"COMPARATIVE STUDY BETWEEN L-LYSINE AND REGULAR DRESSING IN CHRONIC FOOT ULCERS OF PATIENTS ADMITTED AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM".

By

DR.GURUPADAPPA

Dissertation

SUBMITTED TO THE KLE UNIVERSITYBELGAUM, KARNATAKA

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SURGERY (M.S.)

IN

GENERAL SURGERY

Under the guidance of

Dr. A.C.PANGI$_{\text{M.S, FAIS}}$

Professor

DEPARTMENT OF GENERAL SURGERY

JAWAHARLAL NEHRU MEDICAL COLLEGE, BELGAUM-590010, KARNATAKA

MAY – 2011

KLE UNIVERSITY BELGAUM,
KARNATAKA.

DECLARATION

I hereby declare that this dissertation entitled "COMPARATIVE STUDY BETWEEN L-LYSINE AND REGULAR DRESSING IN CHRONIC FOOT ULCERS OF PATIENTS ADMITTED AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"is a bonafide and genuine research work carried outby me under the guidance of Dr.A. C. PANGI M.S,FAISProfessor, Department of Surgery, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum – 590010.

Date:

Place: Belgaum (Dr. GURUPADAPPA)

KLE UNIVERSITY, BELGAUM, KARNATAKA

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled**"**COMPARATIVE STUDY BETWEEN L-LYSINE AND REGULAR DRESSING IN CHRONIC FOOT ULCERS OF PATIENTS ADMITTED AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM**"**is a bonafide research work done by**Dr. GURUPADAPPA.** under my guidance in partial fulfillment of the requirement for the award of the degree of **M.S. (General Surgery)**.

Date :

Place : Belgaum

Dr. A.C.Pangi$_{\textbf{MS.FAIS}}$
Professor,
Department of General surgery,
J. N. Medical College,
Nehru Nagar,
Belgaum-590010.

KLE UNIVERSITY BELGAUM,

KARNATAKA.

COPYRIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the KLE University, Belgaum, Karnataka shall have the rights to preserve, use and disseminate this dissertation in print or electronic format for academic / research purpose.

Date :

Place : Belgaum

(Dr. GURUPADAPPA)

KLE UNIVERSITY BELGAUM, KARNATAKA.

ENDORSEMENT BY THE HOD, PRINCIPAL/HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled**"COMPARATIVE STUDY BETWEEN L-LYSINE AND REGULAR DRESSING IN CHRONIC FOOT ULCERS OF PATIENTS ADMITTED AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"**is a bonafide research work done by **Dr. Gurupadappa**under the guidance of**Dr. A. C. Pangi**$_{\text{M.S.,FAIS}}$Professor, Department of General Surgery, J. N. Medical College, Nehru Nagar, Belgaum-590010.

Seal & Signature of the HOD

Dr. Shashi. M. Uppin$_{\text{M.S.; F.I.C.S}}$
Professor and Head,
Department of General surgery,
J. N. Medical College, Nehru Nagar,
Belgaum-590010.

Date:

Place: Belgaum.

Seal & Signature of the Principal

Dr.V. D. Patil$_{\text{M.D.; D.C.H.}}$
Principal,
J. N. Medical College,
Nehru Nagar,
Belgaum-590010.

Date:

Place: Belgaum.

COPYRIGHT

Declaration By The Candidate

I hereby declare that the KLE UNIVERSITY BELGAUM, Karnataka shall have the rights to preserve, use and disseminate this dissertation in print or electronic format for academic / research purpose.

Date: **Signature of the Candidate**

Place: Belgaum **Dr.GURUPADAPPA**

ACKNOWLEDGEMENT

I take this opportunity to express my respect and heart felt gratitude to all my teachers.

I gladly utilize this opportunity to express my deep sense of gratitude and indebtedness to my respected teacher and guide Dr**. A. C. Pangi**$_{\textbf{M.S.FAIS}}$ Professor, Department of Surgery without whose everlasting inspiration, incessant encouragement and criticism, with valuable suggestions for improvement, the completion of this study would not have been possible.

I am extremely grateful and indebted to **Prof. Shashi. M. Uppin**$_{\textbf{M.S.;FICS}}$ Professor and Head of the Department of surgery, J. N. Medical College, Belgaum, for his valuable advice and guidance in completing this dissertation.

I also wish to express my deepest gratitude to **Dr. V. D. Patil** $_{\textbf{M.D.;D.C.H.}}$ Principal, J. N. Medical College, Belgaum, for allowing me to conduct this study.

I am thankful to **Dr. M. V. Jali**$_{\textbf{M.D.}}$ Medical Director, KLES Dr. PrabhakarKore Hospital and Medical Research Centre, Belgaum, for allowing me to carryout the dissertation work.

I express my sincere gratitude to **Dr. V. B. Dhaded**$_{\text{M.S.;FICS.,}}$**Dr. A. S. Godhi**$_{\text{M.S.; FICS,}}$**Dr. M. S. Sangoli**$_{\text{M.S.,}}$ **Dr. V. M. Uppin**$_{\text{M.S.,}}$ **Dr. S. S. Shimikore**$_{\text{M.S.,}}$ **Dr. I. V. Uppin**$_{\text{M.S.,}}$ **Dr. A. S. Gogate**$_{\text{M.S.,}}$**Dr. B. V. Gogeri**$_{\text{M.S., FRCS}}$ (Late) and **Dr. S. C. Metgud** $_{\text{M.S.,}}$**Dr P. S. Pattanshetti**$_{\text{M.S}}$Professors who have encouraged me during the course of study. I thank them for their inspiration and moral support.

I owe my sincere gratitude to**,Dr. Santosh B. Patil**$_{\text{M.S.,}}$ for their constant support and endeavourance throughout my course. I thank **Dr. R. R. Rao**$_{\text{M.S.,}}$**Dr. BasavarajKajagar**$_{\text{M.S.,}}$ Associate Professors, Department of Surgery, for their valuable guidance throughout the course of this study.

I express my sincere gratitude to **Dr. R. S. Koujalagi**M.S., .**Dr. V. M. Pattanshetti**M.S.,**Dr. S. N. Halabhavi**M.S., **Dr. Manoj Togale** M.S., **Dr Rahul. K** M.S.**DrAman. Mahajan** M.S., **DrParag. Hawaldar**M.S.,**DrPushpa S Kumar** Assistant Professors, Department of Surgery, who have provided me with moral support during the study.

I would like to extend a vote of thanks & appreciation to **Dr. SantoshKurbet**M.S.;MCH,and**DrPrashantHombal**M.S., **Dr PrashantBabanavar** M.S., Senior Residents, Department of Surgery.

I whole heartedly thank **Dr Manoj KumarBhutte** M.S., **Dr PrakashMahantshetti**M.S.for their immense help.

From the bottom of my heart I convey my heartfelt gratitude to **All Patients** without whose co-operation this study would have been incomplete.

No amounts of words can measure up my deep sense of gratitude and fullness that I feel towards my parents **Shri. C. G.Parappanavar(late)**and **Smt. I. C. Parappanavar**and**Shri. B. S. Mannangi(late)** and **Smt. S. B. Mannangi** other friends and family members.

I express my sincere thanks to my friends **Dr. SantoshChikraddi, Dr. Shailesh, Dr. Devendra, Dr Satyajit, Dr. P Umashankar, Dr Sunil Reddy, Dr Amit K, Dr Biju, Dr Santoshi, Dr SiddharthChako, Dr Krishna** for their constant help, support, encouragement and cooperation in designing my dissertation.

Date:

Place: Belgaum Dr. Gurupadappa

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF IMAGES & PHOTOGRAPHS

ABSTRACT

Background and objectives

The management of wound and wound dressing is an important aspect of chroniculcer management. Choosing an appropriate dressing can be a complex process. L-lysine is an amino acid which helps in faster wound remodelling.

Objective

The objective of the study was to assess the L-lysine dressings in comparison to conventional betadine dressings in achieving mean percentage wound reduction in patients with chronic foot ulcer of lower extremities more than four weeks duration, using transparency sheet.

Methodology

The present one year randomized controlled trial was conducted in the Department of Surgery, KLES Dr. PrabhakarKore Hospital and Medical Research Centre, Belgaum on 60 patients with infected diabetic foot ulcer during the period of January 2009 to December 2009. The patients were divided into two different groups by number randomization (Group 1 L-lysine and Group 2 conventional betadine dressing). Woundmeasurement was taken on day one and fourteen in both the groups. Percentage area of wound reduction was calculated.

Results

There was no statistical difference in the baseline characteristics like age, sex and initial wound area of the ulcer between the two groups. The percentage of area reduction was 32.30±7.00in patients treated with L-lysine dressings and 17.95±3.77in patients treated with betadine dressings, which is statistically significant ($p<0.001$).

Conclusions

L-lysine dressing can be used for the healing of chronic foot ulcer of lower limb.

Key word

Diabetic ulcers; L-Lysine dressing; betadine dressing; Wound area;

.

"COMPARATIVE STUDY BETWEEN L-LYSINE AND REGULAR DRESSING IN CHRONIC FOOT ULCERS OF PATIENTS ADMITTED AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM".

By
REG.NO BH0108005

DISSERTATION

SUBMITTED TO THE KLE UNIVERSITYBELGAUM,

KARNATAKA

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MASTER OF SURGERY (M.S.)

IN

GENERAL SURGERY

DEPARTMENT OF GENERAL SURGERY
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELGAUM-590010, KARNATAKA
MAY – 2011

KLE UNIVERSITY BELGAUM, KARNATAKA.

ENDORSEMENT BY THE HOD, PRINCIPAL/HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled**"COMPARATIVE STUDY BETWEEN L-LYSINE AND REGULAR DRESSING IN CHRONIC FOOT ULCERS OF PATIENTS ADMITTED AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"** is a bonafide research work done by **REG.NO BH0108005** Department of General Surgery, J. N. Medical College, Nehru Nagar, Belgaum-590010.

Seal & Signature of the
HOD
Dr. Shashi. M. UppinM.S.; F.I.C.S
Professor and Head,
Department of General surgery,
J. N. Medical College, Nehru Nagar,
Belgaum-590010.

Date:

Place: Belgaum.

Seal & Signature of the
Principal
Dr.V. D. PatilM.D.; D.C.H.
Principal,
J. N. Medical College,
Nehru Nagar,
Belgaum-590010.

Date:

Place: Belgaum.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF IMAGES & PHOTOGRAPHS

ABSTRACT

Background and objectives

The management of wound and wound dressing is an important aspect of chroniculcer management. Choosing an appropriate dressing can be a complex process. L-lysine is an amino acid which helps in faster wound remodelling.

Objective

The objective of the study was to assess the L-lysine dressings in comparison to conventional betadine dressings in achieving mean percentage wound reduction in patients with chronic foot ulcer of lower extremities more than four weeks duration, using transparency sheet.

Methodology

The present one year randomized controlled trial was conducted in the Department of Surgery, KLES Dr. PrabhakarKore Hospital and Medical Research Centre, Belgaum on 60 patients with infected diabetic foot ulcer during the period of January 2009 to December 2009. The patients were divided into two different groups by number randomization (Group 1 L-lysine and Group 2 conventional betadine dressing). Woundmeasurement was taken on day one and fourteen in both the groups. Percentage area of wound reduction was calculated.

Results

There was no statistical difference in the baseline characteristics like age, sex and initial wound area of the ulcer between the two groups. The percentage of area reduction was 32.30±7.00in patients treated with L-lysine dressings and 17.95±3.77in patients treated with betadine dressings, which is statistically significant ($p<0.001$).

Conclusions

L-lysine dressing can be used for the healing of chronic foot ulcer of lower limb.

Key word

Diabetic ulcers; L-Lysine dressing; betadine dressing; Wound area;

.

ANNEXURE I

CONSENT FORM

Introduction

Mr./Miss./Mrs. _____ You are invited to participate in our research study that is **"COMPARATIVE STUDY BETWEEN L-LYSINE AND REGULAR DRESSING IN CHRINIC FOOT ULCERS OF PATIENTS ADMITTED TO KLES DR. PRABHAKARKOREHOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM".**

Since you are suffering from foot ulcer, which is not healing since a long time and will be requiring treatment for the same, you are eligible to be part of the study and hence asked to participate. This research is about the beneficial effects of L-lysine on your foot ulcer and the result of this research will help in a better treatment of similar participants in the future.

