	1	3.33	3	10.00	4	6.67
Total	30	100.00	30	100.00	60	100.00
Chi-square=0.4268 P = 0.8087						



EC-Escherichia Coli KP- Klebsiella Pneumonia NOGC- No Organisms Grown in Culture PM-Proteus Mirabilis SA-Staphylococcus Aureus

In our study maximum culture of pus showed no organism growth (80%) .

Table 7: Comparison of group A and group B with respect to FBS scores by independent t test

Group	n	Mean	SD	SE	t-value	p-value
Group A	30	149.33	23.01	4.20	1.9908	0.0512
Group B	30	137.10	24.56	4.48		

In our study it is observed that mean FBS in study group is 149.33±23.01 and control group is 137.10±24.56. The difference between the two is not statistically significant (p=0.0512).

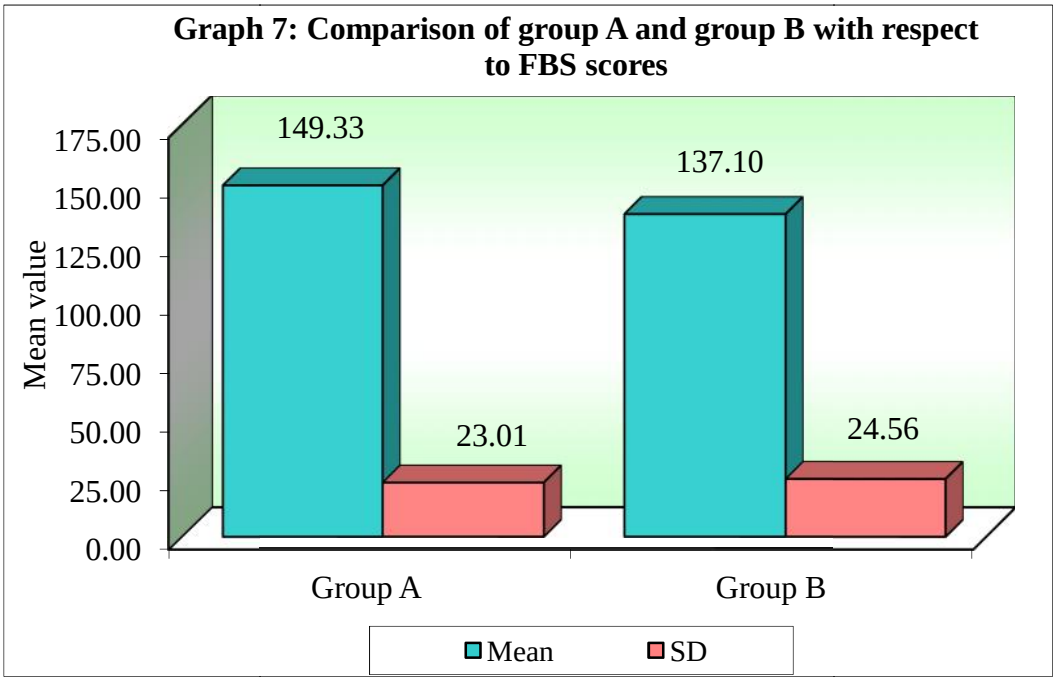
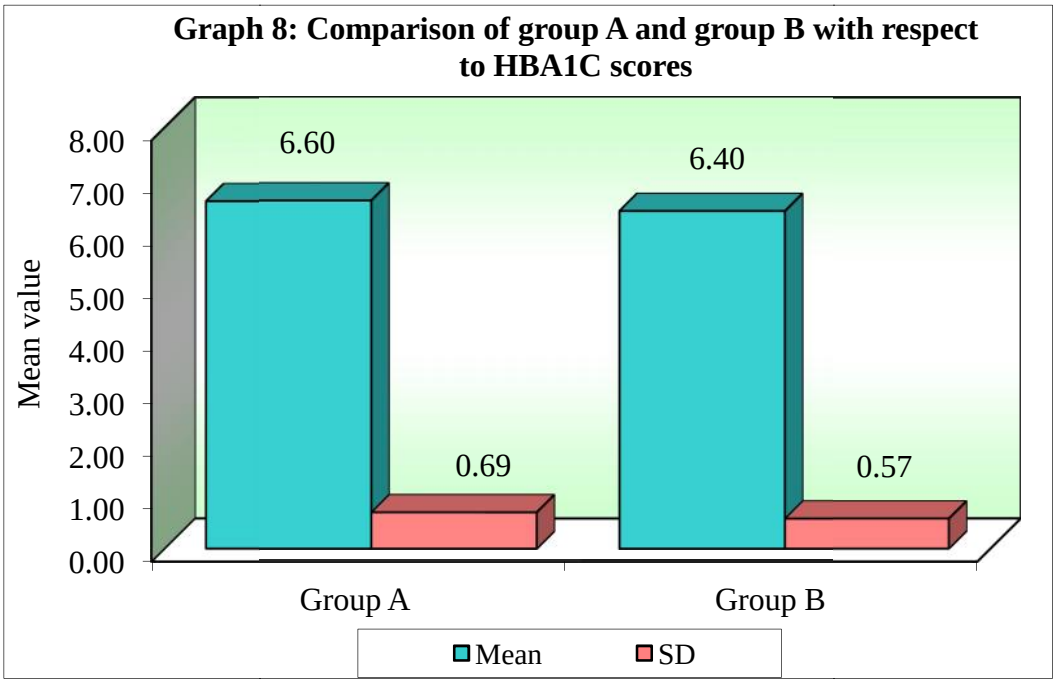


