COMPARATIVE STUDY OF NEGATIVE PRESSURE WOUND THERAPY USING VACUUM ASSISTED CLOSURE WITH GAUZE DRESSING IN THE TREATMENT OF DIABETIC FOOT ULCERS

By

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ABSTRACT

BACKGROUND : Diabetes is one of the most common chronic diseases. The prevalence of Diabetes in the world is 285 million and in India is 50.8 million. Negative pressure wound therapy using vacuum assisted closure, promotes wound healing through creating a moist wound environment, preparing the wound bed for closure, reducing edema and promoting formation and perfusion of granulation tissue.

AIMS AND OBJECTIVES OF THE STUDY: To evaluate safety and clinical efficacy of NPWT using vacuum assisted closure with moist gauze dressing in the treatment of diabetic foot ulcers.

MATERIALS AND METHODS : The cases presented in this study are those patients admitted as in patient basis in the BLDE UNIVERSITYs Shri. B.M.Patil Medical College Hospital and research Centre, Bijapur with diabetic foot in the time period between October 2011 to May 2013. A prospective interventional study was done with 30 randomly selected patients assigned to the topical negative pressure dressing group and 30 patients to the moist gauze dressing group. All patients were studied and clinical findings were recorded, necessary investigations ordered and appropriate treatment given. All cases were followed up to discharge and subsequently for a follow up on 1st week. All the data were analyzed using the Z Test, Student's T test and the results were tabulated. A "p" value of <0.05 was considered statistically significant.

RESULTS : Majority of the patients in the study were male .Majority of the patients in both group presented with ulcer. All the patients in the study were suffering from diabetes of varying duration, with some on regular treatment and the others on

irregular treatment. The efficacy of the dressings was compared as the percent of ulcer surface area covered by granulation tissue such that complete skin closure could be achieved. Granulation tissue fill up of wound was better in TNPD group compared to MGD group at 7,14,21,28 days of follow up. 55.0 % of patients in TNPD had 65-95% 0f granulation fill up with in 21 days compared to only 28.6% in MGD group (pvalve = < 0.001). Mean days to complete recovery was 49 days in TNPD group and 56.6 days in MGD group.

CONCLUSION : The application of Topical Negative Pressure increased the rate of granulation tissue formation and had better graft uptake than the patients who underwent a conventional dressing for diabetic foot ulcers. The patients in the study group had better patient compliance and had a shorter duration of healing of wound when compared to the control group.

KEY WORDS :

NPWT - Negative pressure wound therapy

TNPD - Topical negative pressure dressing

MGD - Moist gauze dressing

LIST OF ABBREVIATIONS

NPWT	:	Negative Pressure Wound Therapy
AMWT	:	Advanced Moist Wound Therapy
VAC	:	Vacuum assisted dressing
TNPD	:	Topical negative pressure dressing
MGD	:	Moist gauze dressing
TNP	:	Topical negative pressure
PDGF	:	Platlet derived growth factor
TGF	:	Transforming growth factor
VEGF	:	Vascular endothelial growth factor
TNF	:	Tumor necrosis factor
PMNs	:	Polymorphonuclear cells
IL	:	Interlukin
WBC	:	White blood cell
TCCs	:	Total contact casts
DFIs	:	Diabetic foot infections
HBOT	:	Hyperbaric oxygen therapy
PRP	:	Platlet rich plasma

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INTRODUCTION

Diabetes is one of the most common chronic diseases affecting the Indian and world population. The prevalence of Diabetes in the world is 285 million and the prevalence of Diabetes in India is 50.8 million in 2010 and is supposed to increase to 87.0 millions by 2030. The disabling complication with the disease is foot ulcer development which leads to non healing chronic wounds that are difficult to treat. [1] The life time risk for a person with Diabetes developing foot ulcers is 15%. [2]

Diabetic foot ulcers and infections are complicated and difficult to treat. They occur in individuals with a systemic illness that has compromising effects on multiple areas of the body, including the nervous, vascular, musculoskeletal and immunologic systems. Each of these compromised systems play a variably weighted role in the occurrence, chronic nature, and eventual recovery or loss of limb in this patient population. [3]

Diabetic foot is a umbrella term for foot problems in patients with diabetes mellitus. Foot disorders such as ulceration, infection and gangrene are the most common complex and costly sequelae of diabetes mellitus .[4]

Diabetic foot ulcers are typically chronic wounds which are difficult to heal. This is due to a range of pathogenic abnormalities in diabetics, which include ischaemia, intrinsic defects in angiogenesis and impaired immunity against infection. The sequence of minor trauma, cutaneous ulceration and failure to achieve wound healing potentially lead to amputations of the lower extremity. Diabetic foot ulcers are found to precede 84% of all non-traumatic amputations in diabetics. An amputation incurres heavy financial cost, adversely affects a person's quality of life and causes a higher risk of mortality. [5]

Various Diabetic foot ulcer treatment have been reported in literature, including Advanced moist wound therapy (AMWT), Bio-Engineered tissue, Skin substitutes, Growth factors, Electric stimulation and Negative pressure wound therapy (NPWT) using vacuum assisted closure.[3] Negative pressure wound therapy using vacuum assisted closure is a non invasive system that creates a localized controlled sub atmospheric negative pressure environment within the wound which promotes wound healing by delayed primary or secondary intention through creating a moist wound environment, preparing the wound bed for closure, reducing edema and promoting formation and perfusion of granulation tissue. With negative pressure wound therapy there is five fold increase in blood flow to cutaneous tissues .[6]

Hence this study was undertaken to compare the outcomes of usage of negative pressure therapy using vacuum assisted closure with the moist gauze dressings in the treatment of diabetic foot ulcers.

OBJECTIVES OF THE STUDY

The purpose of this study was to evaluate safety and clinical efficacy of negative pressure wound therapy (NPWT) using vacuum assisted closure with moist gauze dressing in the treatment of diabetic foot ulcers.

REVIEW OF LITERATURE

Diabetic foot ulcers are a significant health problem affecting more than 1 million patients of diabetes mellitus at some point in their life time. The principles of good wound care includes use of proper footwear, non weight bearing limb support, use of appropriate antibiotics, debridement, aggressive revascularization, control of serum glucose levels and careful monitoring of the ulcer .[7]

The prevalence of diabetes in adults is about 2.4% in rural and 4.0-11.6% in urban dwellers. High frequencies of impaired glucose tolerance shown by the above studies ranging from 3.6-9.1% indicate the potential for further rise in the prevalence of diabetes mellitus in the coming years .[8]

It is believed that every 30 seconds a lower limb is lost somewhere in the world as a consequence of diabetes .[9]

Laing, Patrick (1998): Neuropathy and ischemia, two common complications of diabetes mellitus, are the primary underlying risk factors for the development of foot ulcers and their complications. [10]

Phillips. Pat, Evans. Angela, Popplewell, Phil (2000): Treatment of diabetic foot ulcers involves a number of sequential steps. First, prepare the ulcer for healing, ensuring 5 that the blood supply is adequate, there is no infection, pressure is removed, and the ulcer is clean. The dressing can then facilitate the healing process .[11]

Robson MC.Wound infection. (1997) : Infection in a wound, like infection elsewhere in the body is a manifestation of a disturbed host-bacteria equilibrium in

favor of the bacteria to be able to prevent and manage wound infections requires an understanding of how each prophylactic or therapeutic maneuver works to maintain or reestablish the bacteria-host balance. Only when this equilibrium is in balance can the normal process of wound healing proceed to give a satisfactory healing trajectory .[12]

Van Gils, Carl, et al (1999): The effect of foot ulceration on amputation is not disputed. Failure of normal wound healing after cutaneous ulceration is reported to be the best predictor of amputation risk. Amputation is estimated to occur in 6 – 43 % of diabetic out patients with foot ulceration, depending on ulcer severity. [13]

Blume PA et al conducted a study at 37 Diabetic foot Wound clinics and hospital in Canada and U.S from August 2002 to 2005, on 342 patients in which a complete ulcer closure was seen with negative pressure wound therapy in 43.2% than with moist wound therapy which was 28.9%, after 112 days of treatment .[14]

Townsend CM et al in the Sabiston Textbook of surgery 18th edition volume 1, he mentions a study in which the authors treated 300 wounds with negative pressure therapy, 296 wounds responded favorably with increased rate of granulation tissue. [6]

Nather A et al conducted a study at National University Hospital in department of orthopedic surgery, Singapore from Jan 2008 to Feb 2009, they assessed the effectiveness of vacuum assisted therapy in diabetic foot ulcer among 11 patients, 9 wounds were closed by split skin graft and 2 by secondary closure within 23.3 days .[15]

In a study conducted by Sepuleda G et al at Servicio de Cirugia Vascular, Hospital Dipreca, Sautiago de Chile, Chile. They compared negative pressure wound therapy with standard wound dressing in treatment of diabetic foot ulcer and found

out of 24 patients the average time to reach 90% of granulation was lower in group treated with negative pressure wound therapy. [16]

Nain PS et al conducted a study at Dayanand Medical College and Hospital Ludhiana, they assessed the effectiveness of negative pressure wound therapy in healing of diabetic wound ulcer on 30 patients and divided them into groups A and B. Group A with NPWT showed faster healing by the end of the 4th week. This showed that negative pressure wound therapy is better than saline moist dressings. [17]

Mechanism and clinical applications of Topical Negative Pressure: The use of subatmoshperic pressure dressings has been shown to be effective to accelerate wound healing. The optimal sub atmospheric pressure for wound healing appears to be around 125mmHg utilizing an alternating pressure cycle of 5 minutes of suction followed by 2 minutes off suction. The sub atmospheric pressure optimizes blood flow, decreases local tissue edema and removes excessive fluid from the wound bed[18]

Negative pressure wound therapy seems to be safe and effective treatment for complex diabetic foot wounds and could lead to a higher proportion of healed wounds, faster healing rates and potentially fewer re-amputations than standard care.[19]

HISTORICAL ASPECTS OF WOUND HEALING

Back to about 2000 B.C., when the Sumerians employed two modes of treatment: A spiritual method consisting of incantations and a physical method of applying poultice-like materials to the wound.

The Egyptians were the first to differentiate between infected and diseased wounds compared to noninfected wounds. In 1650 B.C. Edwin Smith Surgical Papyrus, describes at least 48 different types of wounds. A later document (Ebers Papyrus, 1550 B.C.) relates the use of concoctions containing honey (antibacterial properties), lint (absorbent properties), and grease (barrier) for treating wounds. These same properties are still considered essential in contemporary daily wound management.

Galen of Pergamum (120–201 A.D), emphasized the importance of maintaining a moist environment to ensure adequate healing . It took almost 19 centuries for this important concept to be proven scientifically, when it was shown that the epithelialization rate increases by 50% in a moist wound environment when compared to a dry wound environment.

Robert Wood Johnson, impressed on antiseptic dressing in the form of cotton gauze impregnated with iodoform. Since then, several other materials have been used to impregnate cotton gauze to achieve antisepsis.

Polymeric dressings were developed in the 1960s and 1970s. These polymeric dressings can be custom made to specific parameters, such as permeability to gases (occlusive vs. semiocclusive), varying degrees of absorbency, and different physical forms. Due to the ability to customize, the available range of materials that aid in

wound care has grown exponentially to include an ever-expanding variety. Currently, the practice of wound healing encompasses manipulation and/or use of, among others, inflammatory cytokines, growth factors and bioengineered tissue. [20]

ANATOMY

Foot

The foot is the region of the lower limb distal to the ankle joint. It is subdivided into the ankle, the metatarsus and the digits.

There are five digits consisting of the medially positioned great toe (digit I) and four more laterally placed digits, ending laterally with the little toe (digit V).

The foot has a superior surface (**dorsum of foot**) and an inferior surface (**sole)**

Bones

There are three groups of bones in the foot

- Seven tarsal bones, which form the skeletal framework for the ankle;
- Metatarsals (I to V), which are the bones of the metatarsus;
- Phalanges, which are the bones of the toes-each toe has three phalanges, except for the great toe, which has two

Joints

- Ankle joint
- Intertarsal joints
- Subtalar joint (Talo calcaneo navicular joint)
- Calcaneocuboid joint
- Tarsometatarsal joints
- Metatarsophalangeal joints
- Interphalangeal joints

Arches Of The Foot

The bones of the foot do not lie in a horizontal plane. Instead, they form longitudinal and transverse arches relative to the ground , which absorb and distribute downward forces from the body during standing and moving on different surfaces.

Plantar Aponeurosis

The plantar aponeurosis is a thickening of deep fascia in the sole of the foot .It is firmly anchored to the medial process of the calcaneal tuberosity and extends forward as a thick band of longitudinally arranged connective tissue fibers. The fibers diverge as they pass anteriorly and form digital bands, which enter the toes and connect with bones, ligaments and dermis of the skin.

Arteries

Blood supply to the foot is by branches of the posterior tibial and dorsalis pedis arteries.

Veins

There are interconnected networks of deep and superficial veins in the foot. The deep veins follow the arteries. Superficial veins drain into a dorsal venous arch on the dorsal surface of the foot over the metatarsals.