If you agree to be part of this research, we would ask you some relevant clinical history. You are free to not to answer to which ever questions you think are not relevant. A clinical examination will be done. On the first day empirical antibiotics will be given and regular betadine/L-lysine dressing will be done.

There are chances you may have a speedy and better recovery with this therapy and it will also help in the treatment if participants with similar complaints in the future. Your decision of whether or not to participate in this study will not affect

the quality of treatment you receive. Further you may withdraw from the study at any time.

All the new information collected about you during this course of study will be kept confidential to the extent permitted by law. Any information which identifies you personally, will not be released without your written consent.

This study does not have any damaging aspect and there are no chances of injury during the course the course the study, but if injured the investigator is not responsible. There will be no extra cost incurred by you. However you will have to pay for the routine investigations, which are part of existing management protocol for the treatment of chronic ulcer. There is no commitment for any reimbursement or any compensation for the participant. The participation in this study is entirely voluntary and you may withdraw from the study at any time. At any time during or after the study, for any information you may contact the researcher.

Chairman

Institutional ethical committee

Dr V D Patil

Phone: 0831- 2471350

Signature of the participant or legally authorized representative

Subject Name : _____.

Signature or the Left Thumb Print of Subject : _____

Witness Name: _____ ***Signature :*** _____

Investigators Name: _____ Signature : _____

Date : _____ Place : _____

INTRODUCTION

Chronic leg ulceration affects about 1% of the middle-aged and elderly population, most commonly occurs after a minor injury in association with

* Chronic venous insufficiency (45-80%)

* Chronic arterial insufficiency (5-20%)

* Diabetes (15-25%)

Chronic leg ulcers[45] may also be due to skin cancer, which may be diagnosed by a skin biopsy of the edge of a suspicious lesion. There are also many less common causes of ulcers including systemic diseases such as systemic sclerosis, vasculitis and various skin conditions especially pyoderma gangrenosum.

The incidence of diabetes mellitus (DM) and its complications are on a rise, the risk of lower extremity amputations is 15 fold higher in diabetics as compared to non-diabetics. Essential to mention here that chronic diabetic foot ulcer is the leading cause of amputations in these patients, also that 15% of all diabetics develop diabetic ulcer and the commonest site being the foot. Although the fundamental pathophysiologic factors leading to diabetic ulcer remains incompletely understood, the triad of neuropathy, ischemia and infections commonly is considered the most important. These diabetic ulcers are known to be resistant to conventional treatment and may herald severe complications if not treated wisely.

The management of wound and wound dressing is an important aspect of diabetic ulcer management, which is neglected many a time. Care of the wound involves management of the ulcer, care of the exudates and knowledge and rational use of myriad dressing materials.

Basic requirements of the ideal ulcer dressing:

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

Treatment plan for diabetic foot includes surgical debridement of wound, improvement of circulation through surgery or therapy, special dressing and antibiotics. Numerous topical medication and gels are promoted for ulcer care and healing. Relatively few have proved to be more efficacious than saline wet to dry dressings. Topical antiseptic, such as povidine-iodine are usually considered to be toxic to healing wounds.

Wound healing is a complex biological process that is well characterized at the microscopic level, which involves inflammation, angiogenesis and the formation of granulation tissue.

Degradation of extracellular matrix is required to remove damaged tissue and formation to permit vessel formation and cell migration. Tissue remodeling involves various extracellular proteinases particularly those belonging to the serine proteinases & matrix matalloproteinases (MMP)[41].During human skin wound healing MMP 2 & MMP-9 were detected in connective tissue and in migrating keratinocytes which play a major role in tissue repair.

With the above knowledge there is need to study faster methods of tissue repair .L-lysine is a part of matrix matalloproteinases , helps in wound healing at faster rate with better remodeling.

OBJECTIVES

Effectiveness of L-lysine in tissue repair and wound reduction in chronic ulcers of lower limb in comparison with conventional method of dressing.

REVIEW OF LITERATURE

CHRONIC FOOT ULCERS

Leg ulcers is due to skin loss on the leg or foot due to any cause. They occur in association with a range of disease processes, most commonly with blood circulation diseases. Leg ulcers may be acute or chronic.

Acute ulcers are sometimes defined as those that follow the normal phases of healing; they are expected to show signs of healing in less than 4 weeks and include traumatic and postoperative wounds.

Chronic ulcers are those that persist for longer than 4 weeks and are often of complex poorly understood origin.

Chronic leg ulceration affects about 1% of the middle-aged and elderly population. It most commonly occurs after a minor injury in association with:

* Chronic venous insufficiency (45-80%)

* Chronic arterial insufficiency (5-20%)

* Diabetes (15-25%)

Chronic leg ulcers may also be due to skin cancer, which may be diagnosed by a skin biopsy of the edge of a suspicious lesion. There are also many less common causes of ulcers including systemic diseases such as systemic sclerosis, vasculitis and various skin conditions especially pyoderma gangrenosum.

Causes of formation of chronic foot ulcer

- Recurrent infection
- Trauma
- Absence of rest

- Poor blood supply
- Hypoxia
- Oedema of the area
- Loss of sensation

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".[9-15]

Classification[9-15]

Type I

Type Pathology

IA : Autoimmune beta cell destruction which leads to insulin deficiency.

IB : Lack of immunologic markers indicative of an autoimmune destructive process of the beta cells..

Type II

It is a heterogeneous group of disorders characterized by:-

- Impaired insulin secretion.
- Variable degree of insulin resistance.

- Increased glucose production

Chronic Complications of Diabetes Mellitus[9-15]

The chronic complications of DM affect many organ systems and are responsible for the majority of morbidity and morality associated with the disease.

Figure 1: Microvascular complications in diabetes mellitus

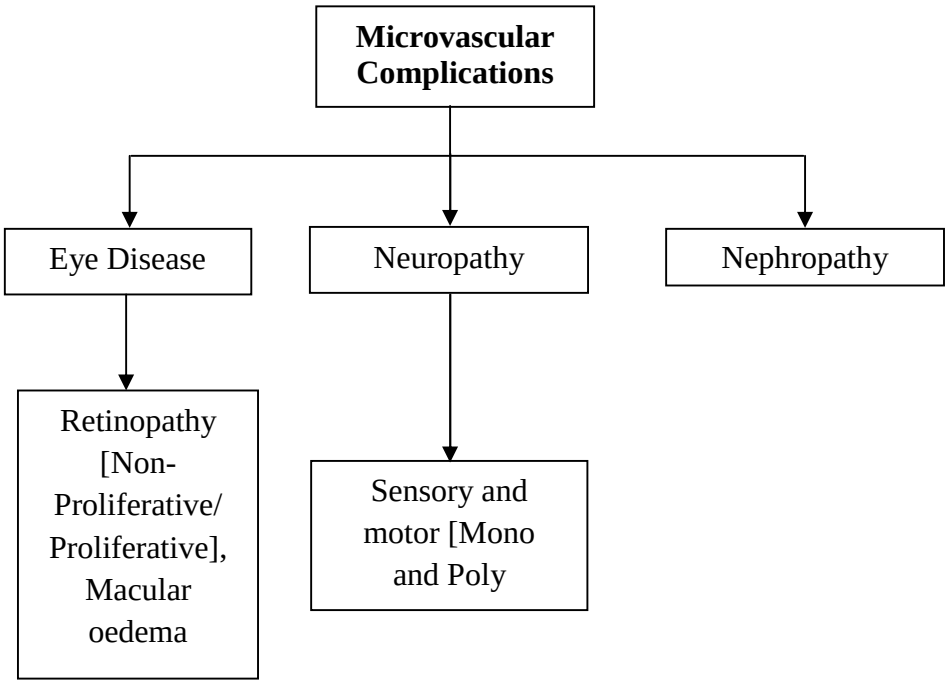
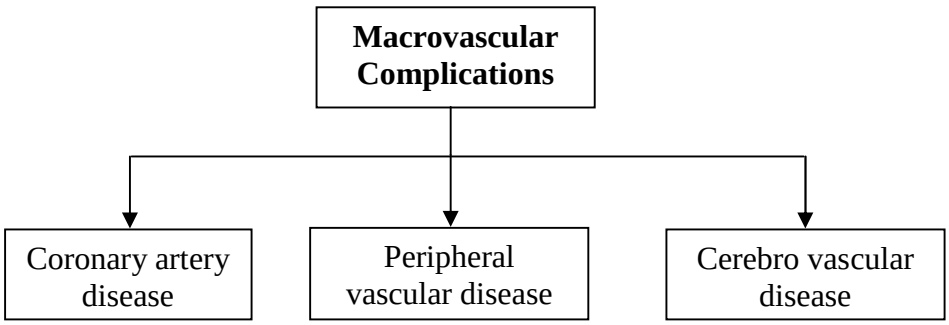


Figure 2: Macrovascular complications in diabetes mellitus



Other complications

- Gastro-intestinal [Gastropareasis, diarrhea]
- Genitor-urinary [Uropathy / Sexual dysfunction]
- Dermatologic
- Infections
- Cataracts and Galucoma

Microvascular complications of both type 1 and type 2 diabetes mellitus results from chronic hyperglycemia.

Lower Extremity Complications and diabetes mellitus[9-15]

- Foot ulcers and infections are a major source of morbidity in individuals with DM.
- The reasons for the increased incidence of these disorders in DM involve the interaction of several pathogenic factors:
    - Neuropathy.
    - Peripheral arterial disease.
    - Abnormal foot biomechanics.

Neuropathy

Neuropathy is present in over 80 percent of patients with foot ulcers.

Peripheral sensory neuropathy

Interferes with normal protective mechanisms and allows the patient to sustain major or repeated minor trauma to the foot, often without knowledge of the injury.

Motor and sensory neuropathy

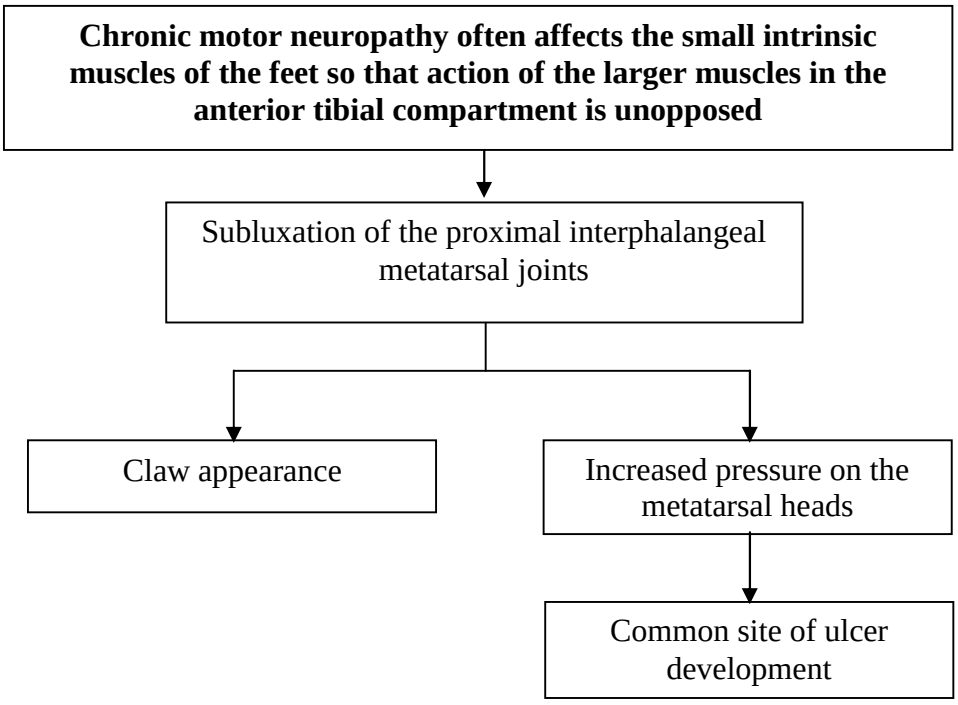
Lead to abnormal foot muscle mechanics and to structural changes in the foot [hammer toe, claw toe deformity, prominent metatarsal heads, Charoct arthropathy].

Charcoat arthropathy (Diabetic neurpathic arthropathy):

It is characterized by collapse of the arch of the mid foot and bony prominences in peculiar places. It is caused by triad of;

a. Small muscle wasting.
b. Decreased sensation.
c. Abnormal distribution of weight when standing.