Table 8: Comparison of group A and group B with respect to HBA1C scores by independent t test

Group	n	Mean	SD	SE	t-value	p-value
Group A	30	6.60	0.69	0.13	1.2180	0.2282
Group B	30	6.40	0.57	0.10		

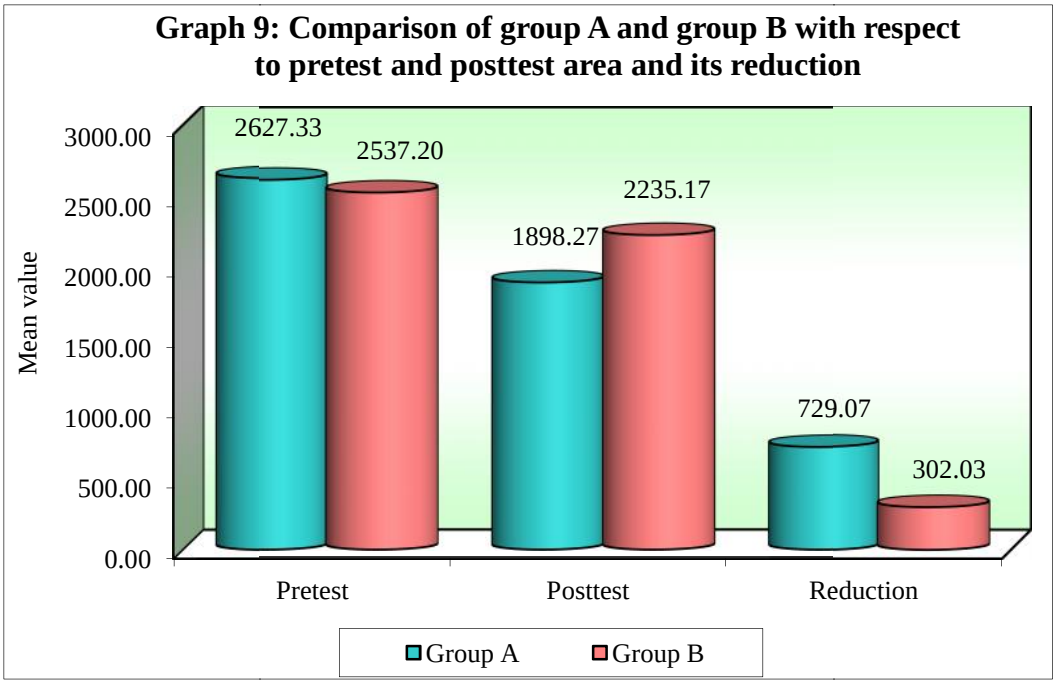


In our study it is observed that mean HBA1C in study group is 6.60±0.69 and control group is 6.40 ±0.57. The difference between the two is not statistically significant (p=0.2282).

Table 9: Comparison of group A and group B with respect to pretest and posttest area and area reduction by independent t test

Variable	Group	n	Mean	SD	SE	t-value	p-value
Pretest	Group A	30	2627.33	711.37	129.88	0.4498	0.6545
	Group B	30	2537.20	835.71	152.58		
Posttest	Group A	30	1898.27	481.17	87.85	-2.0515	0.0447*
	Group B	30	2235.17	759.98	138.75		
Reduction	Group A	30	729.07	364.24	66.50	6.1777	0.0001*
	Group B	30	302.03	103.32	18.86		

*p<0.05



The mean area at the beginning of the study is 2627.3±711.37 mm^2 in study group and 2537.20 ± 835.71mm^2 in the control group. There is no significant difference in the initial mean area between the two groups (p=0.6545).

At the end of the study the mean area are 1898.27±81.17mm^2 in study group and 2235.17±759.98mm^2 in the control group. The difference in final wound area between two groups is significant (p=0.0447).

The study shows that the final wound reduction achieved between the two groups are 729.07±364 .24mm^2 in study group and 302.03±103.32mm^2 in control group which is statistically significant (p<0.0001).