Nerves

The foot is supplied by the tibial, deep fibular, superficial fibular, sural and saphenous nerves. [21]

MUSCLES OF FOOT. [22]

TABLE.NO 1: Muscles of foot

Muscle on dorsal aspect of foot

Muscle	Origin	Insertion	Innervation	Function
Extensor digitorum brevis	Superolateral surface of the calcaneus first muscle layer in the sole of the foot	Base of proximal phalanx of great toe and lateral sides of the tendons of extensor digitorum longus of toes II to IV	Deep fibular nerve [S1,S2]	Extension of metatarsophalangeal joint of great toe and flexion of toes II to IV
LAYERS OF THE SOLE				
FIRST LAYER				
Abductor hallucis	Medial process of calcaneal tuberosity	Medial side of base of proximal phalanx of great toe	Medial plantar nerve from the tibial nerve [S2,**S3**]	Abducts and flexes great toe at metatarsophalangeal joint
Flexor digitorum brevis	Medial process of calcaneal tuberosity and plantar aponeurosis	Sides of plantar surface of middle phalanges of lateral four toes	Medial plantar nerve from the tibial nerve [S2,**S3**]	Flexes lateral four toes at proximal interphalangeal joint
Abductor digiti minimi	Lateral and medial processes of calcaneal tuberosity, and band of connective tissue connecting calcaneus with base of metatarsal V Second layer of muscles in the sole of the foot	Lateral side of base of proximal phalanx of little toe	Lateral plantar nerve from tibial nerve [S2,**S3**	Abducts little toe at the metatarsophalangeal joint
SECOND LAYER				
Quadratus plantae	Medial surface of calcaneus and lateral process of calcaneal tuberosity	Lateral side of tendon of flexor digitorum longus in proximal sole of the foot	Lateral plantar nerve from tibial nerve [S1 to S3]	Assists flexor digitorum longus tendon in flexing toes II to V

Lumbricals	First lumbrical-medial side of tendon of flexor digitorum longus associated with toe II; second, third, and fourth lumbricals-adjacent surfaces of adjacent tendons of flexor digitorum longus third layer of muscles in the sole of the foot	Medial free margins of extensor hoods of toes II to V	First lumbrical-medial plantar nerve from the tibial nerve; second, third, and fourth lumbricals-lateral plantar nerve from the tibial nerve [S2,S3	Flexion of metatarsophalangeal joint and extension of interphalangeal joints
THIRD LAYER				
Flexor hallucis brevis	Plantar surface of cuboid and lateral cuneiform; tendon of tibialis posterior	Lateral and medial sides of base of proximal phalanx of the great toe	Lateral plantar nerve from tibial nerve [**S1**,S2]	Flexes metatar-sophalangeal joint of the great toe
Adductor hallucis	Transverse head-ligaments associated with metatarsophalangeal joints of lateral three toes; oblique head-bases of metatarsals II to IV and from sheath covering fibularis longus	Lateral side of base of proximal phalanx of great toe	Lateral plantar nerve from tibial nerve [S2,S3]	Adducts great toe at metatarsopha-langeal joint
Flexor digiti minimi brevis	Base of metatarsal V and related sheath of fibularis longus tendon Fourth layer of muscles in the sole of the foot	Lateral side of base of proximal phalanx of little toe	Lateral plantar nerve from tibial nerve [S2,S3]	Flexes little toe at metatarsophalangeal joint
FOURTH LAYER				
Dorsal interossei	Sides of adjacent metatarsals	Dorsal expansions and bases of proximal phalanges of toes II to IV	Lateral plantar nerve from tibial nerve; first and second dorsal interossei also innervated by deep fibular nerve [S2,S3]	Abduction of toes II to IV at metatarsophalangeal joints; resist extension of metatarsophalangeal joints and flexion of interphalangeal joints
Plantar interossei	Medial sides of metatarsals of toes III toV	Dorsal expansions and bases of proximal phalanges of toes III to V	Lateral plantar nerve from tibial nerve [S2,S3]	Adduction of toes III to V at metatarsophalangeal joints; resist extension of the metatarsophalangeal joints and flexion of the interphalangeal joints

WOUND HEALING

Phases Of Wound Healing

As noted by John Hunter (1728–1793), a keen observer of biologic phenomena, ".. the injury alone has in all cases a tendency to produce the disposition and the means of a cure." Normal wound healing follows a predictable pattern that can be divided into overlapping phases defined by characteristic cellular populations and biochemical activities: (a) hemostasis and inflammation (b) proliferation and (c) maturation and remodeling.

All wounds need to progress through this series of cellular and biochemical events that characterize the phases of healing to successfully re-establish tissue integrity.

A. Hemostasis And Inflammation

Hemostasis precedes and initiates inflammation, with the ensuing release of chemotactic factors from the wound site. Wounding by definition disrupts tissue integrity, leading to division of blood vessels and direct exposure of extracellular matrix to platelets. Exposure of subendothelial collagen to platelets results in platelet aggregation, degranulation, and activation of the coagulation cascade. Platelet - granules release a number of wound-active substances such as platelet-derived growth factor (PDGF), transforming growth factor beta (TGF), platelet-activating factor, fibronectin, and serotonin. In addition to achieving hemostasis, the fibrin clot serves as scaffolding for the migration into the wound of inflammatory cells such as polymorphonuclear leukocytes (PMNs or neutrophils) and monocytes.

Cellular infiltration after injury follows a characteristic predetermined sequence. PMNs are the first infiltrating cells to enter the wound site, peaking at 24 to 48 hours. Increased vascular permeability, local prostaglandin release, and the presence of chemotactic substances, such as complement factors, interleukin-1 (IL-1), tumor necrosis factor alpha (TNF-α), TGF, platelet factor 4 or bacterial products all stimulate neutrophil migration.

The postulated primary role of neutrophils is phagocytosis of bacteria and tissue debris. PMNs are also a major source of cytokines early during inflammation, especially TNF-α, which may have a significant influence on subsequent angiogenesis and collagen synthesis.

PMNs also release proteases such as collagenases, which participate in matrix and ground substance degradation in the early phase of wound healing. Other than their role in limiting infections, these cells do not appear to play a role in collagen deposition or acquisition of mechanical wound strength. On the contrary, neutrophil factors have been implicated in delaying the epithelial closure of wounds.

The second population of inflammatory cells that invade the wound consists of macrophages, which are recognized as being essential to successful healing. Derived from circulating monocytes, macrophages achieve significant numbers in the wound by 48 to 96 hours postinjury and remain present until wound healing is complete.

Macrophages, like neutrophils, participate in wound débridement via phagocytosis and contribute to microbial stasis via oxygen radical and nitric oxide synthesis. The macrophage's most pivotal function is activation and recruitment of other cells via mediators such as cytokines and growth factors, as well as directly by

cell–cell interaction and intercellular adhesion molecules. By releasing such mediators as TGF, vascular endothelial growth factor (VEGF), insulin-like growth factor, epithelial growth factor, and lactate, macrophages regulate cell proliferation, matrix synthesis, and angiogenesis. Macrophages also play a significant role in regulating angiogenesis and matrix deposition and remodeling T lymphocytes comprise another population of inflammatory/immune cells that routinely invade the wound. Less numerous than macrophages, T-lymphocyte numbers peak at about 1 week postinjury and truly bridge the transition from the inflammatory to the proliferative phase of healing. Although known to be essential to wound healing, the lymphocytes' role in wound healing is not fully defined. A significant body of data supports the hypothesis that T lymphocytes play an active role in the modulation of the wound environment. Depletion of most wound T lymphocytes decreases wound strength and collagen content, whereas selective depletion of the $CD8^+$ suppressor subset of T lymphocytes enhances wound healing. However, depletion of the $CD4^+$ helper subset has no effect. Lymphocytes also exert a downregulating effect on fibroblast collagen synthesis by cell-associated interferon , TNF-α and IL-1. This effect is lost if the cells are physically separated, suggesting that extracellular matrix synthesis is regulated not only via soluble factors but also by direct cell–cell contact between lymphocytes and fibroblasts.

B. Proliferation

The proliferative phase is the second phase of wound healing and roughly spans days 4 through 12 . It is during this phase that tissue continuity is re-established. Fibroblasts and endothelial cells are the last cell populations to infiltrate the healing wound, and the strongest chemotactic factor for fibroblasts is PDGF. Upon entering

the wound environment, recruited fibroblasts first need to proliferate and then become activated, to carry out their primary function of matrix synthesis remodeling. This activation is mediated mainly by the cytokines and growth factor s released from wound macrophages.

Fibroblasts isolated from wounds synthesize more collagen than nonwound fibroblasts, they proliferate less and they actively carry out matrix contraction. Although it is clear that the cytokine-rich wound environment plays a significant role in this phenotypic alteration and activation, the exact mediators are only partially characterized. Additionally, lactate, which accumulates in significant amounts in the wound environment over time (~10 mmol), is a potent regulator of collagen synthesis through a mechanism involving adenosine 5'-diphosphate–ribosylation.

Endothelial cells also proliferate extensively during this phase of healing. These cells participate in the formation of new capillaries (angiogenesis), a process essential to successful wound healing. Endothelial cells migrate from intact venules close to the wound. Their migration, replication and new capillary tubule formation are under the influence of such cytokines and growth factors as TNF, TGF and VEGF. Although many cells produce VEGF, macrophages represent a major source in the healing wound and VEGF receptors are located specifically on endothelial cells.

MATRIX SYNTHESIS

Biochemistry Of Collagen

Collagen, the most abundant protein in the body, plays a critical role in the successful completion of adult wound healing. Its deposition, maturation and subsequent remodeling are essential to the functional integrity of the wound.

Although there are at least 18 types of collagen described, the main ones of interest to wound repair are types I and III. Type I collagen is the major component of extracellular matrix in skin. Type III, which is also normally present in skin, becomes more prominent and important during the repair process.

Biochemically, each chain of collagen is composed of a glycine residue in every third position. The second position in the triplet is made up of proline or lysine during the translation process. The polypeptide chain that is translated from messenger RNA (mRNA) contains approximately 1000 amino acid residues and is called “protocollagen”. Release of protocollagen into the endoplasmic reticulum results in the hydroxylation of proline to hydroxyproline and of lysine to hydroxylysine by specific hydroxylases. Prolyl hydroxylase requires oxygen and iron as cofactors ketoglutarate as cosubstrate, and ascorbic acid (vitamin C) as an electron donor. In the endoplasmic reticulum, the protocollagen chain is also glycosylated by the linking of galactose and glucose at specific hydroxylysine residues. These steps of hydroxylation and glycosylation alter the hydrogen bonding forces within the chain, imposing steric changes that force the protocollagen chain to assume a helical configuration. Three-helical chains entwine to form a right-handed superhelical structure called “procollagen”. At both ends, this structure contains nonhelical peptide domains called registration peptides. Although initially joined by weak ionic bonds,

the procollagen molecule becomes much stronger by the covalent cross-linking of lysine residues. Extracellularly, the nonhelical registration peptides are cleaved by a procollagen peptidase and the procollagen strands undergo further polymerization and cross-linking. The resulting collagen monomer is further polymerized and cross-linked by the formation of intra- and intermolecular covalent bonds.

Collagen synthesis, as well as posttranslational modifications, is highly dependent on systemic factors such as an adequate oxygen supply, the presence of sufficient nutrients (amino acids and carbohydrates), cofactors (vitamins and trace metals) and the local wound environment (vascular supply and lack of infection). Addressing these factors and reversing nutritional deficiencies can optimize collagen synthesis and deposition.

Proteoglycan Synthesis

Glycosaminoglycans comprise a large portion of the "ground substance" that makes up granulation tissue. Rarely found free, they couple with proteins to form proteoglycans. The polysaccharide chain is made up of repeating disaccharide units composed of glucuronic or iduronic acid and a hexosamine, which is usually sulfated. The disaccharide composition of proteoglycans varies from about 10 units in the case of heparan sulfate to as much as 2000 units in the case of hyaluronic acid.

The major glycosaminoglycans present in wounds are dermatan and chondroitin sulfate. Fibroblasts synthesize these compounds, increasing their concentration greatly during the first 3 weeks of healing. The interaction between collagen and proteoglycans is being actively studied. It is thought that the assembly of collagen subunits into fibrils and fibers is dependent on the lattice provided by the sulfated proteoglycans. Furthermore, it appears that the extent of sulfation is critical

in determining the configuration of the collagen fibrils. As scar collagen is deposited, the proteoglycans are incorporated into the collagen scaffolding. However, with scar maturation and collagen remodeling, the content of proteoglycans gradually diminishes.

C. Maturation And Remodeling

The maturation and remodeling of the scar begins during the fibroplastic phase and is characterized by a reorganization of previously synthesized collagen. Collagen is broken down by matrix metalloproteinases and the net wound collagen content is the result of a balance between collagenolysis and collagen synthesis. There is a net shift toward collagen synthesis and eventually the re-establishment of extracellular matrix composed of a relatively acellular collagen-rich scar.

Wound strength and mechanical integrity in the fresh wound are determined by both the quantity and quality of the newly deposited collagen. The deposition of matrix at the wound site follows a characteristic pattern: Fibronectin and collagen type III constitute the early matrix scaffolding, glycosaminoglycans and proteoglycans represent the next significant matrix component and collagen type I is the final matrix. By several weeks postinjury the amount of collagen in the wound reaches a plateau, but the tensile strength continues to increase for several more months. Fibril formation and fibril cross-linking result in decreased collagen solubility, increased strength, and increased resistance to enzymatic degradation of the collagen matrix. Scar remodeling continues for many (6 to 12) months postinjury, gradually resulting in a mature, avascular and acellular scar. The mechanical strength of the scar never achieves that of the uninjured tissue.

There is a constant turnover of collagen in the extracellular matrix, both in the healing wound, as well as during normal tissue homeostasis. Collagenolysis is the result of collagenase activity, a class of matrix metalloproteinases that require activation. Both collagen synthesis and lysis are strictly controlled by cytokines and growth factors. Some factors affect both aspects of collagen remodeling. For example, TGF increases new collagen transcription and also decreases collagen breakdown by stimulating synthesis of tissue inhibitors of metalloproteinase. This balance of collagen deposition and degradation is the ultimate determinant of wound strength and integrity.

Epithelialization

While tissue integrity and strength are being re-established, the external barrier must also be restored. This process is characterized primarily by proliferation and migration of epithelial cells adjacent to the wound. The process begins within 1 day of injury and is seen as thickening of the epidermis at the wound edge. Marginal basal cells at the edge of the wound lose their firm attachment to the underlying dermis, enlarge and begin to migrate across the surface of the provisional matrix. Fixed basal cells in a zone near the cut edge undergo a series of rapid mitotic divisions and these cells appear to migrate by moving over one another in a leapfrog fashion until the defect is covered. Once the defect is bridged, the migrating epithelial cells lose their flattened appearance, become more columnar in shape and increase their mitotic activity. Layering of the epithelium is re-established and the surface layer eventually keratinizes.

Re-epithelialization is complete in less than 48 hours in the case of approximated incised wounds, but may take substantially longer in the case of larger

wounds, in which there is a significant epidermal/dermal defect. If only the epithelium and superficial dermis are damaged, such as occurs in split-thickness skin graft donor sites or in superficial second-degree burns, then repair consists primarily of re-epithelialization with minimal or no fibroplasia and granulation tissue formation. The stimuli for re-epithelialization remain incompletely defined; however, it appears that the process is mediated by a combination of a loss of contact inhibition; exposure to constituents of the extracellular matrix, particularly fibronectin; and cytokines produced by immune mononuclear cells. In particular, epithelial growth factor, TGF, basic fibroblast growth factor, PDGF and insulin-like growth factor I have been shown to promote epithelialization.

Wound Contraction

All wounds undergo some degree of contraction. For wounds that do not have surgically approximated edges, the area of the wound will be decreased by this action (healing by secondary intention); the shortening of the scar itself results in contracture. The myofibroblast has been postulated as being the major cell responsible for contraction and it differs from the normal fibroblast in that it possesses a cytoskeletal structure. Typically this cell contains -smooth muscle actin in thick bundles called stress fibers, giving myofibroblasts contractile capability.

The smooth muscle actin is undetectable until day 6 and then is increasingly expressed for the next 15 days of wound healing. After 4 weeks this expression fades and the cells are believed to undergo apoptosis. A puzzling point is that the identification of myofibroblasts in the wound does not correspond directly to the initiation of wound contraction, which starts almost immediately after injury.

Fibroblasts placed in a collagen lattice in vitro actively move in the lattice and contract it without expressing stress fibers. It is postulated that the movement of cells with concomitant reorganization of the cytoskeleton is responsible for contraction. [23]

DIABETES AND WOUND HEALING

Infection is an important contributing factor to the morbidity of diabetic patients with foot problems. It is uncertain if they have a greater susceptibility to infection as a result of impaired resistance, or whether reduced blood supply allows infections to become established and the neuropathy permits the infection to go unrecognized.