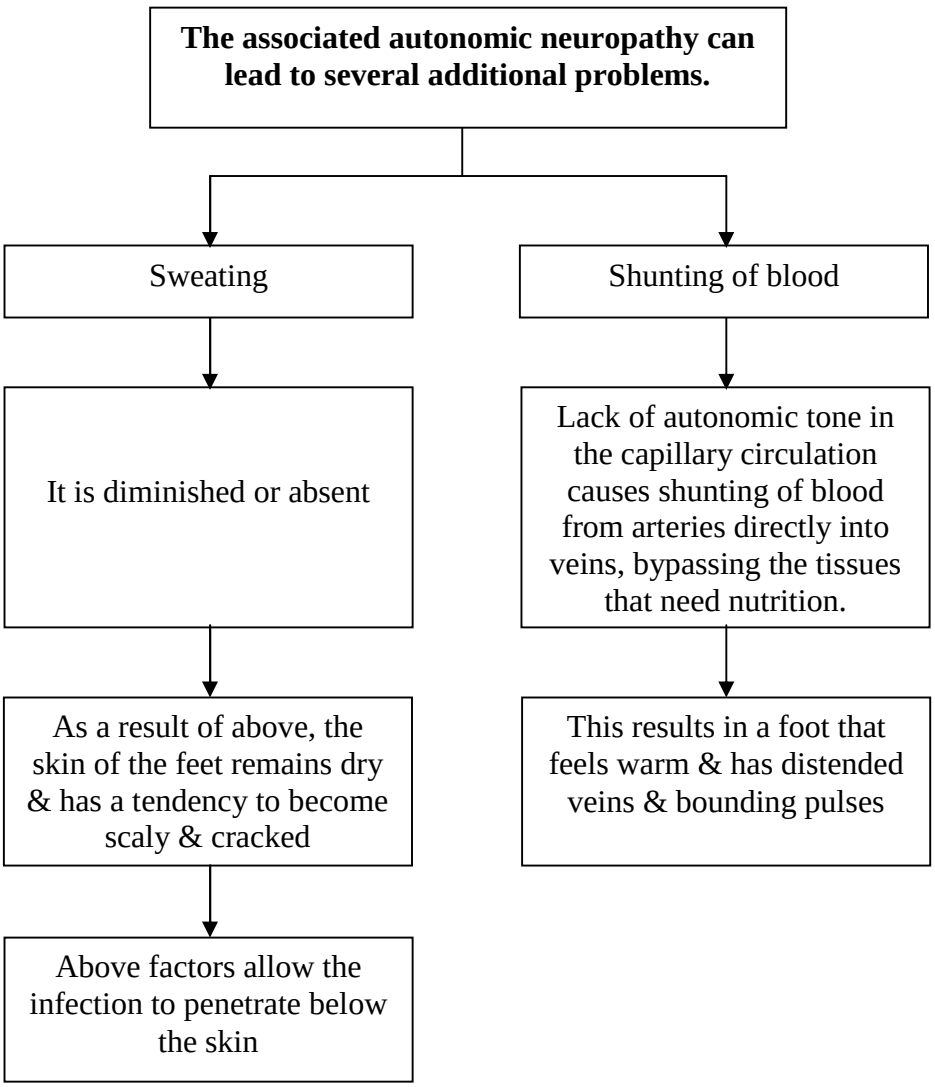
Figure 3: Pathophysiology of Charcoat arthropathy



Autonomic neuropathy

Results in anhidrosis and altered superficial blood flow in the foot, which promotes drying of the skin and fissure formation.

Figure 4: Pathophysiology of Autonomic Neuropathy in Diabetes Mellitus



Peripheral arterial disease and poor wound healing

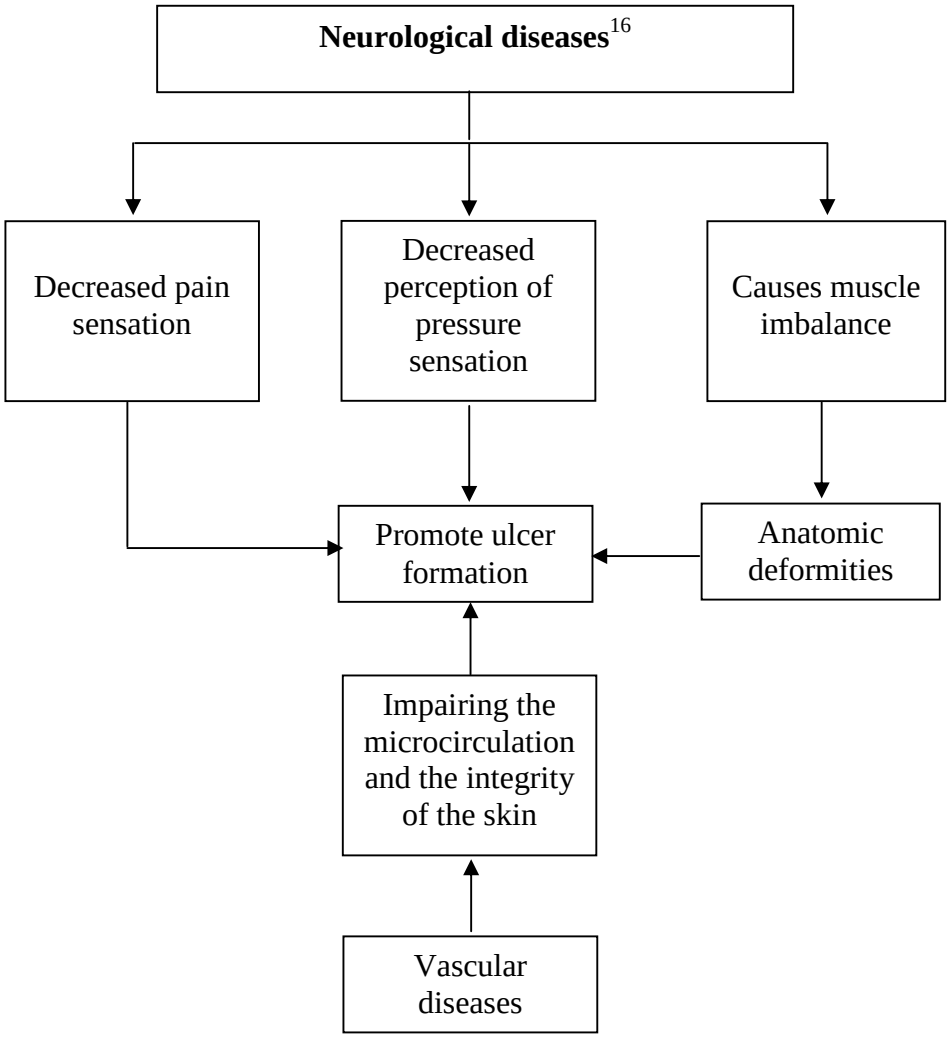
Development of arhtosclerosis is accelerated in DM leading to increased morbidity and mortality. All the large vessels are involved in this process and

clinical manifestations are apparent as a result of atherosclerotic narrowing and thrombosis of coronary, cerebral and leg vessels. It impedes resolution of minor breaks in the skin of the lower limb, allowing them to enlarge and to become infected.

Abnormal foot biomechanics

Disordered proprioception causes abnormal weight bearing while walking and subsequent formation of callus or ulceration.

Figure 5: Pathogenesis of diabetic foot



Changes in foot caused by diabetes

1. Dryness of skin and callus formation due to peripheral neuropathy.
2. High pressure at bony prominences due to
    - Decrease plantar tissue thickness
    - Weak intrinsic muscles of foot
    - Imbalances of flexors and extensors causing clawing of foot
    - Pulling away fat padding from metatarsal heads
3. Limited joint mobility due to
    - Collagen abnormality
    - Thickening of skin tendons and joint capsule
    - Decreased tissue flexibility
    - Increased plantar pressure

Recommendations[17]

- The feet should be examined at least annually in patients with Type-2 diabetes and in those with Type-1 diabetes for more than five years.
- A detailed neurological examination and assessment for Peripheral vascular disease should be performed.
- We recommend using the quantitative foot assessment for neurologic symptoms.
- Patients should be considered at particularly high risk for future plantar ulceration if they have[18]
    - A Previous history of foot ulceration or amputation.

- Neuropathic foot deformities, especially with overlying bunions or calluses.

Prophylactic foot care

It is important that prophylactic advice on foot care be given to any patient whose feet are at high risk. The recommendations for prophylactic foot care are.

Avoid:

- Smoking
- Walking barefoot
- The use of heating pads or hot water bottles
- Stepping into a bath without checking the temperature.

The feet should be:

- Washed daily in tepid water.
- Mild soap should be used and the feet should be dried by gentle patting.
- A moisturizing cream or lotion should then be applied.

Toe Nails:

The toe mails should be:

- Trimmed to the shape of the toe
- Filed to remove sharp edges.

Shoes:

- The patient's shoes should be snug, not tight,

- Patients who have misshapen feet or have had a previous foot ulcer may benefit from the use of special customized shoes.

Socks:

Socks should be

- Cotton
- Loose fitting
- Should be changed every day

Inspection of feet:

- The feet should be inspected daily. Looking between and underneath the toes and at pressure areas for skin breaks, blisters, swelling, or redness. The patient may need to use a mirror or, if vision is impaired, have someone else perform the examination.

Examination of foot by medical person:

- A particularly effective strategy is to make specific recommendations to the patient in the form of a 'contract' and to advise the patient to request that his or her feet be examined at every visit to the doctor or nurse.[19]

Risk factors for foot ulcers or amputation

- Male sex
- Diabetes> 10 years duration
- Peripheral neuropathy [9-15,20,21]
- Abnormal structure of foot [bony abnormalities, callus, thickened nails]

- Peripheral arterial disease
- Smoking
- History of previous ulcer or amputation.[9-15,20,21]
- Poor glycemic control. [9-15,20,21]

ULCER

Definition

An ulcer is defined as break in the continuity of an epithelial surface, characterized by progressive destruction of the surface epithelium.

Acute wound

It is defined as the traumatic loss of normal structure and function to recently uninjured tissue after a noxious insult.[22]

Chronic wound

Wounds more than or equal to four weeks duration, is known as chronic wounds. Disruption in the event of healing regulated by process of cellular, humoral, and molecular events and resulting in a time dependent but predictable and orderly pattern of tissue repair.[23]

Characteristics of chronic wound

Floor is covered with pale granulation tissue, scanty discharge indurated base, edge and surrounding skin.

WOUND HEALING

Historical background

- Wounds were probably earliest problems of human race.
- Early surgeons like Ambrose Pare, John Hunter and Sir James Paget have given some scientific knowledge to their handling of wounds, particularly those resulted from war.[24]
- Halsted was intensely interested in wound healing process.
- In the early 1900's Carrel and his associates made investigation with the scientific approach to wound healing. Later Carrel (1916), Harvey and Howe's (1930), studied incised wounds and contributed to the knowledge of wound healing.[24]

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.

Coagulation

- Helps in preventing blood loss, covering wound surface and holding the wound edges together and thus contributing to the healing process.

- Ross (1980) and Knighton et al (1982) have shown equivocally that fibrin and platelates play an important role in initiating the wound healing.

Granulation phase of wound healing

Granulation tissue[25]

This is a highly vascular tissue, contains largely of

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

Above all are embedded in a matrix consisting.

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 it is pink, soft, granular appearance on the surface of wounds.[25]

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

It is a vital part of proliferative phase of wound healing and repair.[26] Without angiogenesis**,** invasion of the wound bed by macrophages and fibroblasts would cease due to lack of oxygen and nutrients.[26]

In the initial stages, these vessels lack basement membrane and have loose cellular junction and are fragile in nature. Due to this, on slightest touch, the vessels bleed profusely which is a characteristic feature of newly formed capillaries. The leakage facilitates the movement of cells and macromolecules into wound site.[26]

There are four steps in angiogenesis:[25,26]

- *Step-1* Proteolytic degradation of basement membrane of parent vessel is to allow formation of capillary sprout and subsequent cell migration.[26] Angiogenic factors acts on capillary endothelial cells, which releases collagenase. This enzyme degrades the collagen of basement membrane.[25]

- *Step-2* Fragmentation of the collagen of basement membrane, permits the migration of endothelial cells into peri-vascular spaces.[12]

- *Step-3* Endothelial cells migrate into the peri-vascular spaces where they form buds.[26]

- *Step-4* Maturation of endothelial cells and organisation into capillary loops**.**

    - Functional capillary loops: During dermal repair, these buds grow rapidly towards the free surface, where they branch at their tips and 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 and 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 and establish a complete circulation within the wound.