Table 10: Comparison of pretest and posttest area in group A and group B by dependent t test

Groups	Treatment	Mean	Std. Dv.	Mean Diff.	SD Diff.	Paired t	p-value
Group A	Pretest	2627.33	711.37				
	Posttest	1898.27	481.17	729.07	364.24	10.9632	0.0001*
Group B	Pretest	2537.20	835.71				
	Posttest	2235.17	759.98	302.03	103.32	16.0112	0.0001*

*p<0.05

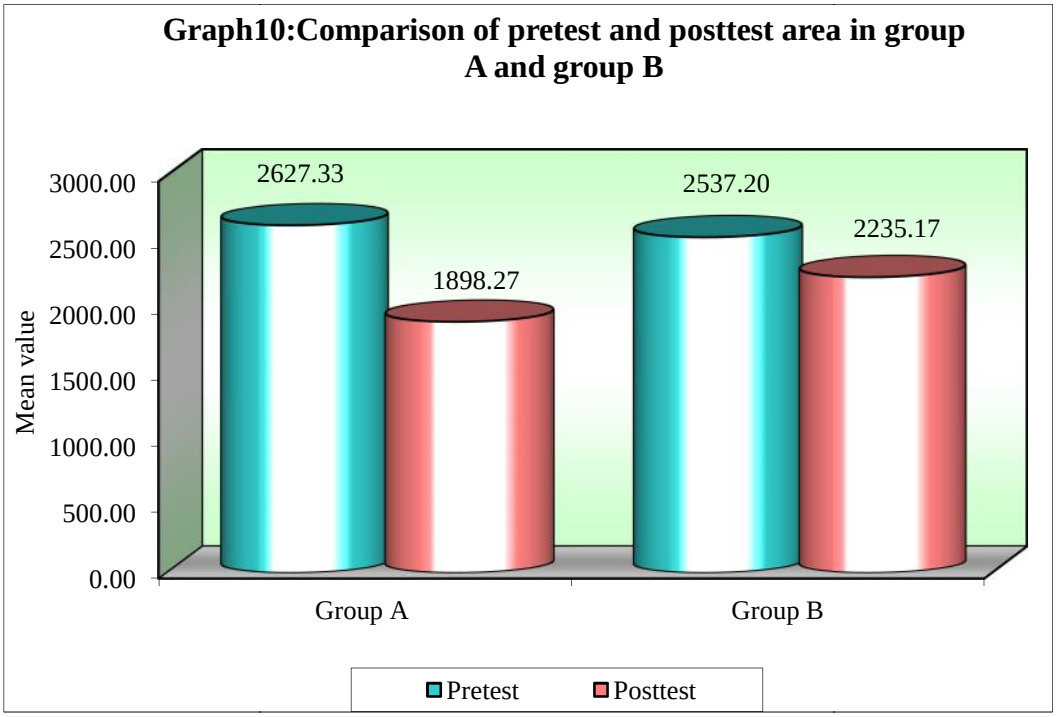
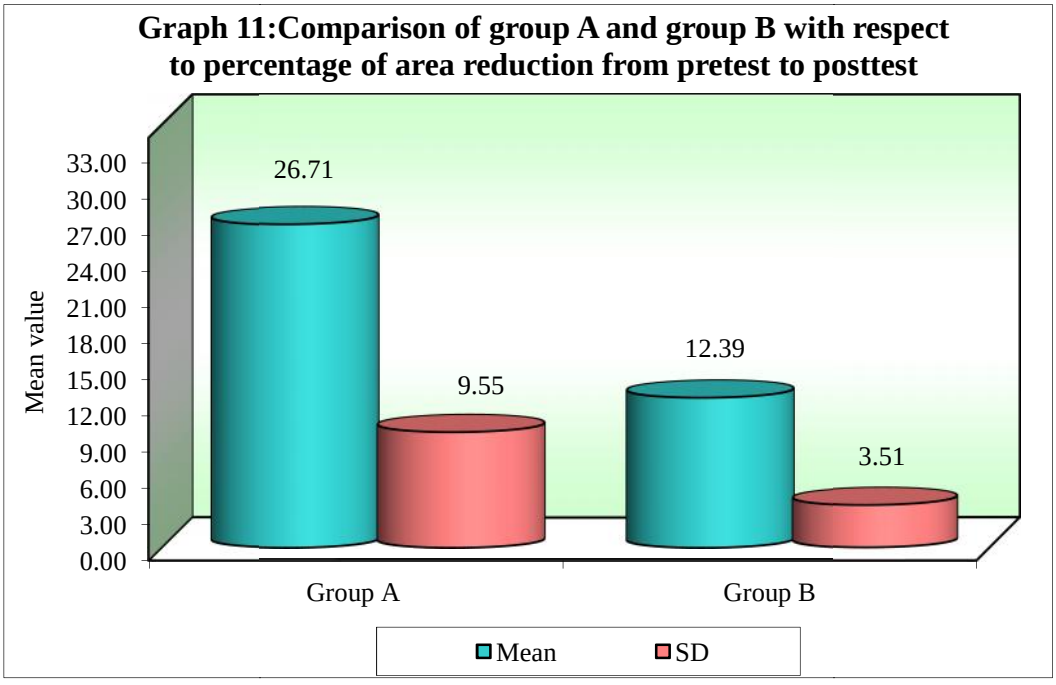


Table 11: Comparison of group A and group B with respect to percentage of area reduction from pretest to posttest by independent t test

Group	N	Mean	SD	SE	t-value	p-value
Group A	30	26.71%	9.55	1.74	7.70 57	0.0001*
Group B	30	12.39%	3.51	0.64		

*p<0.05



The percentage of area reduction were 26.71± 9.55 in study group and 12.39±3.51 in control group, which is statistically significant (p<0.0001).