Diabetes might lead to the impairment of inflammatory and wound healing process by Reducing

a) The blood supply to the affected area.
b) The effectiveness of the inflammatory response.
c) The repair process which results in the formation of fibrous tissue.

a) Impairment of Blood Supply: Reduced blood supply may not be able to sufficiently permit healing of small wounds and as a result, necrosis and infection follow.
   - In ischemic tissue, the growth of anaerobic organisms is favored, particularly if there isconcomitant growth of aerobes.
   - There are several mechanisms by which the microvascular changes in diabetes can impair the response to injury. Blockage of small vessels may prevent the blood flow and impair healing. In addition the capillary basement membrane thickening might alter the permeability and thus interfere with leukocyte migration and fluid exudation.

- Frank wound ischemia is detrimental to all wound healing and may be a contributing factor in the initial formation of chronic wounds. Relative hypoxia, however, is a more common clinical problem and is a significant contributing factor in the formation and the failure to heal wounds. Hypoxia is initially a potent stimulus for fibroblast proliferation and angiogenesis. Higher oxygen tensions are eventually required.
- However wound healing is impeded if hypoxia persists. In an environment of 30 to 40mmHG of oxygen, fibroblasts cannot replicate and collagen production is severely limited. Wound hypoxia also predisposes the wound to bacterial invasion.

b) Formation of Fluid-Cellular Exudates : There is evidence that various inflammatory stages are impaired in diabetes.

- Decreased adhesion of polymorphs to vessel walls and reduced rate of escape from vessels. The abnormality is directly related to the level of fasting blood glucose and returned towards normal with treatment.
- The mobility of white cells towards a chemical stimulus (chemo taxis) is impaired.
- The ability of the polymorphs to ingest and kill bacteria is reduced. Although the various reports are not unanimous in their conclusions, it is likely that the leucocytes from hyperglycemic patients are less efficient at both engulfing and killing bacteria. This defect may be improved by rigorous control of diabetes.
- Wound infection has been shown to impair wound contraction in both acute and chronic wounds. The mechanism by which this occurs is

believed to be the release of bacterial enzymes and metalloproteinase's that may degrade fibrin as well as wound growth factors.

c) Formation of Fibrous Tissue: Goodson and Hunt(1979) demonstrated that the development of strength in an incised wound, which was closely related to the amount of collagen produced in the tissues closest to the wound edge, was decreased in insulin deficiency - Diabetes.

- The experiments of Goodson and Hunt demonstrated that granulation tissue formation could be returned to normal if insulin was given soon after wounding. If the insulin replacement was delayed until the time of greatest collagen formation (about 10 days after wounding) there was no increase in the amount of collagen formed. If this findings can be translated to humans it suggests that the greatest care should be taken to control diabetes in the early postoperative period. In practice this is the time when good control is often most difficult to achieve [24].

Pathophysiology

The pathogenesis is complex and involves the interactive processes of angiopathy, neuropathy and immunopathy.

A. Angiopathy

Diabetic angiopathy is perhaps the most frequent cause of morbidity and mortality in a patient with diabetes.

Angiopathy can be divided into 2 categories: macroangiopathy and microangiopathy

Macroangiopathy:

Macroangiopathy in a diabetic patient presents as a more diffuse disease than in a nondiabetic patient, with more multisegmental involvement and compromised collateral circulation. It is more often seen bilaterally in the lower extremities; the infrapopliteal vessels are more frequently involved than in nondiabetic patients. Vascular impairment, evaluated by resting Doppler ankle pressure, was found to correlate with the development of diabetic foot ulcers. Large vessel disease predisposes a patient with diabetes to foot lesions secondary to ischemic skin changes that, in turn, lead to ulceration and possible infection.

Microangiopathy:

Tooke and Brash discussed the hemodynamic hypothesis of the pathogenesis of diabetic microangiopathy. This hypothesis states that in the early stages, vessel capillaries of diabetic patients have increased microvascular pressure and flow. The increased capillary pressure results in an injury response within the microvascular endothelium. Injury causes release of extravascular matrix proteins, resulting in microvascular sclerosis. Sclerosis is manifested in the arteriole as hyalinosis and in the capillary as basement membrane thickening the ultrastructural hallmark of diabetic microangiopathy. With increasing duration of diabetes, the sclerotic process results in limitation of vasodilatation with reduced maximal hyperemia and in loss of autoregulatory capacity. A key observation has been that nailfold capillary pressure is elevated in the early stages of type 1 diabetes. This has been positively correlated with glycemic control, judged by the glycosylated hemoglobin value at the time of pressure measurement. In addition, pressure appears to be particularly high in those individuals at high risk for microangiopathy, yet relatively normal in patients who have avoided the clinical complications of diabetes over many years.

B. Neuropathy

Neuropathy occurs early in the pathogenesis of diabetic foot problems and is the most prominent risk factor for diabetic foot ulcers. There are three components of diabetic neuropathy namely sensory,motor and autonomic neuropathy. The combined effect of this triad is a foot that cannot respond to pain and is biomechanically impaired, with increased foot pressure, limited joint mobility and poorly hydrated skin that cannot appropriately respond to injury.

Sensory neuropathy:

The damage from sensory neuropathy affects the large myelinated alpha fibres. Its distribution is usually symmetric in stocking and glove pattern as a result, patients are unable to perceive injury to their feet because primary protective or warning systems are defective. This fundamental pathophysiologic impairment is referred to as the loss of protective sensation. Affected patients sustain repetitive, unrecognized injuries to their feet that culminate in full thickness ulceration. Ulcer in an insensate foot is usually painless. Neuropathy can have a wide range of severities and symptoms. Loss of protective sensation does not necessarily mean complete absence of sensation or pain. So called painful or painless ulcers may develop because of ischemia or deep sepsis; these require prompt attention and intervention. This scenario can also represent damage to both large myelinated nerves and small unmyelinated nerves, so the patient may have burning sensation because of small fibre damage and deep, gnawing pain and numbness because of large-fibre neuropathy.

Motor neuropathy

Often occurs in late in course of diabetic peripheral neuropathy and contribute to intrinsic muscle wasting of the feet and hands. Short, weak flexors and extensors

that are over powered by long, strong flexors and extensors in the foot contributes to structural foot deformities such as claw toes, dislocated metatarsophalangeal joints and ankle equinus. Motor neuropathy changes the biomechanics of the foot and directly contributes to increased shear and pressure under the balls of toes, the most common site of neuropathic foot ulcers. Severe motor neuropathy contributes to the development of 'intrinsic minus' foot, or the appearance of high arch structures because of muscle wasting and weakness.

Autonomic neuropathy

Autonomic dysfunction also occurs early in the course of neuropathy. In the foot, autonomic dysfunction results in shunting of blood through direct arteriolevenule communications, diminishing the effectiveness of perfusion. There is loss of hair, sweat and oil gland function, leading to dry, scaly skin that cracks and fissures easily. Vibration, pain and temperature sensations are affected more than touch or proprioception.

C. Immunopathy

The contribution of immunopathy to the development of infection in a patient with diabetes is controversial. Most investigators believe that poor glucose control predisposes patients to infection.

Humoral immunity in the patient with diabetes appears to be normal. Normal to elevated levels of circulating immunoglobulins and normal numbers of B lymphocytes are found. Cell-mediated immune responses are also significantly impaired by elevated glucose concentrations. The impaired host defense mechanism in the diabetic patient appears to occur at the cellular level where impaired leukocyte function and impaired intracellular killing have been observed. Phagocytosis and the intracellular killing function of the leukocyte appear to be

significantly altered in the presence of hyperglycemia. These defects have been partly or completely reversed by improved diabetic control.

MacCuishet demonstrated a decrease in phytohemagglutinin-induced lymphocyte transformation in poorly controlled diabetic patients, but not in well controlled patients or in healthy subjects.A poor response of lymphocytes to staphylococcal antigen has been demonstrated in diabetic patients, regardless of the degree of glycemic control, T lymphocyte immunodeficiency in type 1 diabetes [25].

Diabetic Gangrene

This can occur in neuropathic foot where the arterial tree appears perfectly normal and so are the pulsations throughout the limb.

The gangrene is due to primary infection followed by secondary thrombosis of the digital vessels. The gangrene is slowly progressive and generally remains limited to the area of the foot in which it began.

Necrotizing Fascitis

It is a rare complication of diabetic foot infection. It is an acute infection of subcutaneous tissue and fascia resulting in its necrosis, along with noncrepitus gangrene of the overlying skin.

It is usually due to streptococcus pyogenes but may occasionally be caused by staphylococcus aureus. The affected area is initially red, hot, swollen and painful and the inflammation area is the pathogonomonic sign. This can then progress to frank gangrene. Left untreated, this complication can cause death within days . [27]

Neuropathic foot

The neuropathic foot is a warm, well-perfused foot with bounding pulses and distended dorsal veins due to arteriovenous shunting. Sweating is diminished so skin

and any callus tend to be hard and dry and prone to fissuring. Toes are flexed and the arch of the foot may be raised.

Ulceration commonly develops on the sole of the foot, associated with neglected callus and high plantar pressures. Despite the good circulation, necrosis can develop secondary to severe infection. The neuropathic foot is also prone to bone and joint problems which we refer to as ‘Charcot's osteoarthropathy’.

Neuroischemic foot

The neuroischaemic foot is a cool, pulseless foot with poor perfusion and almost invariably also has neuropathy. The colour of the severely ischaemic foot can be a deceptively healthy pink or red caused by dilatation of capillaries in an attempt to improve perfusion. The neuroischaemic foot may be complicated by swelling, often secondary to cardiac failure or renal impairment.

Ischaemic ulcers are commonly seen around the edges of the foot, including the apices of the toes and the back of the heel and are associated with trauma or wearing unsuitable shoes. The neuroischaemic foot develops necrosis in the presence of infection or if tissue perfusion is critically diminished. Even if neuropathy is present and plantar pressures are high, plantar ulceration is rare. This is probably because the foot does not develop heavy callus, which has good blood flow. [27]

CLINICAL FEATURES

Patients with diabetes are at an increased risk of developing an ulcer on the foot in the presence of established long term complications of the disease. A foot in which arterial disease or neuropathy or both are present is liable to develop major complications.

Presence of sensory neuropathy contributes to the abnormal and prolonged pressure on the foot. Motor neuropathy causes foot deformity, further increasing pressure loading. Loss of innervation to the sweat glands leads to dry skin due to diminished sweating usually in a "stocking" distribution and leads to a dry, cracked skin. These cracks serve as portals of infection that complicate the diabetic neuropathy.

Evidence of neuropathy

- The posture of the foot, clawing of the toes, callus over pressure areas are definitely due to neuropathic changes.
- Glove and stocking distribution of sensory neuropathy .
- Patients complain of cold feet or dead feet describing a sensation of walking on cotton wool. On rare occasions will the foot feel dry and also warm if the blood supply is sufficient.
- Loss of light touch and pain (pin prick) sensation on the toes and foot. In more severe cases this sensory loss may extend to the calf. The loss of the pain sensation my lead to undetected trauma.
- Loss of perception of vibration of foot; at the ankle and at the knee.
- Absence of ankle tendon reflexes and patellar tendon reflexes.

Evidence of ischemia:

- A history of intermittent claudication or rest pain.
- Coldness of the foot
- Absence of ankle pulses.
- Dependent rubor [28].

VARIOUS PRESENTATIONS OF DIABETIC FOOT

Nail Problems

Onychauxis : This is thickening of the nail without deformity, and follows an insult to the nail bed. Without regular reduction onychogryphosis will develop.

Onychogryphosis (ram's horn nail) : This is thickening of the nail with deformity. Onychogryposis is caused by chronic repetitive trauma particularly to the nails on the great toe. The nails may be grossly thickened, hard and very elongated the deformed nail can press against another toe causing ulcerations.

Treatment: can be palliative or surgical. Palliative treatment consists of regular reduction of excessive thickness of the nail plate

Onychocryptosis (ingrowing toe nail) : A section of a nail curves into the adjacent flesh and becomes embedded in the soft tissue. Peeling the nail at the edge or rimming it down at the corners is the most common cause. Other causes are wearing tight shoes or socks which press on the sides of the nail making it curve into the skin. An ingrown nail predisposes to local infection (paronychia) as it provides an entry point for pathogens. Nails should be trimmed in a straight line or removed.

Paronychia : Inflammation of the nail fold. Paronychia, can be acute or chronic.

Acute paronychia is due to bacterial infection, is painful, points and discharges pus. If the margin of the nail plate is pressing on the inflamed area it should be cut back. Collections of pus should be drained. A swab is sent for microscopy and culture and appropriate systemic antibiotics are prescribed.

Chronic paronychia results in the periungual tissues appearing erythematous and oedematous. The infection extends to the nail plate which may develop yellowish-green or yellowish-brown pigmentation. Chronic paronychia is frequently

caused by infection with Candida albicans and the treatment is with terbinafine or itraconazole.

Onychomycosis (fungal nail) : Onychomycosis is a fungal infection of nail. Onychomycosis per se does not cause foot problems, but when it affects the proximal nail it may cause chronic paronychia and serve as a portal for bacteria, resulting in deep tissue infection. It often co-exists with mycosis of the web spaces and it may be superinfected by bacteria, leading to deep tissue infection as well. Treatment with terbinafine hydrochloride, both systemic (tablets 250 mg once daily) and topical (cream), for 3 months with appropriate foot care.

Chronic onychomycosis is classified into two clinical types :

Distal subungual onychomycosis is the most common form.The distal edge of the nail becomes infected and a yellow discoloration, onycholysis and subungual debris develop.

Proximal subungual fungal infection, the second commonest form, Trichophyton rubrum accumulates hyperkeratotic debris under the nail plate and loosens the nail, eventually separating it from its bed.

Itraconazole and fluconazole are also effective in the treatment of chronic onychomycosis.

Lesions under the nail

These can be due to: haematoma, necrosis, melanoma, exostosis.

Fissures : Fissures are moist or dry cracks in epidermis at sites where skin is under tension. Deep fissures may involve dermis. Fissures can occur in dry skin. The treatment involves emollient, such as E45 cream, olive oil or coco butter or in wet skin, where an astringent or antiperspirant such as aluminium chloride is helpful.

Verrucae : Warts may occur anywhere on the foot and may be single or multiple and appear as round flattened papules or plaques. Most will resolve within 2 years without treatment. The recommended treatment for ablation of painful or spreading verrucae in people with diabetes is cryotherapy with liquid nitrogen. Sometimes surgical treatment with excision of the wart is required.