Remodelling of the vasculature

There is constant remodelling of the vasculature, which involves obliteration of many of the capillaries.

As each capillary loop becomes functional, it brings nutrient and oxygen to nearby cells, enabling the fibroblast to secrete materials for the matrix, through which macrophages and other cells can migrate further.

As the scar maturation proceeds, capillaries gradually regress and the red vascular rich wound tissue transforms into a white, relatively avascular poor scar.The above proliferative and migratory processes are repeated sequentially, until wound bed is filled with granulation tissue.

Macrophagia[26]

- It is the point at which protecting and clearing functions of inflammatory response are linked to starting of reparatory process

  Macrophagia is;

  1. Migration of Monocyte [from blood] to tissue injury site.
  2. Conversion of monocyte to Macrophage after migration to tissue injury site.
     - They are key cells in dermal repair
     - Wound macrophages, which appear subsequent to the cells, play pivotal role in healing by liberating various factors.

Functions of macrophages[27]

- 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) stimulate collagen and proteoglycan synthesis.

***Fibroplasia*[27]**

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 platelate-derived cytokines and growth factors, the fibroblast which is normally arrested in G_0 phase, undergoes replication and proliferation.

The primary function of fibroblsts is to synthesize collagen. The rate of collagen 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

Structure[27]

The proline- and glycine- rich collagen molecule is a long, stiff, triple-stranded 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[27]

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[27]

- Connective tissue consists of cellular and non cellular (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[27]

- 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 thickness of 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 ares like back of neck and buttocks.

Timing

Wound contraction starts from about third or fourth day of healing and continues upto 15^{th} or 16^{th} 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 disputable and debatable. 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.
- Unlike healing by fibroplasia where lost parenchymal cells are replaced by non-specific connective tissue, in epithelialisation 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 and
d) Differentiation or restoration of cellular function.

Epithelization which depends on several factors;

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

- Pathological modification of wound

Healing by epithelisation 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.

Types of wound healing[27]

Healing by first intention

The wounds are sealed immediately with simple suturing, skin graft placement, 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.

Heeling by tertiary intention

It is also referred to as delayed primary closure. A contaminated wound in 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 graft placement, or flap design is performed.

MANAGEMENT OF CHRONIC WOUNDS

Wound dressings have been used since antiquity to facilitate the healing process. A material which when applied to the surface of a wound, provides and maintains an environment in which healing can take place at maximum rate; Thomas (1986).[28] The first antiseptic dressing was introduced by Lister in 1867 who soaked the lint and gauze in carbolic acid.[29]

Dressings used in chronic foot 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.[30]

Moist wound environment that these dressings provide are best for wound regeneration and repair and increasing the velocity of healing. Effective wound management aims to strike a balance that is a moist environment to promote healing, but not so wet as to cause maceration and excoriation.

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, helping 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, remove 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.[31]

Basic requirements of the ideal ulcer dressing[2]

- Maintain high humidity between wound and dressing.
- Absorbent, removes excess exudates.
- Non-adherent, allowing easy removal without trauma at dressing change.
- 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 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

- Plate derived growth factors
- Demagraft
- Apligraf
- Granulocyte-colony stimulating factor
- L-lysine

L-LYSINE

Lysine is a basic essential amino acid ,abbreviated as Lys or K with the chemical formula HO2CCH(NH2)(CH2)4NH2.

Its codons are AAA and AAG. Lysine is a base, as are arginine and histidine. The ε-amino group often participates in hydrogen bonding and as a general base in catalysis. Common posttranslational modifications include methylation of the ε-amino group, giving methyl-, dimethyl-, and trimethyllysine. Collagen contains hydroxylysine which is derived from lysine by lysyl hydroxylase

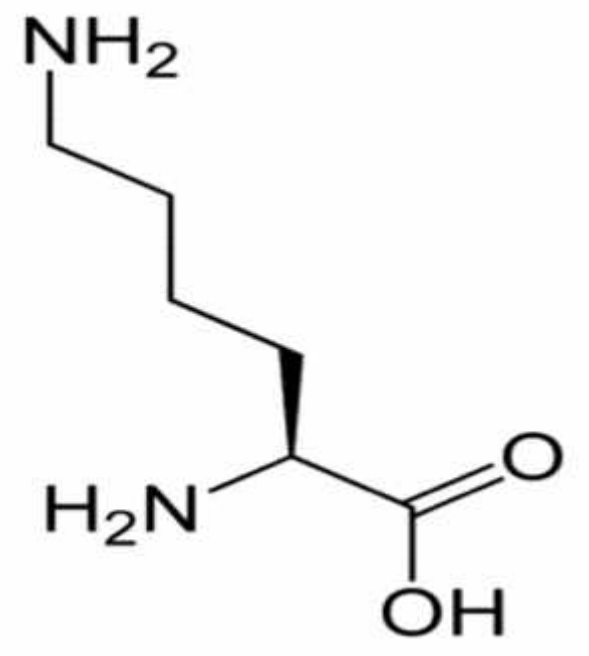
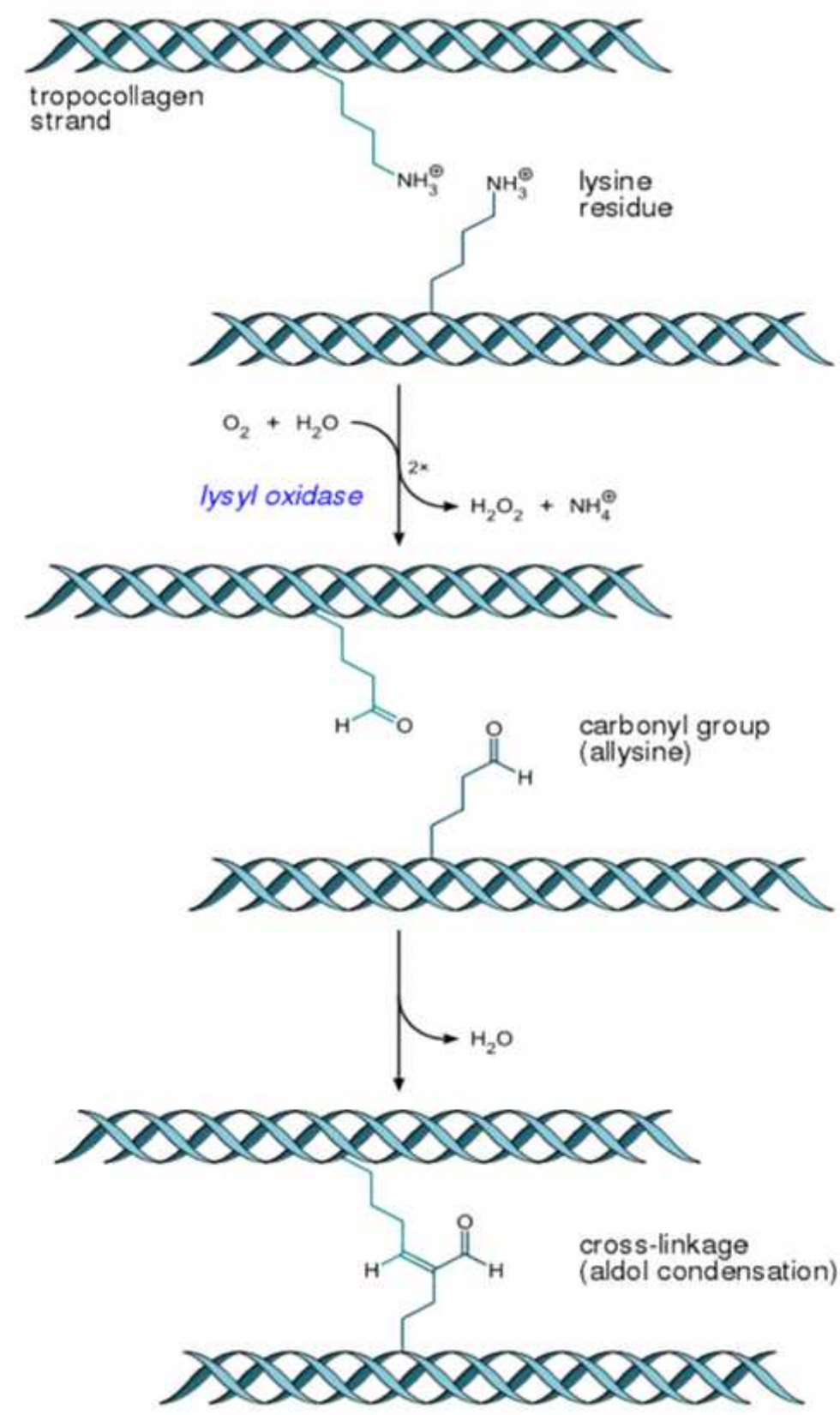


Figure 6: Molecular Structure Of L-Lysine

Physiological aspects of L-lysine

- Synthesis of collagen- L-lysine gives tensile strength by forming cross linkages between peptide chains

Figure 7: Synthesis of Collagen



- It forms a tri-peptide with glysine, histidine wich in turn binds with copper to form a physiological active molecule ie Glysine-L-histidyl-L-lysine- copper (GHK-Cu (2+)).

Actions of GHK-Cu(2+)

- Acts as anti- inflammatory agent that inhibits oxidative damage after tissue injury
- Enhances tissue remodeling
    - Induces blood and tissue macrophages, thus enhances removal of debris a site of wound.
    - Acts on fibroblasts to stimulate m-RNA for synthesis of collagen, elastin, proteoglycans and matrixmetalloproteinases (2 and 9).
    - Potent inducer of angtogenesis.
    - Induces neuronal outgrowth and re-innervation of damaged tissues.
    - Induces re-epthilisation .

Pre- requisits for using L-lysine ointment

The affected should be cleaned with normal saline in case of healthy wound i:e with healthy granulation and active bleeding points.

In chronic foot ulcers were floor is covered with slough , a prior surgical debribrment is to be done to convert it into a healing ulcer and then L-lysine ointment is to be applied.

"COMPARATIVE STUDY BETWEEN L-LYSINE AND REGULAR DRESSING IN CHRONIC FOOT ULCERS"

By

Dr. GURUPADAPPA

Dissertation submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

MASTER OF SURGERY (M.S.)
IN
GENERAL SURGERY

Under the Guidance of

Dr.A. C. PANGI **MS**
PROFESSOR

DEPARTMENT OF SURGERY,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELGAUM – 590 010,
KARNATAKA

MAY - 2011

METHODOLOGY

The present study was conducted in the Department of Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients with infected diabetic foot during the period of January 2009 to December 2009.

Study design

One year randomized controlled trial.

Study period

The present study was conducted during January 2009 to December 2009.

Source of Data

Patients infected with diabetes foot admitted at KLES, Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Sample size

A sample size of 60 cases divided into two groups.

Sampling procedure

As no data was available regarding the bacterial load over the ulcer after the two dressings, the sample size of 30, in each group has been estimated considering last three years hospital statistics of inpatient chronic foot ulcer.

Selection criteria

Inclusion Criteria

- Patients aged between 35 to 65 years.
- Patients with DM (HbA1c < 8.0).
- Patients with infected diabetic foot ulcer with bacterial count of more than 1 X 10^5 CFU per gm wound tissue.
- Ulcer size < 10 X 10 cms.

Exclusion Criteria

- Immuncompromised state
    - Suffering from HIV or TB.
    - On chronic steroid therapy.
    - Severely malnourished.
- Underlying osteomyelitis.
- Vasculopathy.
- Cellulitis.
- Diabetic ketoacidosis.

Procedure

The study was conducted in Department of Surgery at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during one year duration. The study was approved by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belgaum.

After finding the suitability 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 (Annexure–I). Further, descriptive data of the participants like name, age, sex, detailed history, were obtained by interviewing the participants and clinical examination and necessary investigations were recorded on predesigned and pretested proforma (Annexure-II).

In all suitable enrollees, two groups were formed after randomization as group 1 and group 2 . Group 1 with betadine dressing and group 2 with L-lysine dressing . The descriptive data of the participants like name, age, sex, detailed history, were obtained by interviewing the participants and clinical examination and necessary investigations like complete blood count, blood urea and serum creatinine and culture of the ulcer were recorded on predesigned and pretested proforma (Annexure-II).