DISCUSSION

Wound healing without any complications is desired by every surgeon. Successful wound dressing is the one which keeps the wound moist and is devoid of any adverse effects . Diabetic ulcers are stuck in inflammatory phase of healing and show cessation of epidermal growth or migration on the wound surface.

Topical Timolol dressing has shown great promise in healing of chronic ulcers (Venous ulcers and superficial burn wounds). Topical Timolol acts by improving keratinocyte migration and accelerates epithelialization.

The present study at KLE University's Jawaharlal Nehru medical college and KLES DR. Prabhakar Kore Hospital and MRC, Belagavi has been conducted to compare the efficacy of topical Timolol versus normal saline dressing in the treatment of diabetic foot ulcers. Base line characteristics of all the subjects such as age, sex and location of the ulcer were similar in both the groups.

In the present study, the incidence of diabetic foot ulcers was more in males (65%) as compared to females (35%). Diabetic foot ulcers are most commonly seen in 6th decade (50%) followed by the fifth decade (26.67%).As the age increases there are more chances of having diabetic foot ulcers. Patients with pulse less limb and osteomyelitis were excluded.

In this study, 65% of the ulcers were traumatic in origin, trauma being the triggering factor secondary to neuropathy. 35% were spontaneous in origin secondary to blister rupture or unnoticed trivial trauma. 66.66% of the patients had ulcer on the

dorsal surface of the foot , 23.34% on the plantar surface and remaining 10% on the heel of the foot.

Most of the patients (55%) were on Insulin where as 45 % were on Oral Hypoglycaemic agents. The mean ulcer area reduced from 2627.33$mm^2$to 1898.27mm^2 in patients dressed with topical Timolol as compared to ulcer area reduction from 2537.20mm^2 to 2235.17mm^2 in patients dressed with normal saline. The percentage of area reduction is 26.71±9.55% in study group and 12.39±3.51% in control group which is statistically significant ($p<0.0001$).

In the present study 60 patients suffering from Diabetic foot ulcers were enrolled based on inclusion and exclusion criteria. 30 (22 males, 8 females) were in the study group and 30 (17 males and 13 females) were in the control group. Participants of the study group were treated with the topical Timolol 0.5% dressing from day 01 to day 15. All 30 patients selected for topical Timolol treatment complied for the fifteen days period of the study. All 30 patients of the control group were treated with normal saline dressing and complied for the fifteen days period of the study. The initial ulcer area measurement on day 01 and final ulcer area measurement on day 15 were taken on transparent sheets in both the groups.

The following formula was applied to calculate % reduction in area of ulcer after 15days period in both study group and control group.

$$\% \text{ Reduction of ulcer area after 15days} = \frac{\text{Initial area} - \text{Final area}}{\text{Initial area}} \times 100$$

We have found that 26.71% (S.D: 9.55) reduction of ulcer area in the study groups as compared to 12.39% (S.D: 3.51) reduction of ulcer area in control group. Therefore, study group is having more % of ulcer area reduction as compared to control group. On applying independent‘t’ test $p<0.0001$ which is significant.

From our study, we conclude that topical Timolol dressing facilitates early ulcer healing in patients suffering from diabetic foot ulcers.

Limitations of our study:

1. Follow up is short to derive conclusion on long term healing of the ulcers.
2. The cost was not analyzed in this study.

CONCLUSION

Topical Timolol dressing was compared with the normal saline dressing in the treatment of diabetic foot ulcers , the following conclusions were derived:

- ✓ Topical Timolol dressing showed faster and better healing rates .
- ✓ Area reduction and percentage reduction was better in topical Timolol dressing group.
- ✓ There were no adverse effects or reactions due to topical Timolol dressing.

SUMMARY

The present study was conducted in KLES DR Prabhakar Kore Hospital and Medical Research Center, Belagavi on 60 patients with diabetic foot ulcers.

The objective of the study was to compare efficacy of topical Timolol dressing versus normal saline dressing in reducing the ulcer area in patients with diabetic foot ulcers.

The two groups were randomized into study group and control group. The study group received topical Timolol dressing and the other received conventional normal saline dressing.

There was no difference between the groups in the baseline characteristics like age, sex ,site of the ulcer and initial ulcer area.

The final area reduced and percentage of area reduced were statistically significant in the study as compared to the control group.

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ANNEXURE-I

INFORMED CONSENT

TITLE OF THE STUDY:"TO COMPARE THE EFFICACY OF TOPICAL TIMOLOL VERSUS NORMAL SALINE DRESSING IN THE TREATMENT OF DIABETIC FOOT ULCERS – A RANDOMIZED CONTROLLED TRIAL"

PRINCIPAL INVESTIGATOR:

INTRODUCTION AND PURPOSE:

The diabetic foot ulcers are common complication of diabetes mellitus. They are managed by conventional methods of dressings like normal saline, povidone iodine and eusol etc. Topical timolol application could be used as an alternative to currently available methods of dressing. Studies have shown that it has better healing properties than conventional topical agents. This study is being undertaken to compare the efficacy of topical Timolol dressing versus normal saline dressing in diabetic foot ulcer.