Bullae (blisters) : These are superficial accumulations of clear fluid within or under the epidermis which develop following trauma to the skin. Common causes include unsuitable shoes, failure to wear socks and walking in wet footwear. Small flaccid bullae can be cleaned and covered with a sterile non-adherent dressing. Large bullae (over 1 cm in diameter) and all tense bullae should be lanced with a scalpel and drained before dressing, aspiration with a syringe is less useful because the hole frequently seals. Fluid accumulates again and unrelieved hydrostatic pressure causes extension of the blister. The cause of b1isters should always be ascertained and addressed.

Bullosis diabeticorum : This is a rare condition where diabetic patients present with intraepidermal blisters which are not associated with trauma and heal without scarring. Treatment of bullosis diabeticorurn is as for bullae. This can spread to draining lymph nodes. Suspicious lesions should be biopsied. Treatment is surgical excision.

Chilblains (perniosis) : These are localized inflammatory lesions, provoked by cold and injudicious reheating. Chilblains are frequently found on the toes.

Malignancy : Although skin malignancy is rare in the foot, squamous cell carcinoma, malignant melanoma and rarely basal cell carcinoma may present in the foot.

Hyperhydrosis : is excessive sweating of the feet and may be a particular problem in patients who live in tropical climates with high humidity. The skin becomes white,

macerated and rubbery in texture and prone to blistering and fungal infections. It may be due to hyperthyroidism or anxiety.

Hammer toe : Hammer toe is a complex deformity consisting of contraction (hyperflexion) of the proximal interphalangeal joint, while the metatarsophalangeal joint is either dorsiflexed or in the neutral position. The distal interphalangeal joint may be in the neutral position, hyperextended or in plantar flexion. Hammer toe may be flexible or rigid .It is due to loss of balancing lumbrical functions

Claw toes : Claw toes are similar to hammer toes, but with more buckling and greater deformity. There is fixed flexion deformity at the interphalangeal Joint, associated with callus and ulceration of the apex and dorsal aspect of the interphalangeal joint. Although claw toes may be related to neuropathy, they are often unrelated, especially when the clawing is unilateral and associated with trauma or surgery of the forefoot. Claw toes may rarely result from acute rupture of the plantar fascia.

Hallux valgus : Hallux valgus is a deformity of the first metatarsophalangeal joint with lateral deviation of the hallux and a medial prominence on the margin of the foot. This site is particularly vulnerable in the neuroischaemic foot and frequently breaks down under pressure from a tight shoe .[30]

Limited joint mobility (including hallux rigidus) : Limited joint mobility can affect the feet as well as the hands. The range of motion is diminished at the subtalar and first metatarsophalangeal joints. Limited joint mobility of the first metatarsophalangeal joint results in loss of dorsiflexion and excessive forces on the plantar surface of the first toe causing callus formation and ulceration. It is commonly seen in barefooted and sandal wearing populations.

Charcot foot : Bone and joint damage in the tarsometatarsal joints and mid-tarsal joints leads to two classical deformities: the rockerbottom deformity, in which there is displacement and subluxation of the tarsus downwards and the medial convexity, which results from displacement of the talonavicular joint or from tarsometatarsal dislocation. Both are often associated with a bony prominence which is very prone to ulceration and healing is notoriously difficult. When the ankle and subtalar joints are involved, instability of the hindfoot can result

Ischemia : The foot may have a pale white appearance in severe ischemia, especially on elevation. In acute ischemia, the foot is pale, often with purplish mottling. The cause of black appearances is discussed under necrosis.

Necrosis : Areas of necrosis and gangrene can be identified by the presence of black or brown devitalized tissue. Such tissue may be wet (usually related to infection) or dry. Necrosis can be due to infection, when it is usually wet, or to occlusive macrovascular disease of arteries of leg.

Necrosis can involve skin, subcutaneous and fascial layers. In lightly pigmented skin it is easily evident but in the subcutaneous and fascial layers it is not so apparent.

Major Infections

1) Cellulitis : Patients present with cellulitis of the foot involving distal half or whole of the foot because of necrotising skin and subcutaneous tissue, these patients manifest with edema involving dorsum of the foot with shiny skin.

2) Abscess : Abscess may be localized to single toe or multiple toes or in the deep spaces of the sole. Patients may present with or without pain, sometimes even abscess pointing. The most important signs are swelling and redness which can be seen on the dorsum of the web spaces of the foot. However the most characteristic sign is

separation of the toes due to diffuse edema of the deep tissues of the foot and always indicates that there is pus deep in the foot.

3) Ulcer : Ulcer may present on the dorsal or plantar aspect of the foot. Plantar ulcers also called as trophic or penetrating ulcer. They are typically painless and occur over areas that normally carry weight. The earliest change is an area of hyperkeratosis often over a metatarsal head. The commonest site for an ulcer of the toe is on the proximal interphalangeal joint of a clawed toe. Hyperkeratosis or inflammation may precede the breakdown of skin and the development of a small ulcer.

4) Gangrene : Gangrene means tissue death.

There are two kinds of gangrene. Wet gangrene—is caused by infection.

Dry gangrene—is caused by a poor blood supply. When not enough blood reaches a part of the foot, the skin and flesh may die and change colour to brown or black. Areas of gangrene may occur on parts of the foot that are exposed to pressure.

The common sites are heel, the malleoli and the areas of first metatarsal head medially and the base of the fifth metatarsal. Small areas of gangrene may also occur on the parts of the foot not subjected to pressure because of embolism of atheromatous debris. Gangrenous patches may form in the interdigital clefts. If the infection follows, it may spread through tissue which, because of poor blood supply, is unable to confine the process so that further necrosis leads to wet gangrene. The gangrene may be localized to single toe or multiple toes or extend to whole of the foot [29].

Wagner's Classification Of Diabetic Foot Wounds [31]

Grade 0 – Pre- or post-ulcerative lesion completely epithelialized.

Grade 1 – Superficial, full thickness ulcer limited to the dermis, not extending to the subcutis.

Grade 2 – Ulcer of the skin extending through the subcutis with exposed tendon or bone and without osteomyelitis or abscess formation.

Grade 3 – Deep ulcers with osteomyelitis or abscess formation.

Grade 4 – Localized gangrene of the toes or the forefoot.

Grade 5 – Foot with extensive gangrene.

INVESTIGATIONS

I. Blood Examination

- Hemoglobin: It is useful investigation to know about general status of the patient and to know about the fitness of the patient for distinctive operative procedures.
- Total WBC count: Indicates defense mechanism of the body.
- Differential WBC count: Will give a clue to diagnosis, like PMN'S in acute inflammation,l ymphocyte count is increased in tuberculosis, neutrophil reduced in generalized malnutrition,.
- ESR: Increased in tuberculosis etc..
- Bleeding time and coagulation time : Altered levels may require correction when contemplating any surgery of the patient.
- Fasting blood sugar : To Assess degree of control of diabetes.
- HbA1c to know the previous diabetic status.

- Serum creatinine: It is more sensitive indicator of the renal function, which may be hampered in diabetic nephropathy.
- Blood urea: Also indicates renal function, but may vary with hydration of patient.
- Rheumatoid factor test: For diagnosis of rheumatoid arthritis.
- HIV and HBsAG: For universial precautions.

II. Examination of urine

- For Sugar
- For Ketone bodies: Diabetic ketoacidosis.

III. Bacteriological

- Examination of the discharge: This investigation is important in inflammation and spreading ulcer. A baseline bacterial culture with sensitivity result is useful. It provides a guideline for appropriate chemotherapy.

IV. Biopsy

- A biopsy of ulcer when in doubt is useful. It should be performed to exclude unusual cases of ulceration.

V. X-ray of foot

Radiographs of the foot in patients with diabetes commonly reveal a combination of bone alterations, including gross destruction, fragmentation, periosteal new bone formation and pointed bone deformity. If infection is suspected then on plain films defects in soft tissue contour and loss of tissue planes will be seen. Edema or swelling is common.

Other findings include osteosclerosis, fragmentation, periositis and radiolucent areas within the soft tissues which may be air as a result of debridement / open wound (or) from production of gas by microorganisms.

Calcification of arteries (also known as medial arterial calcification or Monckeberg's arteriosclerosis) is a common findings in patients with diabetes. Usually feet are earliest and most frequent site of involvement.

VI. Doppler Ultrasound

Is a useful adjunct to physical examination. Measuring the ankle – brachial ratio is less helpful than in the non – diabetic patient because calcific stenosis may result in artifactually elevated pressures.

The normal Doppler pulse is triphasic, but below a major obstruction it becomes monophasic and this can be readily detected audibly. If all the foot pulses are triphasic, by Doppler then one can assume that the patient does not have significant ischemia. If the pulses are monophasic, then formal non invasive evaluation is indicated.

VII. Duplex Imaging : (Duplex Ultrasound scanning)

This is an investigative technique of major importance in vascular disease. A duplex scanner uses 'B' mode ultrasound to provide an image of vessels. This image is created through the different ability of the tissues to reflect the ultra sound beam. A second type of ultrasound, namely Doppler ultrasound is then used to insonate the vessels and the Doppler shift is analyzed by dedicated computer in the Duplex scanner itself. Such Shifts can give detailed knowledge of vessel blood flow, turbulence. Some scanners have the added sophistication of color coding which

allows visualization of blood flow on the image. The various colors indicate change in direction and velocity of flow: points of high flow generally indicate stenosis.

It allows the cross sectional area of arterial lumen to be measured. By use of color, the flow towards or away from the transducer can be easily distinguished so that peripherally running arterial flow (red) can be immediately distinguished from centrally directed venous flow (blue): the intensity of color increases with the velocity of flow. [32]

TREATMENT

Debridement :

Debridement is widely accepted as the most definitive treatment for the diabetic foot ulcer. Inadequate debridement may lead toprolonged infection, increasing risk for limb amputation.

Sharp debridement of the diabetic foot ulcer stimulates the nonmigratory edge epithelium, releases growth factors and reduces the local inflammatory and proteolytic environment.

The goal of operative debridement is to remove all hyperkeratotic tissue (ie, callus), necrotic tissue, functionally abnormal senescent cells and infected tissue, all of which inhibit wound healing. In this manner, the remaining tissue, although physiologically impaired, can respond to exogenous topical treatment, (ie, growth factors or cell therapy).

Clinical judgment has traditionally defined the margin of debridement, which is recognized as tissue with punctuate bleeding The margin of debridement of the skin edge should extend to the soft tissue beyond the callus. The depth of debridement of

the wound bed should extend to tissue that is free of fibrosis and infection, eg, osteomyelitis, as confirmed by pathology and microbiology. [33]

Infection Control :

Diabetic foot infections (DFIs) are usually a consequence of skin ulceration from ischemia or trauma to a neuropathic foot. The compartmentalized anatomy of the foot, with its various spaces, tendon sheaths and neurovascular bundles, allows ischemic necrosis to affect tissues within a compartment or spread along anatomic tissue planes. Recurrent infections are common, and 10% to 30% of affected patients eventually require amputation.

Diabetic patients are predisposed to foot infections, not only because of the portal of entry and poor blood supply, but also because of defects in humoral immunity (e.g., impaired neutrophil chemotaxis, phagocytosis, intracellular killing) and impaired monocytemacrophage function, which correlate with the adequacy of glycemic control.

Cell-mediated immunity and complement function may also be impaired.

Acute infections are usually caused by gram-positive cocci. S. aureus is the most important pathogen in DFIs. It is often present as a monomicrobial infection, but usually it is also an important pathogen in polymicrobial infections.

Chronic wounds, recurrent infections and infections in hospitalized patients are more likely to harbor complex flora, including aerobic and anaerobic flora. Among gram-negative bacilli, bacteria of the family Enterobacteriaceae are common and Pseudomonas aeruginosa may be isolated from wounds that have been treated with hydrotherapy or wet dressings. Antibiotic-resistant bacteria, especially MRSA,

may be isolated from patients who have received antibiotics previously or who have been hospitalized or reside in long-term care facilities.

Agents that have been shown to be effective for therapy of DFIs in clinical trials include cephalosporins, β-lactamase inhibitor combination antibiotics, fluoroquinolones, clindamycin, carbapenems, vancomycin and linezolid. The optimal duration of therapy for DFIs has not been determined; common practice is to treat mild infections for 1 week, whereas serious infections may require up to a 2-week course of therapy. Adequate débridement, resection or amputation can shorten the necessary durations of therapy. [34]

Offloading therapy :

Neuropathic diabetic foot wounds on the plantar aspect of the foot occur because of a combination of focal pressure and repetitive stress at a given site . The mitigation of either of these variables (pressure or repetitive stress) may reduce risk for ulceration.

Mechanical stress that occurs at right angles to the integument is termed “vertical stress.” This tends to damage healthy tissue through repetitive compressive forces.Stress that is imparted parallel to the plantar aspect of the foot is termed “shear.” This shearing of soft tissue is equally damaging and is evidenced by the characteristic undermined nature of the periphery of poorly off-loaded diabetic foot wounds. Shear and vertical stress work in tandem in the pathogenesis of a diabetic foot wound. So relieving areas of elevated plantar pressure (off-loading) can prevent and heal plantar ulceration.

Methods to offload the foot include bed rest, the use of a wheelchair, crutch assisted walking, total contact casts, felted-foam, half-shoes, therapeutic shoes, custom splints and removable cast walkers.

Total contact casts (TCCs) are considered the gold standard of the off-loading and treatment of neuropathic ulcers The technique is called “total contact casting” because it uses a well-molded, minimally padded cast that maintains contact with the entire plantar aspect of the foot and the lower leg. Total contact casting is effective in treating a majority of noninfected, non-ischemic plantar diabeticfoot wounds, with healing rates ranging from 72% to 100% over a course of 5–7 week . Peak plantar pressures are highest in the forefoot and tend to be generally less significant in the hindfoot and medial arch TCC is effective because it permits walking by uniformly distributing pressures over the entire plantar surface of the foot. TCCs are effective for a number of other reasons besides their ability to off-load. They may help reduce or control edema that can impede healing and, thus, potentially protect the foot from infection. However, the most important attribute of this technique may be its ability to ensure appropriate patient compliance. [35]

Wound bed preparation :

The goal of wound bed preparation is to have well-vascularized granulation tissue with no adjacent cellulites, drainage, or odor with removal of scar tissue. Proper debridement concurrently prepares the wound bed and stimulates the healing process.

The four approaches of wound bedpreparation, which address the different pathophysiological abnormalities underlying chronic wounds, are as follows

(1) Tissue management

(2) Inflammation and infection control

(3) Moisture balance

(4) Epithelial (edge) advancement.

After debridement of an infected wound and wound bed preparation**,** topical antibiotics may be efficacious. [36]

Dressings In Diabetic Foot Disease :

Wound dressings represent a part of the management of diabetic foot ulceration. Ideally, dressings should alleviate symptoms, provide wound protection and encourage healing.

In choosing a dressing for an infected diabetic foot ulcer, several factors have to be taken into account. Infected wounds tend to have a heavy exudate that needs to be controlled to prevent maceration of surrounding tissue. There may be considerable odor associated with infection that may be unpleasant and distressing for the patient and family. A dressing must be comfortable and acceptable for the patient and should help alleviate or, at the very least, not worsen pain, especially at dressing changes. Ideally, the dressing should also aid in the management of the infection itself.