Initial wound measurement was taken in both the groups before starting their respective treatment that is conventional betadine dressing in control group and L-lysine dressing in study group.

Initial wound area measurement

Ulcer examination was done in all these patients and wound was assessed of its characteristics and photographed. Ulcer was assessed by the investigator at the beginning of the study and at the end of the study (Investigator being the staff and residents in the unit excluding the guide). Wound area measurement was

recorded over the transparency sheet on day one in both study groups and control group.

The dressing was changed every third day; similar four dressings were done to all the patients to both the groups. Final wound area was measured on 14th day over the transparency sheet.

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

Statistical Methods

At the end of the study mean area reduction in the wound of the both groups was determined before the first and after the third dressing. Data was compared by using unpaired‘t’ test and a ‘p’ value of < 0.05 was considered significant.

RESULTS

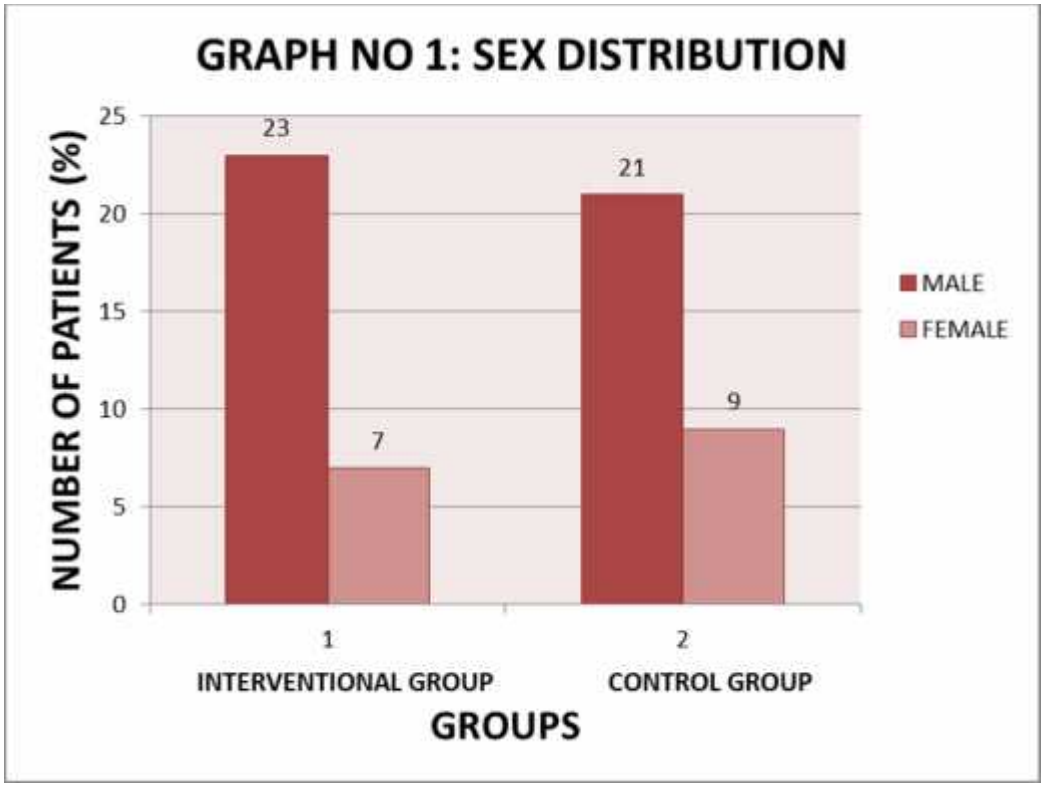
The present study was conducted in KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum and the findings are tabulated as below.

During the study year from January 2009 to December 2009, 60 patients with chronic foot ulcers of the lower limb were randomized into study (L-lysine dressings) and control (betadine) group. These groups were studied for the effect of conventional betadine dressings versus l-lysine dressings on wound reduction.

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

Table 1: Sex distribution

Groups	Interventional Group		Control group	
	Number	Percentage	Number	Percentage
Males	23	76.67%	21	70.00%
Females	7	23.33%	9	30.00%
Total	30	100.00%	30	100.00%



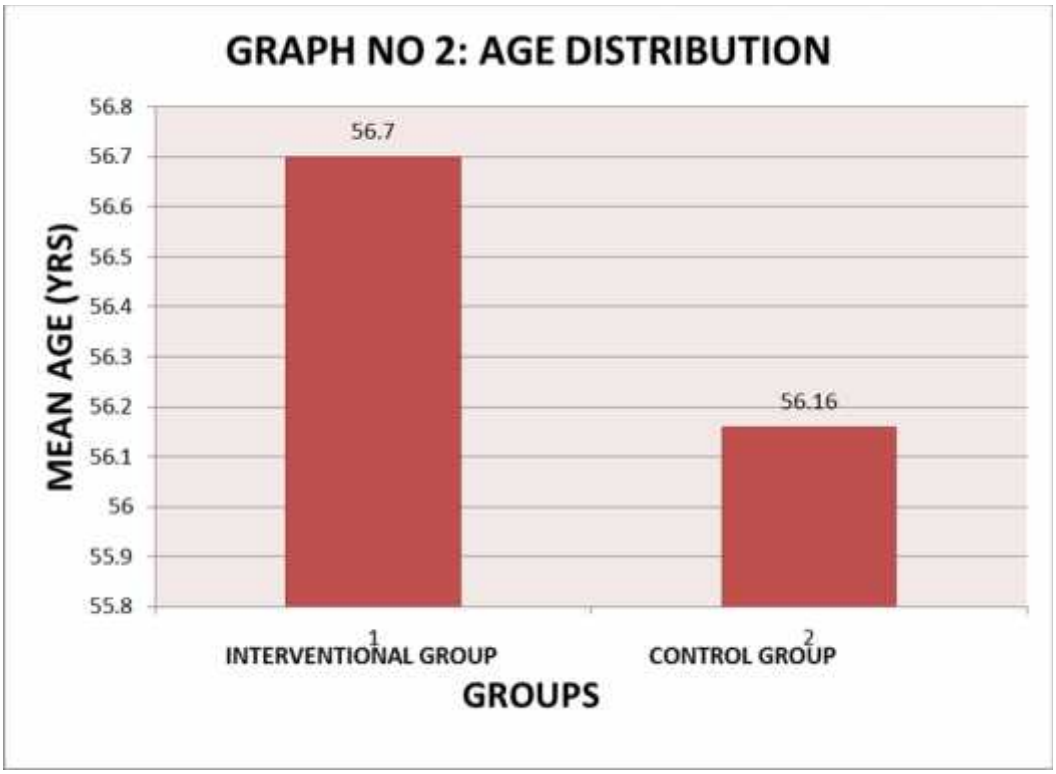
In the interventional group, total number of males and females were 23 (76.67%) and 7 (23.33%) respectively. The male:female ratio was 3.2:1. In control group, total number of male and females were 21 (60%) and 9 (30%) respectively. The male:female ratio was 3:1. Statistically in this study, there was

no significant difference in sex distribution between interventional and control group.

Table 2: Mean age of the patients

Groups	Mean age (Years)	
	Mean	**S.D.**
Interventional	56.7	6.83
Control	56.16	8.11

p= 0.870

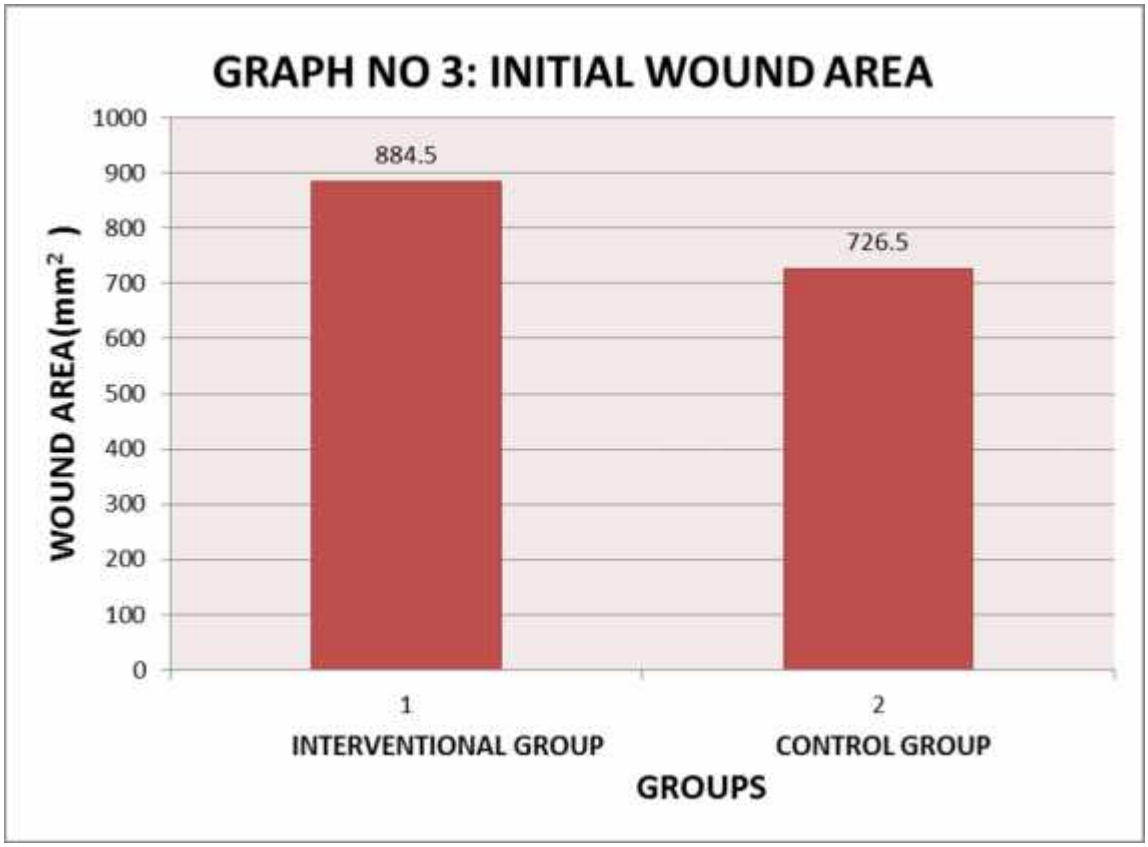


In this study, the mean age in interventional group and control group were 54.30±6.83 and 50.90±8.11 respectively. Statistically there was no significant difference in mean age between interventional and control groups.

Table 3: Initial wound area

Groups	Initial wound area (mm^2)	
	Mean	**S.D.**
Interventional	884.5	428.65
Control	726.5	361.44

p= 0.389

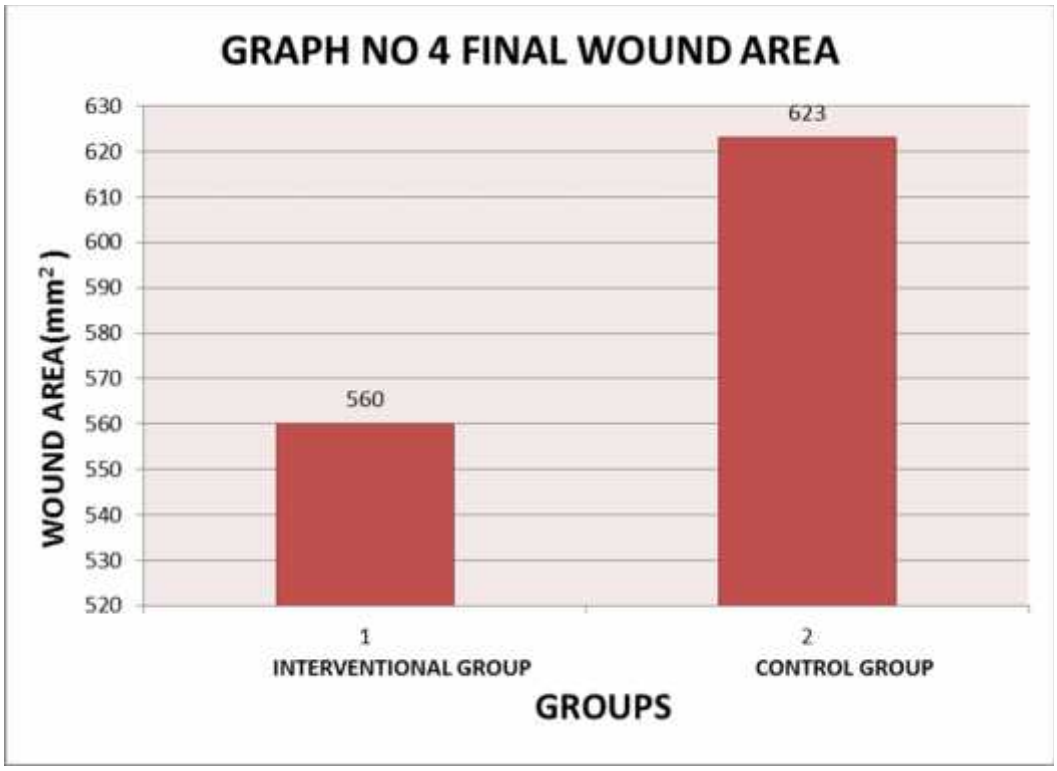


The mean area at the beginning of the study was 884.5±428.65 mm^2 in the HCD and 726.5±361.44 mm^2 in the normal saline group. There was no significant difference in the mean area between the two groups (p=0.389).