PROCEDURE:

I request you to kindly participate in the study titled **"TO COMPARE THE EFFICACY OF TOPICAL TIMOLOL VERSUS NORMAL SALINE DRESSING IN THE TREATMENT OF DIABETIC FOOT ULCERS – A RANDOMIZED CONTROLLED TRIAL"** If you agree to participate in the study please furnish the details pertaining to the study.

BENEFITS:

1. Timolol has the potential to be an inexpensive, noninvasiveand non-labour intensive means to promote wound healing of diabeticfoot ulcers.

2. Timolol (a β2- blocker) helps in the keratinocyte migration and rapid re-epithelialization of ulcers

RISKS:

- No proven side effects

ALTERNATIVES:

If patient is not willing to take part in the study, his / her treatment or any other investigations the patient wants to undergo, in future, in KLE's Dr Prabhakar Kore Hospital and MRC will not be affected by his / her decision.

VOLUNTARY PARTICIPATION/WITHDRAWAL:

Taking part in this study is voluntary. I may choose not to take part in this study, or if I decide to take part I can later change my mind and withdraw from the study. My decision will not change the present or future health care or other services that I receive. The study doctor or the sponsor may stop my participation in this study. I will tell of any important new findings that may change my willingness to continue to take part. If I choose not to take part in the study I will receive the standard treatment.

COSTS: NIL

COMPENSATION:

In the event that I become injured as a result of taking part in this study, treatment will be offered to me, No reimbursement, compensation or free medical care is given.

CONFIDENTIALITY:

All information collected about me during the course of the study will be kept confidential to the extent permitted by the law. The code numbers will identify me in this research record. Information from this study may be published but my identity will be confidential in any publication.

QUESTION:

In case you have any questions about your rights as a study participant you can contact Dr. Ganga Pilli (09448868866).

CONSENT TO PARTICIPATE IN RESEARCH STUDY:

I voluntarily agree to take part in this study by signing on the line below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicated that I have read this entire consent form or it has been read to me, and has been explained to me in my vernacular language and had all my questions answered. I will be given a copy of this consent form.

Signature /Left thumb print of the participant or legally authorized representative.

Participant's Name :…….

Signature/ Left thumb impression .: …….

Name of the legally authorized representative :…….

Signature/ Left thumb impression. :…….

Witness's Name : …….

Signature/ Left thumb Impression of witness :…….

Investigators name and Signature : …….

Date and Place : …….

ANNEXURE-II

PROFORMA

PATIENT IDENFICIATION DATA

GROUP : **CASE NO. :**

I.P/ O.P.D NO.: **D.O.A:**

NAME :

AGE: **D.O.S:**

SEX : **D.O.D:**

OCCUPATION:

MEDICAL HISTORY

	Yes	**No**
Peripheral neuropathy		
Nephropathy		
PVD		
CVD		

DIABETIC STATUS

Type :

Medication :

Drug	Dose	Duration

Complication:

	Yes	No
Neuropathy		
Vasculopathy		

ULCER DETAIL

1. Mode of onset

Traumatic	
Spontaneous	
Pressure	
Others	

2. Duration

WOUND OBSERVATION

1. Site
2. Size
3. Shape
4. Edge
5. Margin
6. Floor
7. Base
8. Discharge
9. Surrounding Skin
10. Slough /necrotic tissue

NEUROLOGICAL EXAMINATION

	Yes	**No**
Sensory Loss		
Motor Weakness		

VASCULAR EXAMINATION

	Right			Left		
	Normal	Weak	Absent	Normal	Weak	Absent
Femoral artery						
Popliteal artery						
Ant. Tibial artery						
Post Tibial artery						
Dorsalis Pedis artery						

FOOT DEFORMITY

	Yes	No
Bunion		
Toe deformity		
Flat foot		
Foot drop		
Charcots foot		

DEBRIDEMENT

Date :

Anesthesia :