Desirable characteristics for wound dressings must incorporate the principles of wound healing. For 3 decades, since the work of Winter and Hinman and Maibach, a moist wound environment has been recognized as optimal for healing. Dressings have since been engineered to maintain this environment while also controlling the growth of microorganisms, allowing gaseous exchange and thermally insulating the wound, which allows atraumatic removal. These dressings must also accommodate practical issues such as allowing observation of the wound and providing mechanical protection and conformability; of course, dressings must also be cost effective .

TABLE NO 2 : Classes of dressings for diabetic foot infections.

Dressing	Advantages	Disadvantages
Low-adherence	Simple Hypoallergenic Inexpensive	Minimal absorbency
Hydrocolloids wounds	Absorbent Can be left for several days Aid autolysis	Concerns about use for infected May cause maceration Unpleasant odor
Hydrogels wounds	Absorbent Aid autolysis	Concerns about use for infected May cause maceration
Foams	Thermal insulation Good absorbency Confirm to contours	Can adhere to wound Occasional dermatitis with adhesive
Alginates	Highly absorbent Bacteriostatic Hemostatic Useful in cavities	May need wetting before removal
Iodine preparations Pregnancy	Antiseptic Moderately absorbent	Iodine allergy Discolors wounds Avoid in case of thyroid disease
Silver-impregnated	Antiseptic Absorbent	Cost No proven advantage

Nonadherent Or Low-Adherence Dressings

Various types of nonadherent or saline-soaked gauze dressings are often regarded as standard treatment for diabetic ulcers and have usually been used as the control arm in studies of dressings.

These dressings are designed to be atraumatic and to provide a moist wound environment. These simple, relatively inexpensive dressings are not designed specifically for managing infection butcan be safely used in conjunction with antibiotic treatments.

Hydrocolloids

Hydrocolloid dressings are semipermeable to vapor, occlusive to wound exudate and absorbent. They are usually presented as an absorbent layer on a film or foam.

Examples of commercially available products include Duoderm(Convatec), Granuflex (Convatec), and Comfeel (Coloplast).

They are found to be the second most popular choice of dressing (behind nonadherent) for all diabetic foot ulcers in a study of British diabetic specialist nurses and chiropodists. Despite their popularity, their use on infected wounds is controversial. Hydrocolloid materials are designed to be occlusive, trapping exudate within the dressing and hydrating the wound.

This creates a hypoxic and moist environment that may also facilitate autolysis of necrotic material. Their use for highly exudative wounds can lead to maceration of the surrounding skin. Concerns persist regarding their use for infected wounds. Some evidence suggests that occlusive dressings may reduce the risk of infection developing in a wound by increasing infiltration of polymorphonuclear leucocytes.

Most authorities, however, have expressed concern that hydrocolloids may increase the risk of infection developing within a wound.

Hydrocolloid dressings are designed to be left on the wound for prolonged periods (1 week); this is useful in managing clean ulcers, but not when regular wound inspection is required. Thus, these dressings are probably more useful in preventing, rather than treating, infection within a woun.

Hydrogels

Hydrogels are designed to facilitate autolysis of necrotic tissue and they donate moisture to extensively dry wounds. Thus, they can lead to maceration when applied to wounds that are moderately to heavily exudating. Their use on a diabetic foot lesion should be as an adjunct to sharp debridement of necrotic eschar. Further, they should be applied cautiously on patients with limb ischemia, because dry gangrene could potentially rapidly progress to wet gangrene, with serious consequences. In vitro studies have shown that hydrogels will not support bacterial growth ,although a reluctance to apply gels to infected wounds persists .

Examples include Aquaform (Maersk Medical) and Intrasite Gel

Foams

Foam-based dressings are another popular choice for diabetic foot ulcers. The dressings have a wide range of absorbency, provide thermal insulation and are easily cut to shape. There have been few published data on their use in diabetic foot ulceration and none on their use in infection. However, their absorbency and comfort would theoretically make them a suitable choice Examples include Allevyn (Smith and Nephew) , Cavicare (Smith and Nephew) and Avance impregnated with bactericidal silver .

Alginates

A wide range of different alginate, or seaweed, products are currently available. They are highly absorbent, pack into cavity wounds, provide hemostasis and are atraumatic at dressing change (but may require wetting). It is important to ensure that all dressing is removed from a cavity wound, because retained dressing may be a source for further infection. The dressings may have some bacteriostatic properties. Calcium alginate dressing inhibited growth of Staphylococcus aureus in vitro, with no increase in growth of Pseudomonas, Streptococcus pyogenes, or Bacteroides fragilis.

Alginates should be safe to use on infected foot ulcers, provided there are regular and thorough dressing changes. Examples include Kaltostat (Convatec) and Sorbsan (Maersk Medical).

Iodine Preparations

Antiseptics, such as iodine-based preparations, are commonly used on wounds, although there is no evidence to support a beneficial effect. Typically they are applied to locally infected wounds, usually in combination with systemic antibiotics.

Iodine comes in 2 main preparations: cadexomer- iodine and povidone-iodine.

Iodine is bactericidal in vitro, with maximal activity at 0.1%–1% . Povidone-iodine has long been used as a skin antiseptic, but its antimicrobial effect on wounds is debatable. Furthermore, some data have shown iodine solutions to be toxic to fibroblasts and keratinocytes.

A randomized controlled trial of cadexomer- iodine versus saline-soaked gauze on clean foot ulcersshowed no significant difference in healing between the

groups. Certain iodine dressings are highly absorbent and therefore useful in preventing skin excoriation in moderately exudating ulcers. In our own clinical practice, .Cadexomer-iodine pastes are used for cavity wounds and povidone-iodine gauze for superficial ulcers. Despite the lack of evidence, many consider iodine preparations to be appropriate dressings for infected diabetic foot ulcers.

Silver-Impregnated Dressings

The use of silver as a topical antimicrobial for acute and chronic wounds is well established. It has been traditionally delivered as silver nitrate (on sticks or roll-ons) or as silver sulfadiazine (e.g., Flamazine ointment). Silver nitrate has cytotoxic effects on host cells, a property often exploited in the treatment of hypergranulating tissue, but its application can be uncomfortable. Silver sulfadiazine, which has the antimicrobial actions of both silver and sulfadiazine, is used on burns and chronic wounds and is generally well tolerated. The antimicrobial effects of silver are complex, including direct inhibition of bacterial cell respiration, inactivation of intracellular enzymes and alterations to the cell membrane. Silver-coated dressings that use elemental silver may be more efficacious at killing bacteria than is silver sulfadiazine or silver nitrate . New silver-impregnated dressings may be suitable for use for infected diabetic foot ulcers.

Examples include Acticoat and Actisorb 220.

There have been no randomized controlled clinical trials of these dressings in diabetic foot ulceration. However, reports of accelerated wound reepithelialization and beneficial antibacterial action in the treatment of burns are encouraging [37].

Biological dressings

Biological Therapy (e.g., bilayered keratinocytes and fibroblasts and platelet-derived growth factor-BB) must be used when patients fail to improve after the approaches described above have been applied for 3 weeks. Biological therapy should be implemented only if wound size cannot be decreased by more than 10 percent within a 3- week time period.

Diabetic foot ulcers exhibit a decreased angiogenic response and a decreased production of growth factors within the wound. Cell therapy, also known as biological therapy, presents an appropriate treatment option in some cases. Biological therapy is an ideal treatment for diabetic foot ulcers, because it adds cells that release growth factors to a growth factor-dependent environment, increases cytokines and matrix proteins and promotes angiogenesis. Thus Accelerating healing time decreases the risk of wound infection. The biological therapy consists of "The bilayer biologically active skin construct", composed of a surface layer of allogenic human keratinocytes over a layer of allogenic human fibroblasts suspended within a collagen matrix. The "Bilayer cell therapy" has been shown to increase the healing rate of diabetic foot ulcers not complicated by osteomyelitis or ischemia. Fibroblasts synthesize collagen and secrete a matrix of growth factors and matrix proteins in physiological concentrations essential for wound healing and epitheliazation. Biological therapy is usually performed after a debridement and after achieving proper hemostasis. Often wounds require several applications, as the biological effect from the cell therapy lasts only up to 6 weeks. [38]

Glycemic control :

According to Diabetes Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study , tight control of blood glucose will decrease rates of retinopathy, nephropathy and neuropathy. Lowering HbAlc may reduce the risk of myocardial infarction and cardiovascular death. The control of glucose levels should be as strict as possible and blood glucose levels above 10mmol/L must be avoided, as they are associated with impaired function of the leucocytes, both polymorphonuclear and mononuclear cells .[39]

Hyperbaric oxygen therapy :

Hyperbaric oxygen therapy (HBOT) is based on the premise that the delivery of supraphysiological concentrations of oxygen to diseased tissues will result in beneficial physiological changes.

The therapy is based on achieving an atmospheric pressure of 2–3 atmospheres pressure which is administered using a sealed polyethylene bag over the affected area and administering 100 percent oxygen to a pressure between 20 and 30 mmHg. Treatments last 2 to 2 ½ hours.

HBOT can be offered to patients who have diabetic foot ulcers for whom at least 30 days of standard wound care has failed and who have a Wagner grade III lesion or higher (meaning the ulcer must penetrate to tendon, bone, or joint and may be associated with deep abscess, osteomyelitis, gangrene, or septic arthritis) In the case of diabetic foot ulceration, it is believed both that the function of phagocytic cells is improved, assisting in the fight against any infection and that wound healing is independently aided through effects on cellular processes .Thus, it has been suggested

that HBOT is useful for the treatment of infection and for the healing of chronic diabetic wounds. [40]

Growth Factors :

PDGF-beta (becaplermin; available as Regranex) has been developed as a topical therapy for the treatment of noninfected diabetic foot ulcers. It is applied in the form of a once-daily gel along with debridement on a weekly basis.

Platelet-rich plasma (PRP) is an autologous product, extracted from the patient's plasma, which includes a high platelet concentration in a fibrin clot that can be easily applied to the ulcer area. The fibrin clot is absorbed during wound healing within days to weeks following its application . There are a few studies reporting a shorter closure time and higher healing percentage in patients using PRP and platelet-derived products.

Granulocyte colony stimulating factor (GCFS) shows faster resolution of the infection and faster healing.

Basicfibroblast growth factor (bFGF) is known to be beneficial in the formation of granulation tissue and normal healing.

Epidermal growth factor (EGF) acts on epithelial cells, fibroblasts and smooth muscle cells to promote healing. [41]

Bioengineered Skin Substitutes :

Tissue-engineered skin substitutes are classified into

- Allogenic cell-containing
- Autologous cell-containing
- Acellular matrices.

The first two types of matrix contain living cells, such as keratinocytes or fibroblasts, while acellular matrices are free of cells and act by releasing growth factors to stimulate neovascularization and wound healing. Accumulating evidence shows that bioengineered skin substitutes may be a promising therapeutic adjunct therapy to the standard wound care for the management of noninfected diabetic foot ulcers.

Extracellular Matrix Proteins is a semisynthetic ester of hyaluronic acid which facilitates the growth and movement of fibroblasts and controls hydration.

Collagen seems to induce the production of endogenous collagen and to promote platelet adhesion and aggregation. It has been reported to be safe and effective as an adjunctive therapy in the management of foot ulceration .[42]

Matrix metalloproteinases modulators regulate the extracellular matrix components. During normal wound healing, there is a balance between the construction and the destruction of the extracellular matrix. In chronic wounds, a high expression of MMP-2 in fibroblasts and the endothelium is detected and is believed to favor destruction. Thus, downregulation of MMP-2 expression may enhance the healing process.

TOPICAL NEGATIVE PRESSURE

Although extensive research is going on in the field of wound management, the treatment modalities available for chronic ulcers are limited. Most of the above mentioned techniques have their own limitations when chronic wound management is concerned. The practice of exposing a wound to sub-atmospheric pressure for an extended period to promote debridement and healing was first described by fleischmann et al in 1993 following the successful use of this technique in 15 patients with open fractures. They reported that the treatment resulted in "efficient cleaning and conditioning of the wound, with marked proliferation of granulation tissue". The science behind topical negative pressure dressings is to apply a sub atmospheric pressure over the wound bed and maintain the negative pressure environment by means of a semi permeable occlusive coverage. Since the wound is occluded from the surrounding environment it is also called " Limited access dressing" [44,45].

In the early studies, negative pressure within the wound was achieved by the use of conventional methods such as wall suction apparatus or surgical vacuum bottles. Both these systems are associated with practical problems in terms of the delivery, control and maintenance of the required levels of negative pressure. In 1995, a commercial system for promoting vacuum assisted closure (VAC) was introduced into the United States market. The heart of the system is a microprocessor-controlled vacuum unit that is capable of providing controlled levels of continuous or intermittent sub-atmospheric pressure ranging from 25 to 200 mmHg.

Principles and mechanism of action

The fundamental principle behind topical negative pressure dressing is the application of sub atmospheric pressures ranging from –25 to –200 mm of Hg at the

wound bed. A number of factors are found to be involved in delayed wound healing in chronic wounds, when conventional methods of wound dressings are used.

These factors mainly include

- Peripheral oedema and circulatory compromise at wound bed.
- Bacterial colonisation.
- Granulation tissue formation.

Argenta and Morykwas first published experimental work on Topical negative pressure therapy in 1997 using animal and scientific studies. Using an acute wound model in swine, Morykwas postulated a multimodal mechanism of action and the effective pressure that needs to be generated within the wound for action [43,46]. The exact mechanism of action of topical negative pressure on the wounds is still debated. Several theories have been proposed to describe the possible mechanism of action of TNP in the treatment of wounds. It is thought that TNP promotes closure of the wound by promoting the rapid formation of granulation tissue as well as by mechanical effects on the wound. It concurrently provides a moist wound environment and removes excess wound exudates thus aiding in the creation of the "ideal wound healing environment".

Usage of a subatmospheric pressure causes

- Fourfold increase in blood flow in the local wound environment. (As measured by a laser Doppler technique.)
- Induces mechanical stress which causes an increase in cellular activity, the nature of which varies with the cell type and methodology. Accelerated cell cycling and DNA synthesis have been seen which causes increased fibrogenesis in the wounds. In wounds, exposure to sub-atmospheric pressure alters the cytoskeleton of the cells in the wound bed. This alteration disrupts

the integrin bridges of the cytoskeleton, triggering the release of intracellular secondary messengers, which in turn up regulate cell proliferation. Thus, the increased rate of granulation tissue formation observed with the intermittent pressure cycle may be, in part, attributable to the repeated release of secondary messengers that occur with each cycle of sub-atmospheric pressure.