Table 4: Final wound area

Groups	Final wound area (mm^2)	
	Mean	**S.D.**
Interventional	560	261.67
Control	623	309.14

P=0.187

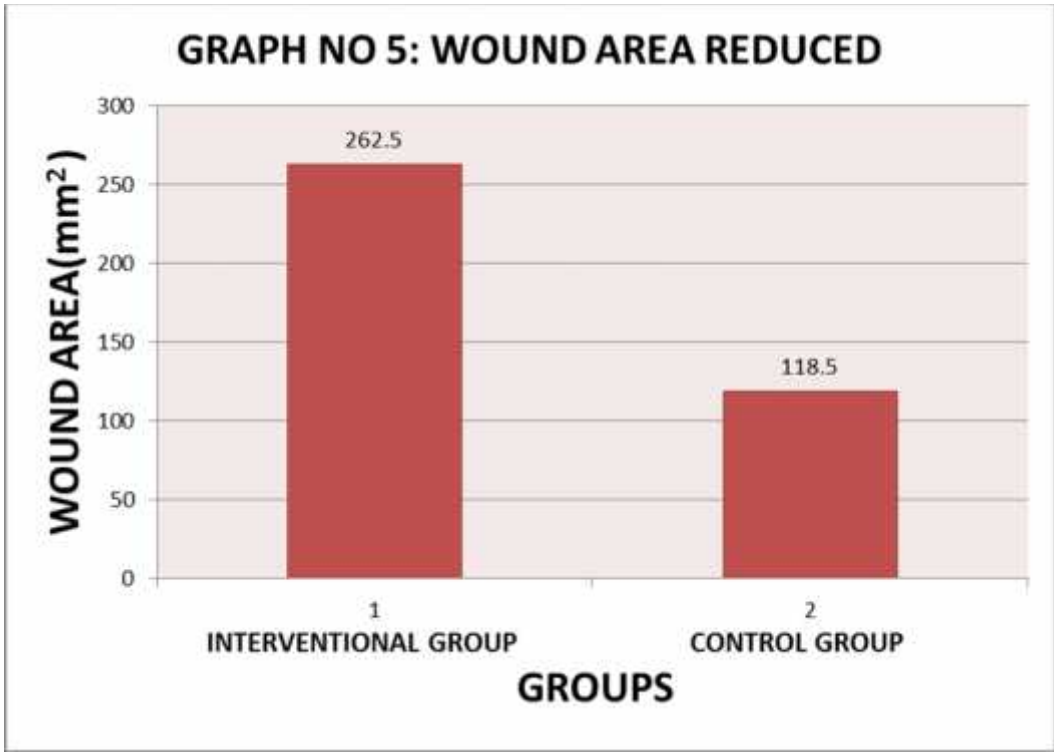


At the end of the study the mean area were 560 ± 261.67 mm^2 in the group treated with HCD dressings and 623±309.14 mm^2 in the group treated with normal saline dressings.

Table 5: Wound area reduction

Groups	Reduction wound area (mm^2)	
	Mean	**S.D.**
Interventional	262.5	168.92
Control	118.5	58.53

$p<0.001$

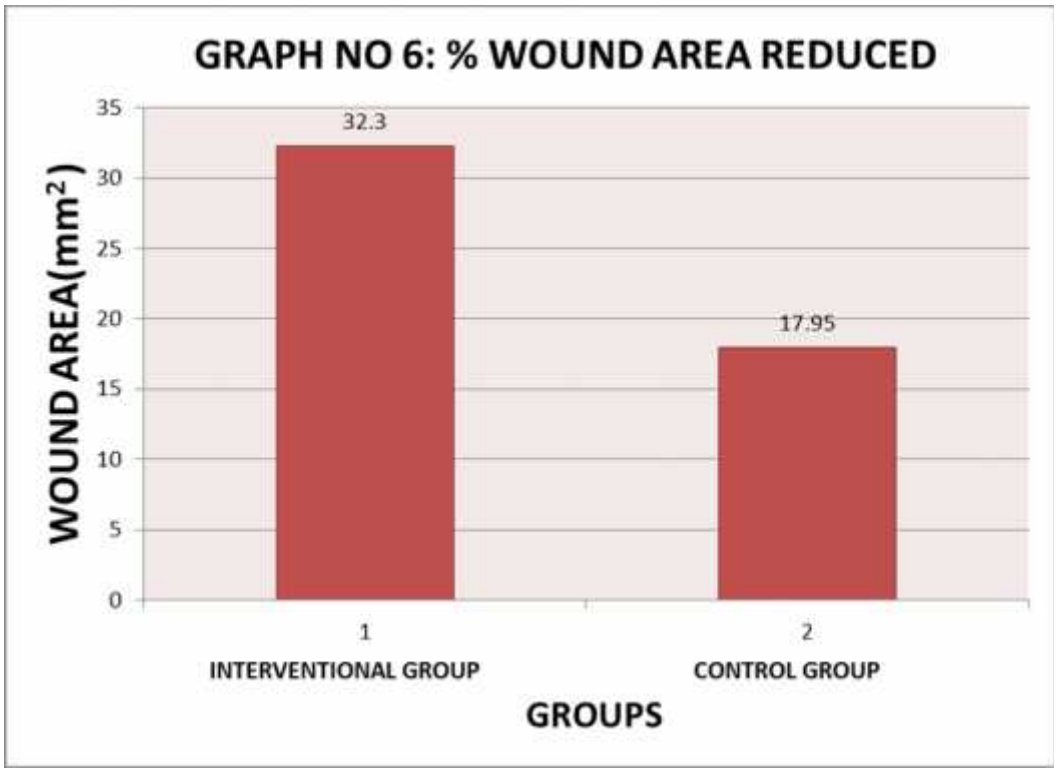


The study shows that the final wound reduction achieved between the two groups were 262.5±168.92 mm^2 in patients treated with L-lysine dressing and 118±58.53 mm^2 in patients treated with betadine dressing, which is statistically significant ($p<0.001$).

Table 6: Percentage of reduction in wound area

Groups	Percentage of reduction	
	Mean	**S.D.**
Interventional	32.30	7.00
Controls	17.95	3.77

p<0.001



The percentage of area reduction were 32.30±7.004 in patients treated with L-lysine dressing and 17.95±3.77 in patients treated with betadine dressing, which is statistically significant (p<0.001).

Introduction

Objectives

Review of Literature

Methodology

Results

Discussion

Conclusion

Summary

Bibliography

Annexure-I

Annexure-II

Annexure-III

Annexure-IV

DISCUSSION

It is every surgeon's desire that after dressing the wound, it should heal without any complications. Successful wound dressing should keep the wound moist and be devoid of any adverse reactions such as infection, maceration and allergy. Chronic foot ulcers are stuck in inflammation phase and shows cessation of epidermal growth or migration over the wound surface.

L-lysine dressing has shown great promise as a modulator for healing of chronic wounds (Venous ulcers, pressure sores, superficial burn wounds, small donor site wounds and minor abrasions).

It is suggested that L-lysine dressings may be used on chronic foot ulcers, although there is much debate on this issue. L-lysine is a recent drug released into the market with no phase 4 trials.

In the present study, an attempt has been made to establish better healing rates with use of L-lysine dressing in chronic foot ulcer of lower limb. In this study the base line characteristics such as age, sex and location of the ulcer were similar in the patients who received L-lysine dressing in the study group and in patients who received normal saline dressing in the control group.

This study is a comparative study which aimed to document the safety and performance of L-lysine dressing in the treatment of established foot ulcers. Participants had an ulcer bigger than one cm^2 and less than eight cm^2 in any direction. The treatment period was 15 days. The mean wound area reduced from 884.5mm^2 to 560mm^2. Relative wound area reduced from 100% at baseline to

40% at 15th day. This study demonstrates that treatment of chronic foot ulcer with L-lysine dressing results in considerable wound area reduction and prevents any deterioration in maceration.

The percentage of area reduction was 32.30±7.004 in patients treated with L-lysine dressing and 17.95±3.77 in patients treated with betadine dressings.

However, the final area of the ulcer (in mm^2) was significantly reduced in patients with L-lysine dressing group as compared to the patients in betadine group at the end of the study. The percentage reduction in the area of the ulcer was more in the L-lysine dressing group as compared to the Normal Saline group and this difference was statistically significant.

We have applied the following formula to calculate % reduction in area of wound after two weeks period in both cases and controls.

$$\% \text{ Reduction of wound after two weeks} = \frac{\text{Initial area} - \text{Final area}}{\text{Initial area}} \times 100$$

Overall this study shows that L-lysine dressing is a safe and effective in treating chronic foot ulcers of lower limb. This study was conducted only for 15 days and complete epithelialization and wound reduction was not awaited.

Limitations of our study

- Not a blinded study
- Follow up is short to derive conclusion on long term healing of the ulcers.
- The cost involved was not analyzed in this study.

Scope for further study

There is further scope of study among infective diabetic wound with respect to anti-infective properties of L-lysine dressing.

CONCLUSION

With the use of L-lysine dressing in comparison with the conventional betadine dressing for the treatment of chronic foot ulcers of lower limb, the following conclusions were derived:

- L-lysine dressing showed faster and better healing rates among the study group.
- Area reduction and percentage reduction was better in L-lysine dressing group.
- There was no adverse effect or reactions seen when L-lysine dressing was applied over the ulcer.
- Appearance of granulation tissue was earlier as compared to regular dressing.
- Patient compliance was better due to early grafting and recovery.

SUMMARY

The present study was conducted in KLES' Prabhakar Kore Hospital and Medical Research Centre, Belgaum on 60 patients with chronic diabetic ulcers of lower limb.

The objective of the present study was to assess the L-lysine dressing in comparison to conventional betadine dressing in achieving mean percentage reduction in patients with chronic ulcer of lower extremities more than four weeks duration using transparency sheet.

The two groups were randomized into study (L-lysine) and conventional (betadine) group. One group received treatment in the form of L-lysine dressing and other received conventional betadine dressing.

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

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

BIBLIOGRAPHY

1. Most RS, Sinnock P, Epidemiology of lower extremity amputation in diabetic individuals. Diabetes Care 1983; 2: 87-91.

2. Mann CV, Russel RCG, Williams NS. Bailey and Love's Short Practice of Surgery. 24th Ed. New York: Hodder Arnold Publication; 1995.

3. Hutchinson JJ, Lawrence JC. Wound infection under occlusive dressings. J Hospital Infection 1991; 17: 83-94.

4. Lawrence JC. What materials for dressing? Injury 1982; 13: 500-12.

5. Verghese ML, Balin AK, Carta DM, Caldwel D. Local environment of chronic wounds under synthetic dressings. Arch Dermatol 1986; 122: 52-7.

6. Gill D. The use of hydrocolloids in the treatment of diabetic foot. J Wound Care 1999; 8 (4): 204-6.

7. Foster AVM, Spencer S, Edmonds ME. Deterioration of diabetic foot lesions under hydrocolloid dressings'. Pract Diabetes Int 1997; 14(2): 62-4.