INVESTIGATIONS

CBC

FBS ,PPBS,HbA_1C

Blood Urea

Sr. Creatinine

Urine : Routine

Microscopy

X-ray Foot AP view

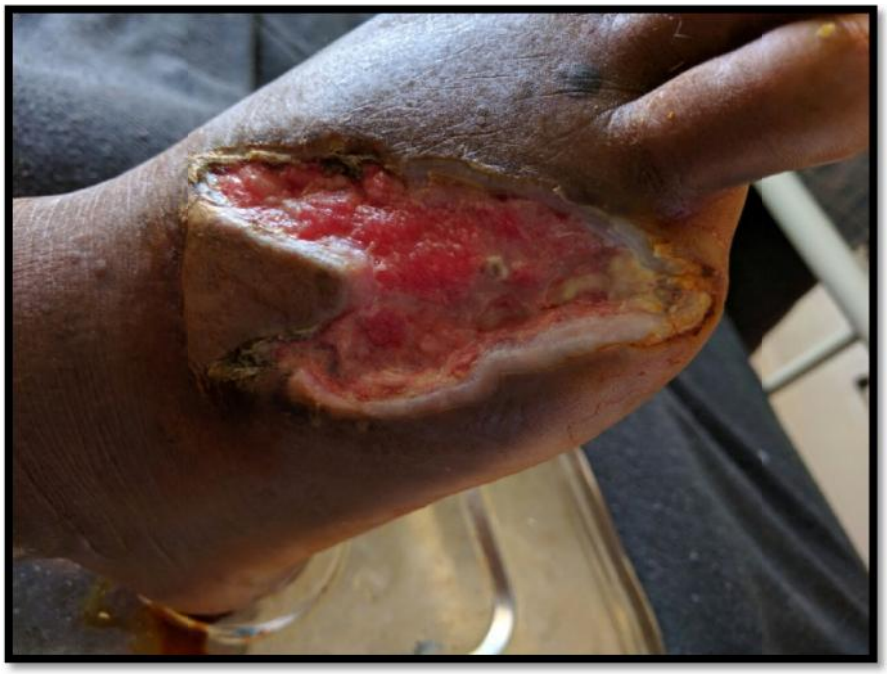
Lat. View

Tissue culture/ sensitivity

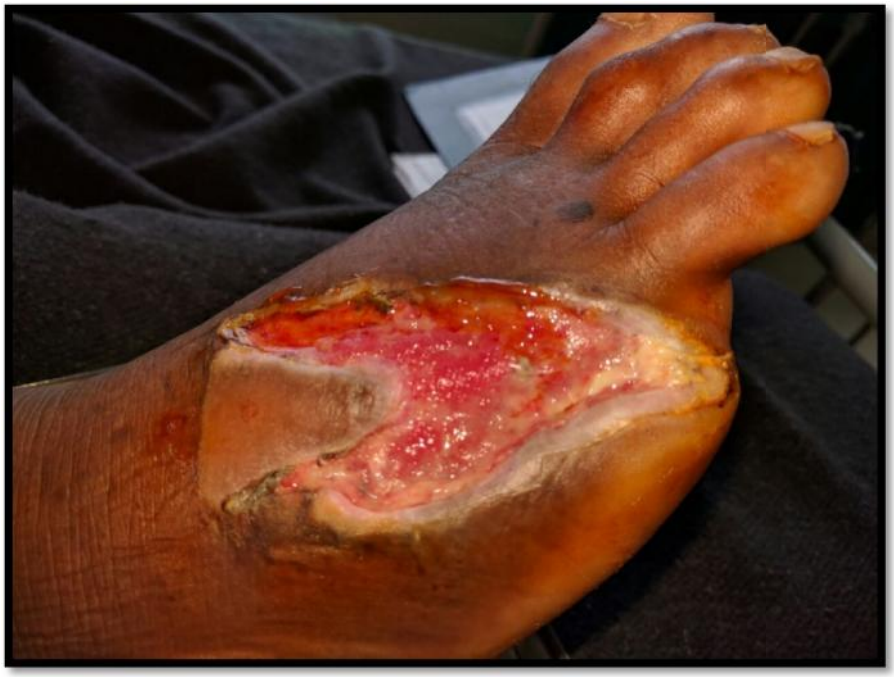
Colour doppler

ANNEXURE III – PHOTOGRAPHS

CONTROL GROUP :