- Increase in the rate of granulation tissue formation and reduction in the bacterial load in the wound.
- Clinically TNP removes large amounts of fluid from wounds especially acute wounds. The resulting reduction in oedema is thought to aid in the enhancement of blood and nutrient flow into the wound. However, this removal of exudates (which will include metalloproteinase's and other inflammatory mediators) from the wound and oedema from the surrounding tissues encourages nutrient movement into the wound area even if blood flow is not increased. Removal of fluid prevents a build up of inflammatory mediators and encourages diffusion of further nutrients into the wound. This is all beneficial to the healing process especially in the case of chronic wounds where it has been hypothesised that an imbalance of metalloproteinase's can inhibit healing. Anecdotally the volume of wound exudate gathered from acute wounds decreases significantly over the first three to four days signifying a decrease in wound oedema.
- The mechanism behind the ability of the TNP to decrease bacterial count may be attributable to three properties: increased blood flow, decreased interstitial edema and removal of harmful enzymes from the wound bed. Morykwas et al.quantified blood flow to wounds by inserting laser Doppler needle probes. As mentioned above, cyclical application of negative pressure increases local

blood flow at the wound surface. The increased blood supply to the wound bed delivers increased oxygen and leukocytes to better combat bacterial infection. In addition to the increase in blood flow, the VAC decreases local tissue edema. Edema is a normal consequence of increased capillary permeability that occurs during the inflammatory response. However, as the accumulation of interstitial fluid increases, the distance between the capillaries and the healing cells increases as well. This decreases oxygen and nutrient transport and increases the distance for white blood cells to diapedese, thereby adversely affecting the capacity of the immune system to clear an infection. Removing the excess interstitial fluid improves oxygen and nutrient delivery and decreases the distance the white blood cells have to diapedese to reach the wound site. Similarly, the sub-atmospheric pressure applied by the VAC continuously removes any fluid that would normally accumulate on the wound surface. This decreases the concentrations of harmful wound and bacterial byproducts such as metalloproteases. These proteases (elastases and collagenases) inhibit the formation of granulation tissue and slow down the healing process. Their removal facilitates the formation of new granulation tissue [43,46,47].

- The TNP therapy equipment consists of a reticulated foam dressing that is inserted in the wound and sealed in place with the use of an adhesive dressing and this is in turn connected to a suction apparatus to provide the negative pressure.

Indications For Vacuum Assisted Closure

- Acute and Traumatic wounds.
- Pressure ulcers.
- Chronic wounds
- Flaps
- Grafts
- Wound Dehiscence

Application of the vacuum assisted closure device

The wound is thoroughly debrided and devitalized tissue removed. A perforated drain tube is placedon top of the wound bed and other end is brought out subcutaneously a little away from main wound. The dressing consists of a polyurethane (PU) or polyvinyl-alcohol (PVA) foam that is cut to fit the wound cavity exactly. The foam is covered with an adhesive drape which creates a sealed environment for moist healing. This is in turn connected to the negative pressure generator- a source for suction and drainage. The negative pressure generator maintains the pressure at 125mmHg sub atmospheric level which is the optimum pressure to ensure wound healing and adequate perfusion to the tissues. The TNP can be applied in two settings either as a continuous or intermittent setting (five minutes on and two min off). The rate of granulation tissue formation is faster in the later setting than the former. TNP dressings should be changed every 48–56 hours except in exceptional circumstances (for example, over a skin graft) with more frequent dressing changes in the presence of aerobic infection. If dressings are routinely left for longer periods of time (>56 hours) this can lead to increased discomfort at the time of dressing changes because of in growth of granulation tissue into the foam [18].

The TNP device can be applied over any type of tissue or material, including dermis, fat, fascia, tendon, muscle, blood vessels, bone, Gortex graft, synthetic mesh and hardware. There are two important prerequisites:

- The wound must be debrided (i.e. free of necrotic tissue); and
- The wound must be well vascularised.

To avoid the risk of promoting a deeper or systemic infection, the wound should always be completely debrided before application of topical negative pressure.

TNP therapy has greatly simplified wound management. It is currently well accepted as an excellent initial dressing after wound debridement in all but ischemic wounds because it effectively reduces wound edema, controls local bacterial growth, and promotes the formation of granulation tissue. It provides a safe temporary wound environment so that reconstructive surgery can be electively planned rather than performed urgently.

Use of the VAC also allows the surgeon to choose a less complex mode of reconstructive surgery. The available options for facilitating wound healing range in complexity from allowing the wound to heal by secondary intention, healing by delayed primary closure, use of a skin graft, use of a local flap, use of a pedicled flap and finally use of a microsurgical free flap. By promoting the rapid formation of granulation tissue, the VAC decreases the three-dimensional size of the wound. The surgeon can therefore allow the wound to heal by secondary intention or with a simple skin graft and/or local flap. Without the VAC, the same wound would have needed to be treated with a pedicled or microsurgical free flap.

Complications

While complications associated with VAC therapy are usually infrequent and of low morbidity, serious events, although rare, have been reported. Most of these are related to technique, i.e. the wound was not clinically ready for the VAC, there was insufficient protection between a vital structure and the sponge, the VAC was not changed frequently enough, or inadequate pressures were applied. The key to minimize the risk of this complication is to place the VAC only on clean healthy wounds. Less serious complications affecting up to 25% of patients associated with VAC therapy include pain, skin irritation or maceration, pressure from the tubing, odor, tissue necrosis, bleeding and infection. Most of these complications can be avoided with proper technique, management and patient selection.

Pain upon application of the VAC in a sensate patient can be mitigated by starting with a low pressure of 50mm Hg and slowly increasing to 125mm Hg. Intermittent suction can be painful and this may necessitate switching the modality to continuous suction. Changing the sponge can also be painful, especially when granulation tissue has grown into the sponge. This can be addressed by wetting the sponge with topical xylocaine without epinephrine (adrenaline). The alternative option is to change the sponge more frequently, even daily, if rapid tissue in-growth continues to be a problem. This is often necessary in children, who have a rapid wound healing response.

Bleeding from the wound may occur with dressing changes as a result of excessive growth of granulation tissue into the sponge. This is seen more commonly in pediatric patients, in whom the rate of granulation tissue formation is more rapid than in adult patients. Bleeding can generally be stopped by manual pressure and can be minimized bychanging the sponge dressing more frequently.

In a poorly sealed system, an air leak can develop and potentially lead to wound desiccation. Damage to adjacent tissue from the VAC occurs when the dressing is inappropriately placed. Careful placement of the tube to avoid skeletal pressure points (e.g. the heel) is critical. Another minor complication is a rash on the skin around the wound resulting from contact with the foam sponge.

Contraindications to vac therapy

- These include fragile skin: Skin integrity should be examined prior to use of the VAC system. Patients with thin skin because of age, chronic corticosteroid use or secondary to a collagen vascular disorder can experience shearing or skin avulsion when the adhesive dressing is lifted from the skin during dressing changes. Therefore, patients who cannot tolerate skin adhesives should not be treated with the VAC device.
- Ischemic tissue / Necrosis: Similarly, patients with ischemic wounds may experience further necrosis at the skin edge with VAC therapy. When dealing with an ischemic wound, the VAC cannot be applied until the wound has been revascularized.
- Osteomyelitis / Fistulas: In wounds where devitalised tissue is present, especially in case of osteomyelitis, all the dead tissue including dead bone must be removed and any underlying infection must be treated prior to application of topical negative pressure. This is believed to be due to the fact that presence of devitalised tissue acts as a medium for bacterial growth and thus impedes healing. In cases where fistulas are associated with the wound, topical negative pressure application may prove more dangerous. The suction

device may not have sufficient capacity to accommodate the discharge removed by suction especially in case of high output fistulas. The negative pressure may also cause more fluid leakage through the fistulous tract leading to delayed healing of fistula.

- Presence of malignancy: VAC therapy is contraindicated in patients with neoplasm because it may stimulate further tumour growth. Whenever neoplasm is suspected or found, it should be excised with adequate margins prior toapplication of the VAC. [18,48]

AMPUTATION

The indications for amputations are as follows:

1. Infective gangrene
2. Trauma – Crush injury with tissue loss
3. Frostbite.
4. Ischaemic gangrene of the toes, or forefoot, from peripheral arterial occlusive disease

Various types of amputations

Pre operative management

i. Control diabetes
ii. Control infection: Period of antibiotic therapy is essential for about 24-48 hours prior to surgery, except in case of spreading anaerobic infection.

1. **Ray amputation**

   The most common amputation in the foot is a ray amputation of the affected toe with the distal half of the associated metatarsal. This also allows good drainage of infected deep spaces of the foot

2. **Toe Amputations, Single Toe**

3. **All(remaining) toes**

   Clawed toes on a neuropathic foot have negligible role in walking but vulnerable to minor trauma which many cause morbidity. If no doubt about the adequacy of blood supply of the foot, amputation of healthy toes is sometimes justified.

4. **Transmetatarsal, Tarsometatarsal And Midtars Alamputations**

   These are also satisfactory amputations for distal gangrene with adequate perfusion of the hindfoot, and leave a patient with a weight-bearing heel.

5. **Syme's Amputation**

   This classical ankle amputation, first described by Syme in 1842, produces a durable weight bearing stump .It consist of a bone section at the distal tibia and fibula 0.6 cm proximal to the periphery of ankle joint and passing through the dome of ankle centrally.

6. **Below-Knee Amputations**

   These operations are most commonly performed for diabetic with peripheral arterial occlusive disease and the standard technique is designed to maximize the use of well-perfused tissue. It is not always possible to retain the ideal 15 cm of tibia, but if less than 8 cm can be retained there will be difficulty in fitting a satisfactory prosthesis.

7. Disarticulation Through The Knee

This amputation produces a stump which is functionally satisfactory and which can sustain end weight-bearing. A through-knee amputation has advantages in children in order to preserve final femoral length.

8. Above-Knee Amputations

These are common amputations for ischaemia . In general, the longer the stump the better the control of the prosthesis and ideally 70 per cent of the femur (or around 25–30 cm as measured from the tip of the greater trochanter) should be retained. [49]

METHODOLOGY

Source of data

All patients attending the surgery OPD and/or admitted patients in B.L.D.E.U's Shri. B. M. Patil Medical College, Hospital and Research Centre, Bijapur with diabetic foot ulcer during the period of October 2011 to May 2013 were taken for the study.

Method of collection of data

- Period of study was from October 2011 to May 2013.
- The patients were allocated to study group and control group alternatively.
- A Proforma was used to collect all the relevant data from the patients.
- Detailed history was taken, thorough clinical examination and investigations were performed for all the patients in both the study groups.
- All cases were followed up to discharge and subsequently for a follow up till wound healing.
- 'Primary efficacy end point' include complete ulcer closure. 'Secondary efficacy end points' include a reduction in ulcer surface area over a time or time to achieve ulcer closure by either skin grafting or secondary suturing.

Sampling

- Prospective, interventional study.
- A minimum of 30 cases each for the vacuum assisted closure dressings and normal gauze dressings which were allocated alternatively.
- The life time risk for a person with Diabetes developing foot ulcers is 15%.[2] The allowable error is 10%.
- Formula for estimating sample size :

$$n = \frac{z^2_{\alpha}\, pq}{E^2}$$

Where : n = Sample size to be estimated.

Z_{α} = Z value at α% level of significance

p = Prevalence rate.

q = 1 – prevalence

E = Allowable error is 10%.

- Calculated sample size was 51.
- In this study 60 cases were studied, in each group 30 cases which were allocated alternatively.

Statistical Analysis

- Statistical tools like measure of Central tendency and dispersion were used to describe the data .
- Statistics like Z statistics were used for the analysis of data and to draw valid conclusion.

Inclusion Criteria

- All cases of diabetic foot ulcers presented to the hospital during the study period with Wagner's grade 1 – 3.

Exclusion Criteria

- Diabetic patient with foot ulcers resulting from electrical, radiation burns and those with collagen vascular disease.
- Wagner's grade 4 and 5
- Patients on medications such as corticosteroids, immunosuppressive medications, or chemotherapy.
- Pregnant or nursing mothers.
- Diabetic foot ulcers with gangrene and osteomyelitis which need amputation.
- Cases of diabetic foot ulcers with skin cancer.

Procedure

Wounds were debrided till slough were removed. Glycerin gauze or magnesium sulfate or Vaseline gauzes were kept over the wound. Sterile foam were cut to the approximate size of the wounds with scissors and placed gently into position over wound area. The perforated drain tube was then located on the top of the foam and the second piece of foam placed over the top. For shallower wounds, a single piece of foam might be used and the drainage tube was inserted inside it.

The foam together with the few inches of the drainage tube and the surrounding area of healthy skin, was then covered with adhesive transparent membrane supplied.

FIGURE 1 : VACUUM SUCTION APPARATUS

The distal end of the drain was connected to the vacuum assisted closure unit which is programmed to produce the required level of negative pressure of wound (50-150mm of Hg)[14,22]. Once the vacuum was switched on, the air was sucked out of the foam causing it to collapse inwards drawing the edges of the wound with it. Fluid within the wound was taken up by the foam and transported into disposable container within the main vacuum unit.