8. Seheiz M, Rauterberg A, Weib J. Allergic contact dermatitis from hydrocolloid dressings'. Contact Dermatitis 1996; 34(2): 146.

9. American diabetes association: Clinical practice recommendations 2002. Diabetes Care 2004; 27: 51.

10. Clement S. Management of diabetes & hyperglycemia in hospitals. Diabetes Care 2004; 27: 553.

11. Kirpichnikov D. Metformin: An update. Ann Intern Med 2002; 137: 25.

12. Knowler WC for the Diabetes prevention program research group. Reduction in the incidence of type-2 diabetes with lifestyle intervention of metformin. N Engl J Med 2002; 346: 393.

13. Saltiel AR, Kahn CR: Insulin signaling & the regulation of glucose & lipid metabolism, Nature 2001; 414: 799.

14. The writing team for the diabetes control & complications trial/ Epidemiology of the diabetes interventions & complications research group: Effect of intensive therapy on the microvascular complications of type-I Diabetes mellitus. JAMA 2002; 287: 2563.

15. UK Prospective diabetes study group: Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment & risk of complications in patients with type-2 diabetes (UKPDS 33). Lancet 1998; 352: 1998.

16. Pecoraro, RE, Reiber, GE, Burgess, EM. Pathways to diabetic limb amputation: Basis for prevention. Diabetes Care 1990; 13: 513.

17. Pham, H, Armstrong, DG, Harvey, C, Harkless LB, Giurini JM, Veves A. et al. Screening techniques to identify people at high risk for diabetic foot ulceration: a prospective multicenter trial. Diabetes Care 2000; 23: 606.

18. Liniger, C, Albeanu, A, Bloise, D. The tuning fork revisited. Diabet Med 1990; 7: 859.

19. Litzelman DK, Slemenda CW, Langefeld CD, Hays LM, Welch MA, Bild DE, et al. Reduction of lower extremity clinical abnormalities in patients with non-insulin – dependent diabetes mellitus: A randomized controlled trial. Ann Intern Med 1993; 119: 36.

20. Litzelman, DK, Marriott, DJ, Vinicor, F. Independent physiological predictors of foot lesions in patients with NIDDM. Diabetes Care 1997; 20: 1273.

21. Lehto, ST, Ronnemaa, T, Pyorala , K, Laksoo M. Risk factors predicting lower extremity amputation in patients with NIDDM. Diabetes Care 1996; 19: 607.

22. Leaper DJ, Harding KG. Wounds: biology and management. Oxford: Oxford University Press; 1998.

23. David L. Steed MD. Wound healing trajectories. Surg Clinics North Am 1997; 77(3): 773-7.

24. Yardley PA. A brief history of wound healing. Yardley, PA: Oxford Clinical Communications; 1998.

25. Kumar V, Cotran RS, Robbins SL. Robbins Basic Pathology. 7th Ed. Philadephia: W.B. Saunders Company; 2003.

26. Halloran CM. Pathophysiology of wound healing. Surgery 2002; 2: 1-5.

27. Townsend CM, Beauchamp RD, Evers BM, Mattox KL. Sabiston Textbook of Surgery; The biologic basis of modern surgical practice. 18th Ed. Philadelphia: Saunders; 2008.

28. Morris PJ, Wood WC. Oxford textbook of surgery. 2nd Ed. Oxford University Press; 2000.

29. Gerald TL, WT Lawrence. Wound dressings. Surg Clin North Am 2003; 30: 617.

30. Lim JK, Saliba L, Smith MJ, Tavish, Raine C. Normal saline dressing: Is it really Normal Br. J Plast Surg 2000; 53(1): 42-5.

31. Pendsey S. Diabetic Foot: A Clinical Atlas. New Delhi: Jaypee Brothers; 2004.

32. Thomas,S. Hydrocollod. J Wound Care 1992; 1(2): 27-30.

33. Cherry GW, Ryan TJ. Enhanced wound angiogenesis with a new hydrocolloid dressing. In: An environment for healing - the role of occlusion. International Congress and Symposium Series No. 88 (ed T J Ryan) p 62-8 Royal Society of Medicine, London 1985

34. Gilchrist B, Reed C. The bacteriology of chronic venous leg ulcers treated with occlusive hydrocolloid dressings' British Journal of Dermatology 1989; 121: 337-344.

35. Winter GD. Formation of the scab and rate of epithelisation of superficial wounds in the skin of the young domestic pig. Nature 1962; 193: 293-4.

36. Thomas S, Loveless P. A comparative study of the properties of twelve hydrocolloid dressings. World Wide Wounds (serial online) 1997. Available at http://www.worldwidewounds.com /1997/ThomasHydronet /hydronet.html. Accessed February 4, 2002.

37. Heenan A. Frequently asked questions: hydrocolloid dressings. World Wide Wounds. www.worldwidewounds.com/1998/april/Hydrocolloid-FAQ/hydrocolloid-question.html (Last accessed 2nd February 2007).

38. Punder R (2001) Hydrocolloid dressings in wound management JCN. www.jcn.co.uk/journal.asp?MonthNum=04&YearNum=2001&Type= backissue&ArticleID=343(Last accessed 7 th February 2007)

39. Lohmann M, Thomsen JK, Edmonds ME, Harding KG, Apelqvist J, Gottrup F. Safety and performance of hydrocolloid dressing for the treatment of diabetic ulcer. J Wound Care 2004; 13 (3): 118-20.

40. Apelqvist J, Larson J, Stenstrom A. Tropical treatment of necrotic foot ulcers in diabetic patients: A comparative trial of zinc oxide tape and hydrocolloid dressing. Br J Dermatol 1990; 123(6): 787-92.

41. Simeon ET AL. expression and activation of matrix metalloproteinases in wounds : Modulation by the Tripeptide- copper Complex Glysyl-L-HComplexities in Leg Ulcer Management

42. Complexities in Leg Ulcer Management Module Codes: Level 3 - 3NMH0019 or Level M - MNMH0003\

43. Franqois XM, Loren PS, Maryvonne LM, Philippe GS, Jean CM and Jacques PB; Stimulation of collagen synthesis in fibroblast cultures by the tripeptide-copper complex glycyl-L-histidyl-L-lysine-Cu2+:Volume 238, number 2, 343-346 FEB 06385 October 1988

44. Michael SO, O'Reilly MW, Dmitri WO, William GS, Stevenson SS, Judah FD, and Marsha A. Moses Regulation of Angiostatin Production by Matrix Metalloproteinase-2 in a Model of Concomitant Resistance: The Journal Of Biological Chemistry Vol. 274, No. 41, Issue of October 8, pp. 29568–29571, 1999

45. Ed Rook A, Wilkinson DS, Ebling FJB, Champion RH, Burton JL Textbook of Dermatology, . Fourth edition

46. Gadi B Copper's Role In Wound Healing: Review Of Literature , may2004

ANNEXURE I

CONSENT FORM

Introduction

Mr./Miss./Mrs. _____

You are invited to participate in our research study that is **"COMPARATIVE STUDY BETWEEN L-LYSINE AND REGULAR DRESSING IN CHRONIC FOOT ULCERS OF PATIENTS ADMITTED TO KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM".**

Since you are suffering from foot ulcer, which is not healing since a long time and will be requiring treatment for the same, you are eligible to be part of the study and hence asked to participate. This research is about the beneficial effects of L-lysine on your foot ulcer and the result of this research will help in better treatment of similar participants in the future.

If you agree to be part of this research, we would ask you some relevant clinical history. You are free to not to answer to which ever questions you think are not relevant. A clinical examination will be done. On the first day empirical antibiotics will be given and regular betadine/L-lysine dressing will be done.

There are chances you may have a speedy and better recovery with this therapy and it will also help in the treatment if participants with similar complaints in the future. Your decision of whether or not to participate in this

study will not affect the quality of treatment you receive. Further you may withdraw from the study at any time.

All the new information collected about you during this course of study will be kept confidential to the extent permitted by law. Any information which identifies you personally, will not be released without your written consent.

This study does not have any damaging aspect and there are no chances of injury during the course the course the study, but if injured the investigator is not responsible. There will be no extra cost incurred by you. However you will have to pay for the routine investigations, which are part of existing management protocol for the treatment of chronic ulcer. There is no commitment for any reimbursement or any compensation for the participant. The participation in this study is entirely voluntary and you may withdraw from the study at any time. At any time during or after the study, for any information you may contact the researcher.

Dr . Gurupadappa
Room no 76, Chanakya Hostel
J N Medical College,
Nehru nagar, Belgaum,
Karnataka
Phone no – 9844324220

OR

Chairman

Institutional ethical committee

Dr V. D. Patil .

Phone: 0831- 2471350

Signature of the participant or legally authorized representative

Subject Name : _____.

Signature or the Left Thumb Print of Subject : _____

Witness Name: _____ Signature : _____

Investigators Name: _____ Signature : _____

Date : _____ Place : _____

ANNEXURE II

PROFOMA

I) <u>PATIENT IDENTIFICATION DATA</u> :

NAME IP/OPD NO.

AGE DOA :

SEX DOD:

OCCUPATION

ADDRESS

II) <u>CHIEF COMPLAINTS</u> :

<u>MEDICAL HISTORY</u> :

Peripheral Neuropathy : ( )

Nephropathy ( )

Retinopathy ( )

PVD ( )

CVD ( )

<u>DIABETIC STATUS</u> :

TYPE :

DURATION :

MEDICATION : Oral Hypoglycemics Insulin

( ) ( )

COMPLICATION	Neuropathy	(	)
	Vasculopathy	(	)

ULCER DETAIL :

1.Mode of Onset	Traumatic	(	)
	Spontaneous	(	)
	Pressure	(	)
	Others	(	)

2. Duration

3. Progress

WOUND OBSERVATION:

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

NERUROLOGICAL EXAMINATION

VASCULAR EXAMINATION	Left	Right
Popliteal a.	( )	( )
Ant . Tibial	( )	( )
Post Tibial	( )	( )
Dorsalis Pedis	( )	( )

ANY FOOT DEFORMITY PRESENT

Toe deformity

Bunion

Charcots foot

Foot drop

IF AMPUTATION HAS BEEN DONE

SPECIFY : Date

: Side

: Level

: Cause for amputation

FOOT WEAR ASSESSMENT

Does patient wear appropriate shoes.

Does patient require contact cast immobilization.

INVESTIGATION

CBC

FBS 1st _____ Date :_____ Time :_____

2nd (24 hr apart) _____ Date :_____ Time : _____

Sr. Creatinine

UKB

Urine : Routine

Microscopy

X-ray Foot

AP View

Lat. View

Wound C/s

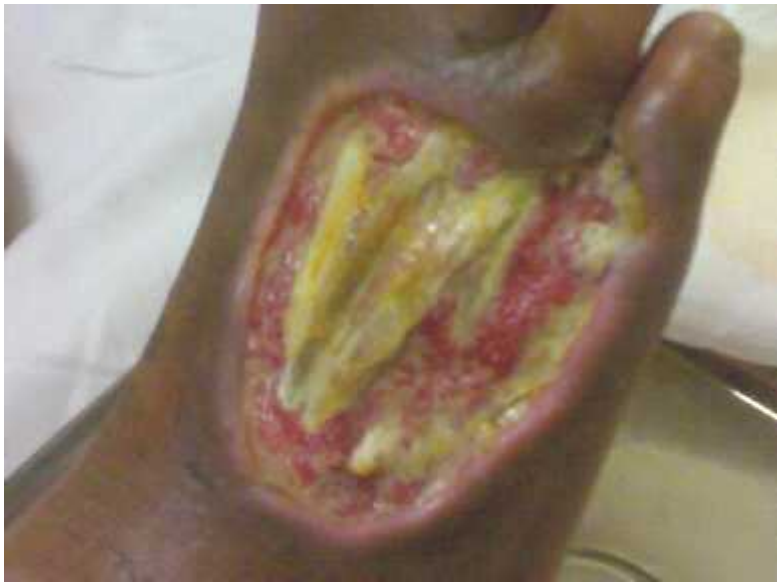
WOUND AREA MEASUREMENT ON D_1 in cm^2

Type of Dressing – Betadine ( )