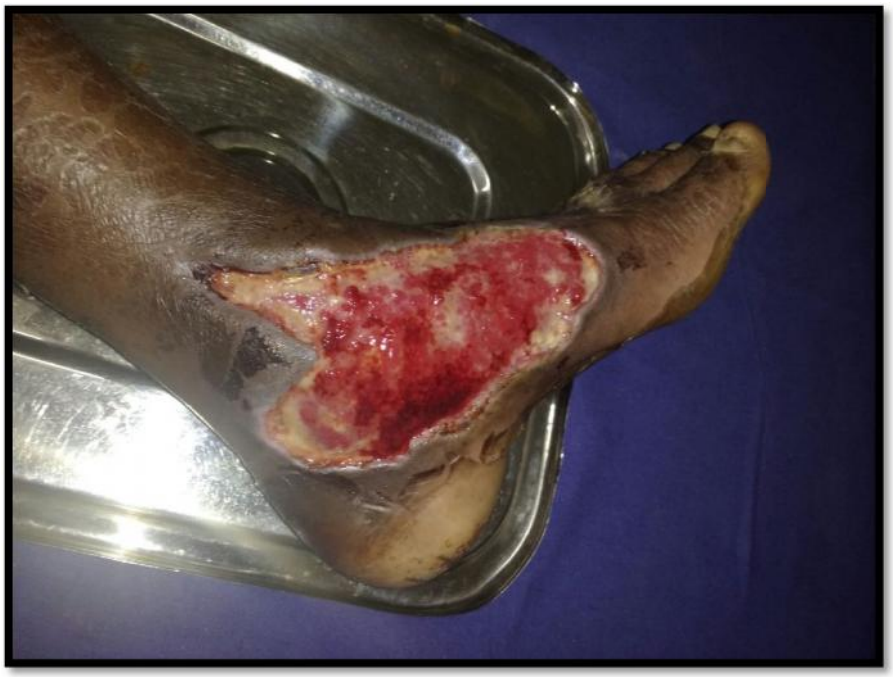


Photographs 1 : Ulcer on day 1

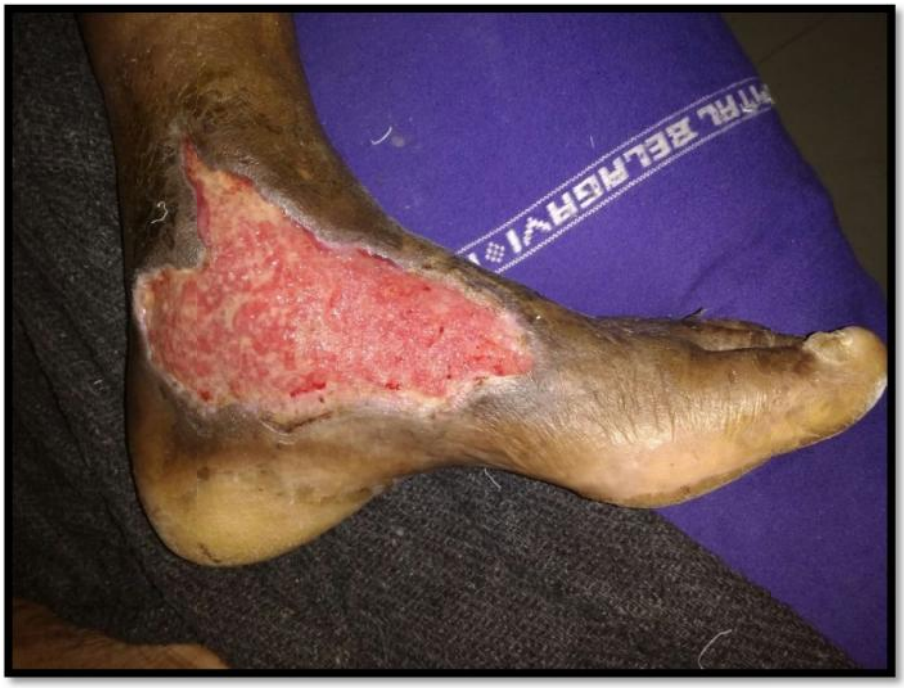


Photographs 2: Ulcer on day 15 using normal saline dressing

STUDY GROUP :



Photographs 3: Ulcer on day 1



Photographs 4: Ulcer area on day 15 using topical Timolol (0.5%)solution

Photographs 5: Topical Timolol (0.5%)

ANNEXURE IV–MASTERCHART

STUDY GROUP -A

SL.NO	IP.NO	AGE/SEX	Onset	SITE	ANTI DM RX	FBS	HBA1C	C/S	INITIAL AREA	FINAL AREA	AREA REDUCED	%REDUCTION IN AREA
1	719677	52/F	Spontaneous	DRF	INSULIN	156	6	NOGC	2734	1656	1078	39
2	723919	60/M	Traumatic	DLF	OHA	130	7	NOGC	3110	2200	910	29
3	719701	56/M	Traumatic	DRF	OHA	183	7	NOGC	3455	2820	635	18
4	716163	44/M	Traumatic	PRF	INSULIN	136	7	NOGC	1783	1596	187	10
5	723857	52/M	Traumatic	DRF	OHA	130	7	NOGC	2525	1950	575	23
6	725171	62/M	Spontaneous	DRF	INSULIN	120	7	NOGC	3450	2400	1050	30
7	721742	64/M	Traumatic	DRF	INSULIN	140	7	KP	2586	2250	336	13
8	721460	38/M	Traumatic	DRF	OHA	150	6	NOGC	3563	2100	1463	41
9	725282	45/M	Traumatic	HRF	OHA	160	6	PM	3966	3000	966	24
10	734841	40/M	Traumatic	DLF	INSULIN	182	8	NOGC	2350	1896	454	19
11	734888	52/F	Spontaneous	PRF	OHA	138	8	NOGC	2370	1920	450	19
12	734473	48/M	Traumatic	PLF	INSULIN	156	6	NOGC	3240	2050	1190	37
13	739179	36/M	Spontaneous	DLF	INSULIN	94	6	NOGC	1430	1286	144	10
14	749977	56/F	Spontaneous	DRF	INSULIN	156	7	SA	1540	1200	340	22
15	742893	52/M	Traumatic	DLF	OHA	144	7	NOGC	2540	1560	980	39
16	740395	62/M	Traumatic	DRF	OHA	178	6	NOGC	2720	2030	690	25
17	741508	64/F	Traumatic	PLF	INSULIN	192	6	EC	3300	2120	1180	36
18	743354	48/M	Spontaneous	DLF	OHA	145	7	NOGC	2540	1726	814	32
19	743891	52/F	Traumatic	HLF	INSULIN	158	6	NOGC	1550	1166	384	25
20	748722	56/M	Spontaneous	DRF	OHA	145	7	NOGC	2750	1720	1030	37
21	754116	60/M	Traumatic	DLF	INSULIN	149	6	PM	3600	2570	1030	29
22	755166	52/M	Spontaneous	DRF	OHA	185	8	NOGC	2368	1490	878	37
23	755796	48/M	Traumatic	PRF	INSULIN	172	5	NOGC	3420	2200	1220	36
24	755954	56/F	Traumatic	DLF	INSULIN	164	6	NOGC	2196	1980	216	10
25	753453	42/M	Spontaneous	DRF	OHA	140	6	NOGC	2460	2030	430	17
26	758053	40/M	Traumatic	DLF	INSULIN	112	7	NOGC	1430	1010	420	29
27	758467	56/M	Spontaneous	PRF	OHA	118	7	NOGC	2456	2078	378	15
28	765285	61/M	Traumatic	PLF	INSULIN	134	7	NOGC	1560	1120	440	28
29	761389	53/F	Traumatic	PRF	INSULIN	168	6	NOGC	3280	2200	1080	33
30	760115	56/F	Spontaneous	DRF	OHA	145	7	NOGC	2548	1624	924	36