OBSERVATIONS AND RESULTS

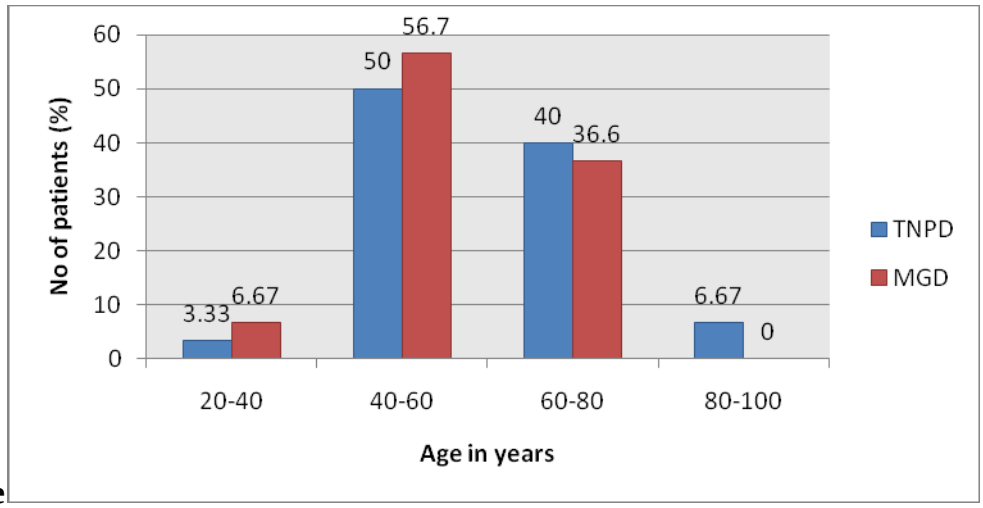
The 60 patients admitted for the study group were divided into two equal and comparable groups of 30 patients each, which were allocated alternatively. Patients were divided into two group classified as TNPD (Topical Negative Pressure Dressing) Group and MGD (Moist Gauze Dressing) Group . The patients characteristics in both the Groups were well matched as shown below

DISTRIBUTION OF PATIENTS ACCORDING TO AGE

TABLE NO 3: **Frequency and Percentage distribution of patients according to age.**

Age in years	TNPD		MGD		Total
	Frequency	Percentage	Frequency	Percentage	
20-40	01	3.33	02	6.67	03
40-60	15	50.0	17	56.7	32
60-80	12	40.0	11	36.6	23
80-100	02	6.67	00	00	02
Total	30	100	30	100	60

GRAPH NO 1: Percentage distribution of patients according to age



The mean age in TNPD Group was 61.3 years (Standard deviation of 11.6)

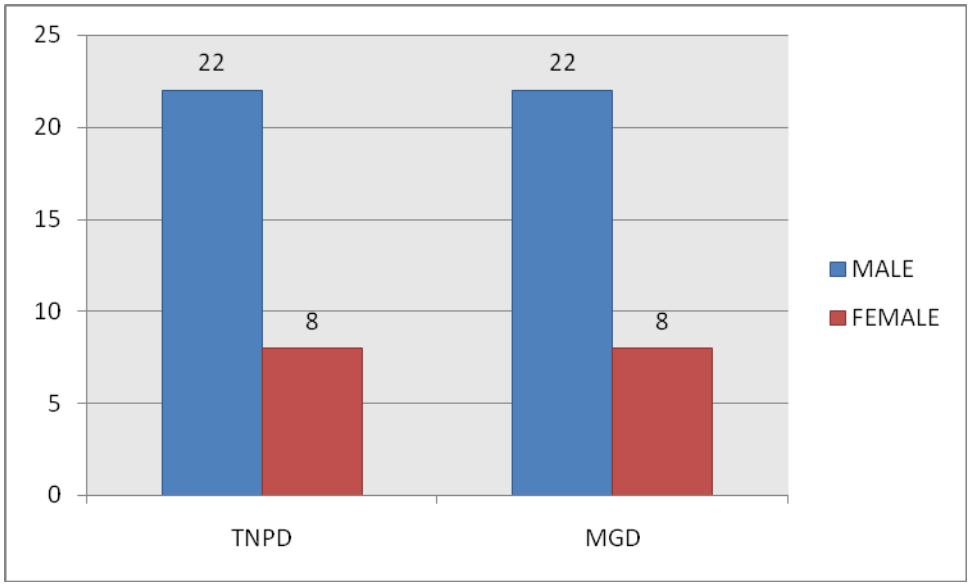
The mean age in MGD Group was 58.1 years (Standard deviation of 12.9)

DISTRIBUTION OF PATIENTS ACCORDING TO SEX

TABLE NO 4 : **Frequency and Percentage distribution of patients according to sex**

Sex	TNPD		MGD		Total
	Frequency	Percentage	Frequency	Percentage	
Male	22	73.3	22	73.3	44
Female	08	26.7	08	26.7	16
Total	30	100	30	100	60

GRAPH NO 2: Distribution of patients according to sex



Male : Female ratio in TNPD group was M : F 22: 8

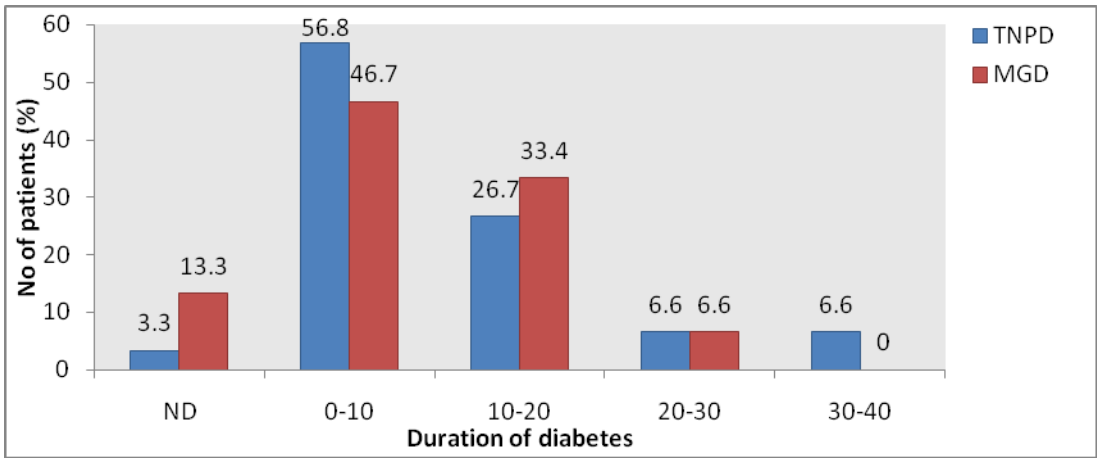
Male : Female ratio in MGD group was M : F 22: 8

DISTRIBUTION OF PATIENTS ACCORDING TO DURATION OF DIABETES

TABLE NO 5 :Frequency and Percentage distribution of patients according to duration of diabetes.

Duration in years	TNPD		MGD		Total
	Frequency	Percentage	Frequency	Percentage	
ND (Newly Detected)	01	3.3	04	13.3	05
0-10	17	56.8	14	46.7	31
10-20	08	26.7	10	33.4	18
20-30	02	6.6	02	6.6	04
30-40	02	6.6	00	00	02
Total	30	100	30	100	60

GRAPH NO 3: Percentage distribution of patients according to duration of diabetes.



All the patients in the study were suffering from diabetes of varying duration, with some on regular treatment and the others on irregular treatment. A few patients were detected of having diabetes upon admission to the hospital for their ulcers.

17 (56.7 %) of the patients in TNPD Group were suffering from diabetes for 0-10 years as compared to 14 (46.7 %) of the patients in MGD Group . The mean duration of suffering from Diabetes was 10.9 years in TNPD Group (Standard

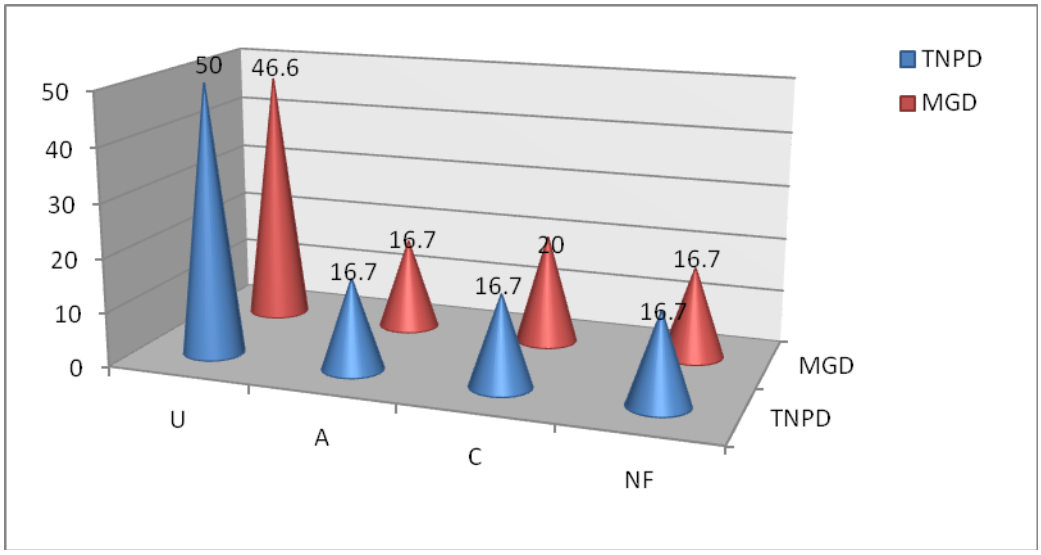
deviation of 8.15) when compared to 7.4 years in MGD Group (Standard deviation of 6.23).

DISTRIBUTION OF PATIENTS ACCORDING TO MODE OF PRESENTATION

TABLE NO 6 : Frequency and Percentage Distribution of patients according to mode of presentation.

Mode of presentation	TNPD		MGD		Total
	Frequency	Percentage	Frequency	Percentage	
Ulcer (U)	15	50.0	14	46.6	29
Abscess(A)	05	16.7	05	16.7	10
Cellulitis(C)	05	16.7	06	20.0	11
Necrotizing fasciitis(NF)	05	16.7	05	16.7	10
Total	30	100	30	100	60

GRAPH NO 4 : Percentage distribution of patients according to mode of presentation.



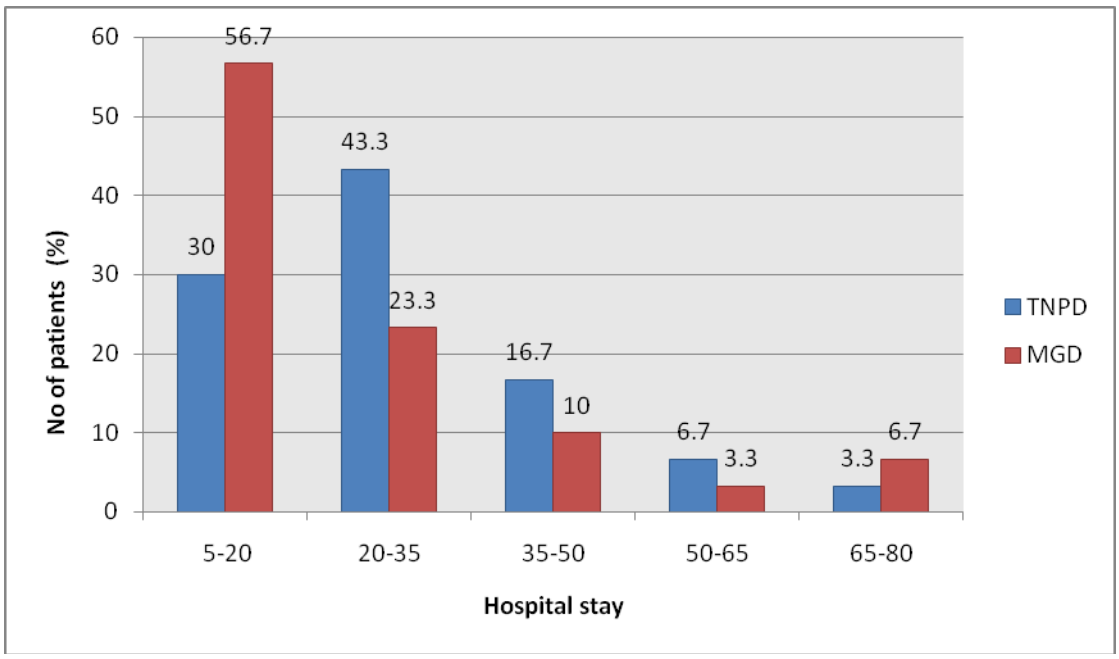
Ulcers were the most common form of presentation of diabetic foot in both TNPD (50%) and MGD (46.6%) group.

DISTRIBUTION OF PATIENTS ACCORDING TO HOSPITAL STAY

TABLE NO 7 : Frequency and Percentage distribution of patients according to days of hospital stay

	TNPD		MGD		
Days	**Frequency**	**Percentage**	**Frequency**	**Percentage**	**Total**
5-20	09	30.0	17	56.7	26
20-35	13	43.3	07	23.3	20
35-50	05	16.7	03	10.0	08
50-65	02	6.7	01	3.3	03
65-80	01	3.3	02	6.7	03
Total	30	100	30	100	60

GRAPH NO 5: Percentage distribution of patients according to days of hospital stay



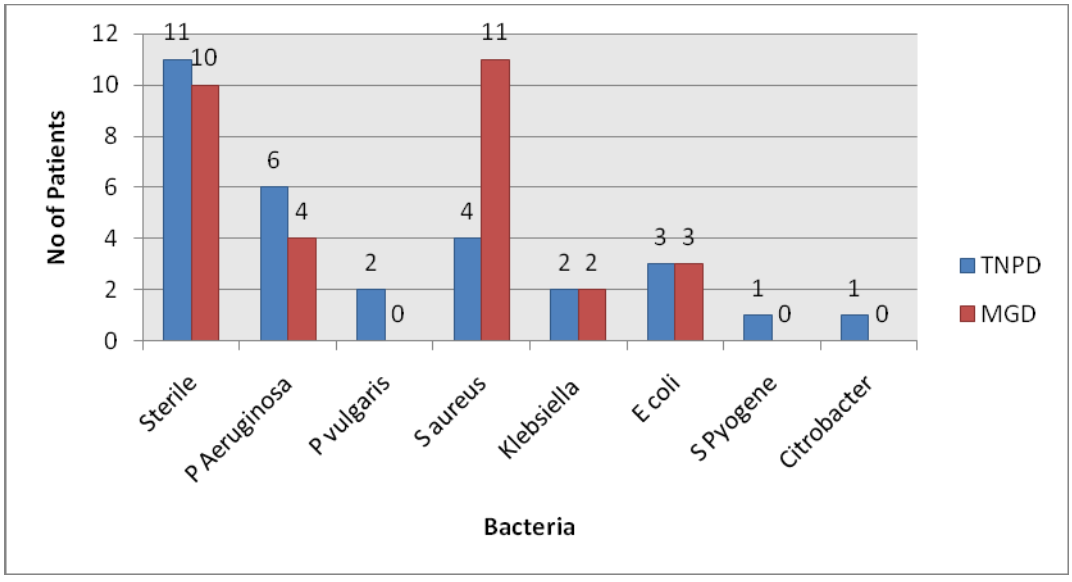
The mean hospital stay in TNPD Group was 29.4 days (Standard deviation of 15.8) and that on MGD Group was 23.3 days (Standard deviation of 15.5)

DISTRIBUTION OF PATIENTS ACCORDING TO BACTERIAL GROWTH ON CULTURE

TABLE.NO 8 : Frequency and Percentage distribution of patients according to Bacterial growth on culture

Bacteria	TNPD		MGD	
	Frequency	Percentage	Frequency	Percentage
Sterile	11	36.7%	10	33.3%
P Aeruginosa	6	20.0%	4	13.3%
P vulgaris	2	6.7%	0	0
S aureus	4	13.3%	11	36.7%
Klebsiella	2	6.7%	2	6.7%
E coli	3	10.0%	3	10.0%
S Pyogene	1	3.3%	0	0
Citrobacter	1	3.3%	0	0
Total	30	100.0%	30	100.0%

GRAPH NO 6: Distribution of patients according to Bacterial growth on culture in TNPD and MGD group



The discharge from the ulcers was analyzed to determine the most common organism causing the infection. In TNPD group culture showed no growth of organism on most of occassions. In MGD group Staphylococcus Aureus was the most common organism to be found on culture.