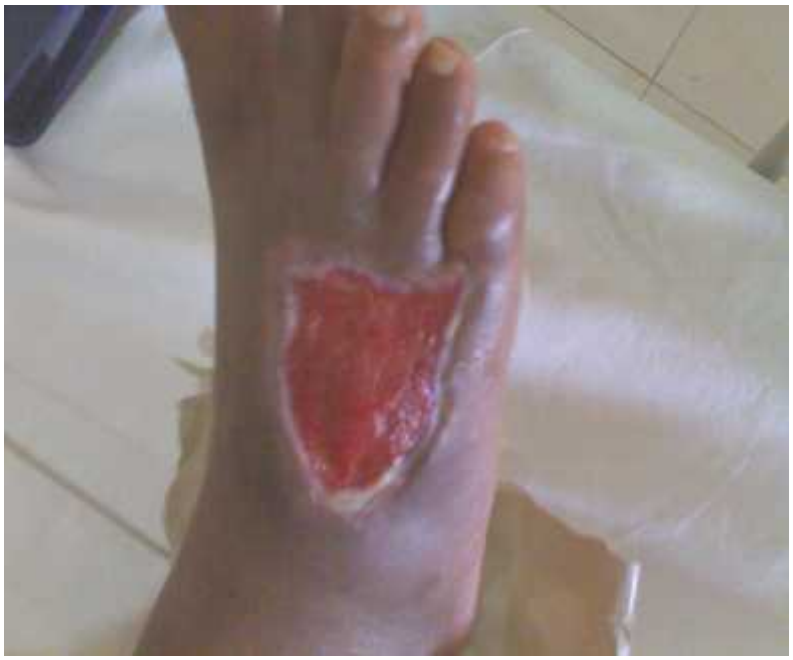
L-lysine ( )

ANNEXURE III

PHOTOGRAPHS



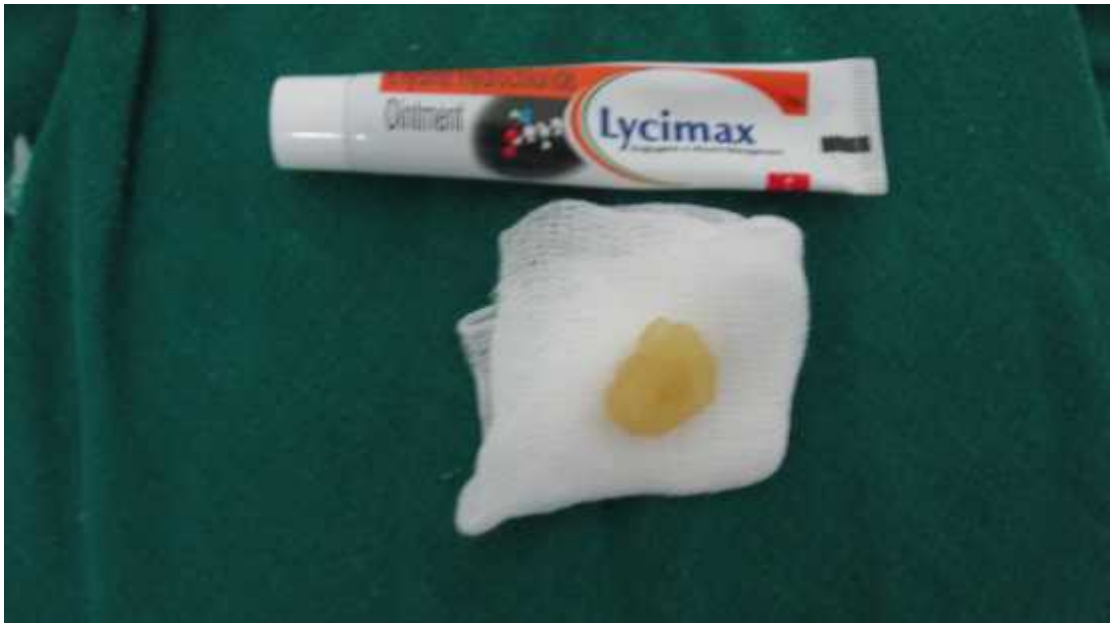
Photographs 1: Ulcer1 size on day one



Photographs 2: Ulcer1 size on day 14 using L-lysine dressing

Photographs 3: Ulcer2 size on day one

Photographs 4: Ulcer2 size on day 14 using L-lysine dressing



Photographs 5: L-lysine hydrochloride

Photographs 6: Betadine and Hydrogenperoxide

ANNEXURE IV

S. No	I.P No	GROUP	AGE /	SITE	SITE	ANTI DM RX	X-Ray	C/S	INTITIAL AREA	FINAL AREA	AREA REDUCED	% AREA REDUCTION	SEX	NAME
1	326170	CONTROL	56	T	SRF	I	N	NOGC	390	318	72	18.46	F	RACHAWWA
2	336604	CONTROL	70	T	DRF	O	N	NOGC	425	343	82	19.29	M	DIAS
3	327925	CONTROL	55	T	DLF	O	N	NOGC	370	303	67	18.01	M	SAKHARAM
4	350001	CONTROL	75	S	SLF	I	N	NOGC	357	293	64	17.9	M	GOPAL
5	330862	CONTROL	68	S	HRF	I	N	NOGC	430	348	82	19.06	F	GANGAWWA
6	325191	CONTROL	36	T	SRL	0	N	NOGC	913	717	196	21.46	M	DAYANAND
7	328993	CONTROL	62	S	DLF	I	N	NOGC	826	698	128	15.49	M	BASANGOUDA
8	298179	CONTROL	40	T	SLF	O	N	NOGC	569	493	76	13.35	M	VIRUPATHI
9	311067	CONTROL	26	S	LMLL	I	N	NOGC	716	624	92	12.84	M	SANTOSH
10	312012	CONTROL	34	T	LMRL	I	N	NOGC	1310	1161	149	11.37	M	RAJU
11	338500	CONTROL	54	S	SLL	O	N	NOGC	1396	1206	190	13.61	M	GUNDHAR
12	320927	CONTROL	60	T	DRF	I	N	NOGC	976	813	163	16.71	M	IRAYYA
13	304084	CONTROL	61	S	SLF	I	N	NOGC	980	782	198	20.02	F	PARVATHI
14	326155	CONTROL	65	T	DLF	O	N	NOGC	802	613	189	23.57	M	MUTAPPA
15	342986	CONTROL	60	T	SRL	O	N	NOGC	842	704	138	16.38	F	SUNDRAWWA
16	340853	CONTROL	68	T	SLL	I	N	NOGC	929	747	182	19.59	M	CHANAPPA
17	329307	CONTROL	28	S	SRL	O	N	NOGC	1026	896	130	12.67	M	KRISHNA
18	328334	CONTROL	75	T	LMLL	I	N	NOGC	891	723	168	18.85	F	NAGAWWA
19	353072	CONTROL	65	S	LMRL	O	N	NOGC	1492	1322	170	11.39	F	SAVAKKA
20	330340	CONTROL	41	T	HRL	O	N	NOGC	737	665	72	9.7	F	ZARINA
21	329023	CONTROL	60	T	SRL	I	N	NOGC	1588	1290	238	18.76	M	PARASHURAM
22	341341	CONTROL	68	T	SLF	I	N	NOGC	1435	1153	282	19.65	M	SHIVANGOUDA
23	350431	CONTROL	56	S	GLL	O	N	NOGC	712	622	90	12.64	M	MAHADEVAPPA
24	345052	CONTROL	46	S	DRL	I	N	NOGC	506	397	109	21.54	F	SUREKA
25	331915	CONTROL	57	T	DLF	O	N	NOGC	299	236	63	21.07	M	GOPAL
26	347460	CONTROL	90	S	DLF	I	N	NOGC	700	601	99	14.14	M	MALAPPA
27	304076	CONTROL	50	S	MMRL	I	N	NOGC	711	572	139	19.54	M	SURESH
28	306510	CONTROL	45	T	ATRL	O	N	NOGC	576	493	83	14.40	F	LAXMI
29	305124	CONTROL	58	S	SLF	O	N	NOGC	513	408	105	20.46	M	RAJU
30	311828	CONTROL	56	T	DRF	I	N	NOGC	440	393	47	10.68	M	GURUSIDAPPA

MASTER CHART – CONTROL GROUP

CASE GROUP

S. No	I.P No	GROUP	AGE /SEX	SITE	SITE	ANTI DM RX	X-Ray	C/S	INTITIAL AREA	FINAL AREA	AREA REDUCED	% AREA REDUCTION	SEX	NAME
1	324110	CASE	43	T	DRF	I	N	NOGC	499	352	147	29.45	M	SIDAPPA
2	327893	CASE	39	T	GLL	I	N	NOGC	411	273	138	33.57	M	SHANTARAM
3	327189	CASE	70	S	DLF	O	N	NOGC	1527	428	49	9.29	M	YAMANAPPA
4	328976	CASE	60	T	GRL	I	N	NOGC	335	223	112	33.43	M	CHANDRASHEKAR
5	301795	CASE	60	T	DRF	O	N	NOGC	441	302	139	31.51	M	SHASHIKANTHA
6	298412	CASE	30	S	DLF	O	N	NOGC	1260	843	417	33.09	M	ASHOK
7	325420	CASE	71	T	DRF	I	N	NOGC	957	598	356	37.13	M	THIMMANAGOUDA
8	325985	CASE	60	S	DLF	I	N	NOGC	876	553	323	36.89	F	GANGAWWA
9	316089	CASE	55	S	GLL	I	N	NOGC	925	652	273	29.51	M	MALLAPPA
10	329403	CASE	58	T	DRF	O	N	NOGC	1363	817	546	40.05	M	VAMAN
11	337766	CASE	42	S	DRF	I	N	NOGC	1417	938	479	33.80	M	MALLAPPA
12	306344	CASE	45	T	DLF	O	N	NOGC	1601	897	704	43.97	F	BHAGIRATHI
13	319889	CASE	50	T	GRL	O	N	NOGC	1253	738	515	41.10	M	SHIVALINGAPPA
14	316191	CASE	60	S	GLL	I	N	NOGC	1351	849	502	37.15	M	SANGAPPA
15	321932	CASE	72	S	DLF	I	N	NOGC	983	644	339	34.48	M	MARUTHI
16	344495	CASE	68	S	DRF	I	N	NOGC	819	567	252	30.76	F	SHANTAWWA
17	353072	CASE	65	T	GLL	O	N	NOGC	1147	774	373	32.51	F	SAVAKKA
18	333884	CASE	63	T	DLF	O	N	NOGC	665	439	226	33.98	M	MAHADEV
19	353930	CASE	54	T	DRF	I	N	NOGC	1231	902	329	26.72	F	SAVITHRI
20	353038	CASE	62	T	DRF	I	N	NOGC	689	473	216	31.34	M	VASANTH
21	347846	CASE	65	S	GRL	O	N	NOGC	1658	1191	467	28.16	M	SIDAPPA
22	342536	CASE	65	S	GLL	O	N	NOGC	893	617	276	30.90	M	VENDAMIA
23	335476	CASE	46	S	DLF	I	N	NOGC	335	232	103	30.74	F	CHANDAWWA
24	331031	CASE	44	T	DRF	O	N	NOGC	1235	793	442	35.78	M	MARUTHI
25	322866	CASE	55	S	SRL	I	N	NOGC	479	319	148	32.10	M	SHANKAR
26	333792	CASE	65	T	DLF	O	N	NOGC	461	319	148	32.10	M	KALLAPA
27	325080	CASE	51	S	GLL	I	N	NOGC	551	348	203	36.84	F	SURIA
28	325045	CASE	65	T	DRF	O	N	NOGC	439	387	52	11.84	M	VITTAL
29	324695	CASE	60	T	GRL	I	N	NOGC	381	262	119	31.23	M	BASAVARAJ
30	338765	CASE	58	S	GLL	O	N	NOGC	339	243	96	28.31	M	SIDRAM

KEY TO MASTER CHART

SRF	: Sole of right foot
SLF	: Sole of left foot
DRF	: Dorsum of right foot
DLF	: Dorsum of left foot
GRL	: Gaiter area right limb
GLL	: Gaiter area left Limb
SRL	: Shin right limb
SLL	: Shin left limb
LMLL	: Lateral malleolus left limb
LMRL	: Lateral malleolus right limb
HRF	: Heel right foot
MMRL	: Medial malleolous right limb
ATRL	: achiles tendon right limb
I	: Insulin
O	: Oral hypoglycemic
FBS	: Fasting blood sugar
C/S	: Culture sensitivity
NOGC	: No organism grown