CONTROL GROUP B												
31	710944	56/M	Traumatic	DLF	INSULIN	136	7	NOGC	3546	3182	364	10
32	717604	45/M	Spontaneous	HLF	OHA	160	6	NOGC	3134	2835	299	10
33	718528	35/F	Spontaneous	DLF	OHA	99	6	SA	2681	2366	315	12
34	719160	57/M	Traumatic	PRF	OHA	140	6	NOGC	3547	3070	477	13
35	723768	43/F	Traumatic	DRF	INSULIN	123	7	NOGC	1165	980	185	16
36	720201	50/F	Traumatic	PRF	OHA	129	7	SA	1367	1180	187	14
37	722662	60/M	Spontaneous	DLF	OHA	92	6	NOGC	3523	3167	356	10
38	723664	22/F	Traumatic	HLF	INSULIN	120	7	NOGC	1280	968	312	24
39	725263	56/F	Traumatic	DLF	INSULIN	178	7	NOGC	2900	2537	363	13
40	727624	53/M	Traumatic	DRF	INSULIN	145	7	NOGC	2678	2345	333	12
41	729158	64/M	Traumatic	DLF	INSULIN	123	6	KP	2534	2199	335	13
42	729166	56/M	Traumatic	PLF	OHA	111	7	NOGC	3218	2894	324	10
43	729190	50/M	Traumatic	DLF	INSULIN	156	7	EC	1678	1416	262	16
44	735371	46/M	Traumatic	DRF	INSULIN	123	6	NOGC	980	820	160	16
45	734846	56/F	Traumatic	DRF	INSULIN	144	6	NOGC	920	810	110	12
46	744329	55/F	Traumatic	DLF	OHA	140	7	NOGC	2356	2134	222	9
47	744758	47/F	Spontaneous	PLF	OHA	96	7	PM	1472	1256	216	15
48	743003	45/M	Traumatic	DRF	OHA	160	7	NOGC	3180	2791	389	12
49	743490	58/M	Spontaneous	HRF	INSULIN	122	6	NOGC	2560	2286	274	11
50	743355	62/F	Spontaneous	DRF	INSULIN	136	6	NOGC	1967	1777	190	10
51	744559	60/M	Traumatic	DRF	INSULIN	172	6	NOGC	3318	2942	376	11
52	749185	56/M	Traumatic	PLF	OHA	118	6	SA	3467	2972	495	14
53	749274	52/F	Spontaneous	DRF	INSULIN	110	6	NOGC	2234	1879	355	16
54	749283	48/M	Traumatic	HRF	INSULIN	164	8	NOGC	3426	2966	460	13
55	750420	51/M	Spontaneous	PLF	INSULIN	182	7	NOGC	2500	2378	122	5
56	753458	39/F	Traumatic	DRF	INSULIN	128	6	NOGC	2668	2423	245	9
57	754111	49/M	Traumatic	DLF	OHA	142	6	EC	3065	2767	298	10
58	762108	52/M	Spontaneous	DRF	OHA	178	6	NOGC	2436	2238	198	8
59	765449	60/F	Spontaneous	DRF	INSULIN	156	5	NOGC	3546	3147	399	11
60	765983	50/F	Traumatic	DLF	OHA	130	6	NOGC	2770	2330	440	16

ANNEXURE-V

KEY FOR USING THE MASTER CHART

SL.No	:	Serial number
M	:	Male
F	:	Female
IP No	:	Inpatient Number
DM	:	Diabetes mellitus
FBS	:	Fasting Blood Sugar
C/s	:	Culture sensitivity report
mm2	:	millimetre square
DLF	:	Dorsum of Left Foot
HRF	:	Heel of Right Foot
DRF	:	Dorsum of Right Foot
PLF	:	Plantar of Left Foot
HLF	:	Heel of Left Foot
PRF	:	Plantar of Right Foot
OHA	:	Oral Hypoglycaemic Agents
NOGC	:	No Organisms Grown in Culture
SA	:	Staphylococcus Aureus
KP	:	Klebsiella Pneumonia
PM	:	Proteus Mirabilis
PA	:	Pseudomonas Aeruginosa
EC	:	Eischericia Coli