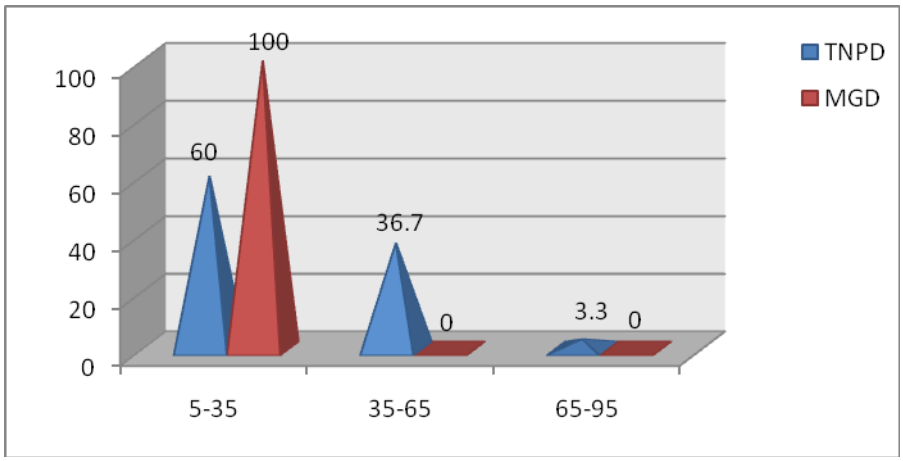
GRANULATION TISSUE FILL UP OF WOUNDS IN DAYS

The efficacy of the dressings was compared as the percent of ulcer surface area covered by granulation tissue such that complete skin closure could be achieved. Complete skin closure was defined as skin closure (100 % re-epitheliazation) without drainage or dressing requirements. The ulcer floor surface areas were inspected on the 7th, 14th, 21st and the 28th day for the percentage of granulation tissue covering the ulcer floor.

TABLE NO 9 : Granulation tissue fill up of wounds (%) in 7 days

Granulation fill up (%)	TNPD		MGD		Total	Test
	Frequency	Percentage	Frequency	Percentage		
5-35	18	60	30	100	48	Z value = 4.9 p-value 0.001
35-65	11	36.7	00	00	11	
65-95	01	3.3	00	00	01	
Total	30	100	30	100	60	

GRAPH NO 7: Percentage of Granulation tissue fill up of wounds in 7 days



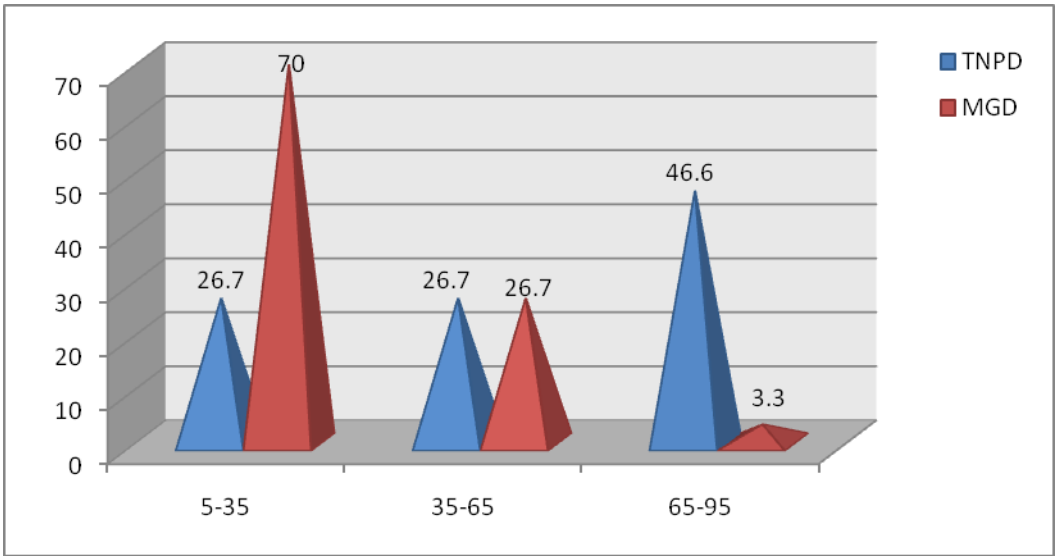
In our study after 7 days, it was seen that 18(60%) of patients in TNPD group had 5-35% of granulation tissue fill up, 11(36%) of patients had 35-65% of granulation tissue fill up and 1(3.3%) of patients had 65-95% of granulation tissue fill up,however in MGD group all 30(100%) of patients had only 5-35% of granulation tissue fill up.

This difference was found to be statistically significant (p value = 0.001) as per Table no 9.

TABLE NO 10 : Granulation tissue fill up of wounds (%) in 14 days

Granulation fill up (%)	TNPD		MGD			
	Frequency	Percentage	Frequency	Percentage	Total	Test
5-35	08	26.7	21	70.0	29	Z value = 4.8
35-65	08	26.7	08	26.7	16	
65-95	14	46.6	01	3.3	15	p-value 0.001
Total	30	100	30	100	60	

GRAPH NO 8: Percentage of Granulation tissue fill up of wounds in 14 days

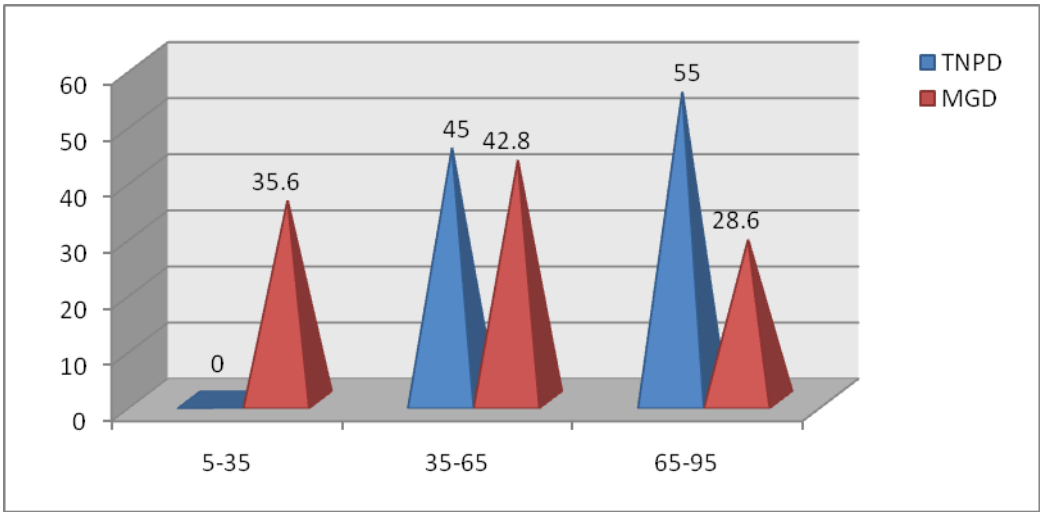


While studying granulation tissue fill up of wounds after 14 days ,it was seen that each 8(26.7%) of patients in TNPD group had 5-35% and 35-65% of granulation tissue fill up and 14(46.6%) of patients had 65-95% of granulation tissue fill up, while 21(70%) of patients in MGD group had 5-35% of granulation tissue fill up , 8(26.7%) of patients had 35-65% of granulation tissue fill up and 1(3.3%) of patients had 65-95% of granulation tissue fill up as per Table no 10. This difference was found to be statistically significant (p value = 0.001).

TABLE NO 11 : Granulation tissue fill up of wounds (%) in 21 days

Granulation fills up (%)	TNPD		MGD			Test
	Frequency	Percentage	Frequency	Percentage	Total	
5-35	00	00	10	35.6	10	
35-65	09	45.0	12	42.8	21	Z value = 3.04
65-95	11	55.0	08	28.6	19	p-value 0.001
Total	20	100	28	100	50	

GRAPH NO 9 :Percentage of Granulation tissue fill up of wounds in 21 days



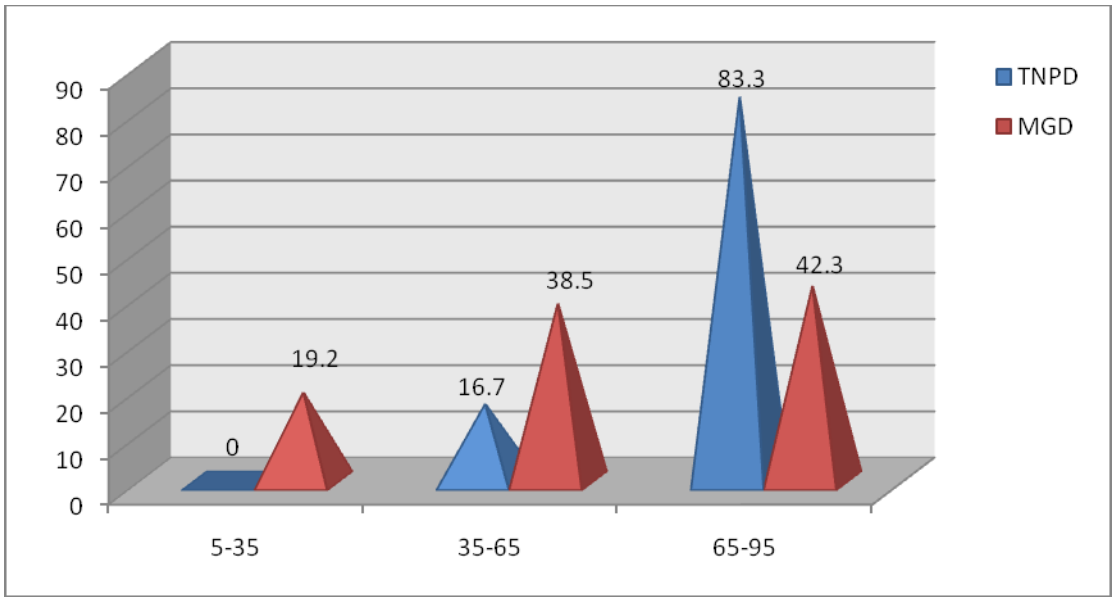
While studying granulation tissue fill up of wounds after 21 days ,it was seen that each 9(45%) of patients in TNPD group had 35-65% of granulation tissue fill up and 11(55%) of patients had 65-95% of granulation tissue fill up, While wound closure was achieved in 10 patients in TNPD group, they were excluded from this table no 11 .

10(35.6%) of patients in MGD group had 5-35% of granulation tissue fill up , 12(45%) of patients had 35-65% of granulation tissue fill up and 8(28.6%) of patients had 65-95% of granulation tissue fill up .This difference was found to be statistically significant (p value = 0.001)

TABLE NO 12 : Granulation tissue fill up of wounds (%) in 28 days

Granulation fills up (%)	Dressing					Test
	TNPD	Percentage	MGD	Percentage	Total	
5-35	00	00	05	19.2	05	Z value = 3.2 p-value 0.001
35-65	02	16.7	10	38.5	12	
65-95	10	83.3	11	42.3	21	
Total	12	100	26	100	38	

GRAPH NO 10: Percentage of Granulation tissue fill up of wounds in 28 days



18 patients in TNPD group and 4 patients in MGD group were excluded from this table no 10, as they have already achieved wound closure. Among 12 patients remaining in TNPD group 2(16.7%) of patients had 35-65% of granulation tissue fill up and 10(83.3%) of patients had 65-95% of granulation tissue fill up, while 5(19.2%) of patients in MGD group had 5-35% of granulation tissue fill up , 10(38.5%) of patients had 35-65% of granulation tissue fill up and 11(42.3%) of patients had 65-95% of granulation tissue fill up. This difference was found to be statistically significant (p value = 0.001)

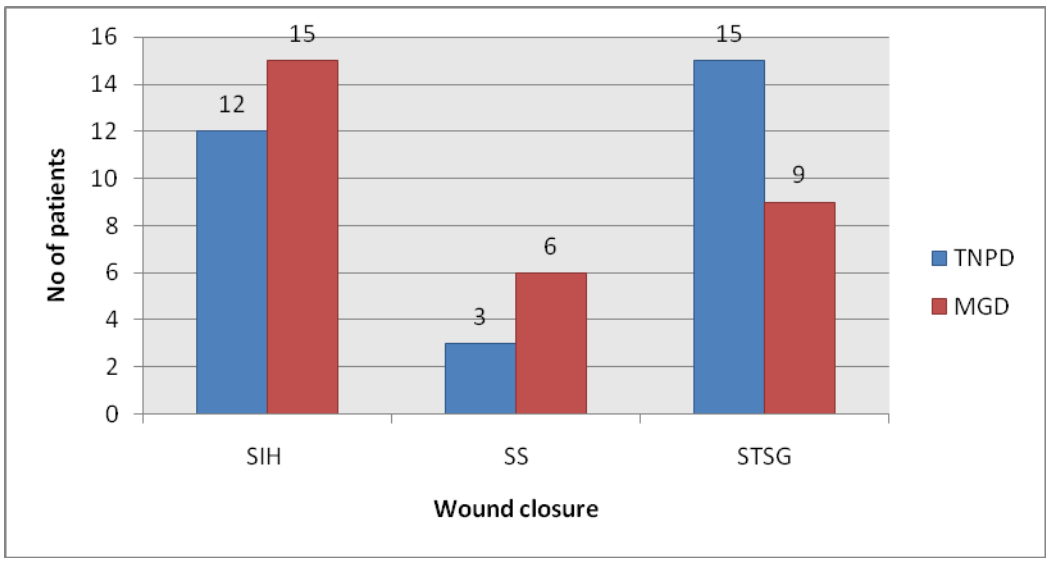
DISTRIBUTION OF PATIENTS ACCORDING TO WOUND CLOSURE

TABLE.NO 13 : Frequency and Percentage distribution of patients according to methods of wound closure

Wound closure	Dressing				
	TNPD	Percentage	MGD	Percentage	Total
SIH	12	40.0.	15	50.0	27
SS	03	10.0	06	20.0	09
STSG	15	50.0	09	30.0	24
TOTAL	30	100	30	100	60

SIH – Secondary intension healing, SS – Secondary suturing, STSG –Split thickness skin graft

GRAPH NO 11: Distribution of patients according to wound closure.



Upon complete appearance of granulation tissue, in some pattients wound were healed with secondary intension and in some patients surgical treatment in the form of Secondary Suturing, Split Thickness Skin Graft were done.

Patients in whom wounds were healed by secondary intension were taken as primary end point. Patients in whom wounds were healed by secondary suturing and STSG were taken as secondary end point. 12(40%) of patients in TNPD group and 15(50%) of patients in MGD group underwent SIH, While 3(10%) of patients in TNPD group and 6(20%) of patients in MGD group underwent SS. 15(50%) of patients in TNPD group and 9(30%) of patients in MGD group underwent STSG

DISTRIBUTION OF PATIENTS ACCORDING TO PERCENTAGE OF GRAFT UPTAKE

TABLE.NO 14 : Frequency and Percentage distribution of patients according to Graft uptake

Graft uptake(%)	Dressing				
	TNPD	Percentage	MGD	Percentage	Total
60-80	06	40	07	77.7	13
80-100	09	60	02	22.3	11
Total	15	100	09	100	24

GRAPH NO 12: Distribution of patients according to Graft uptake

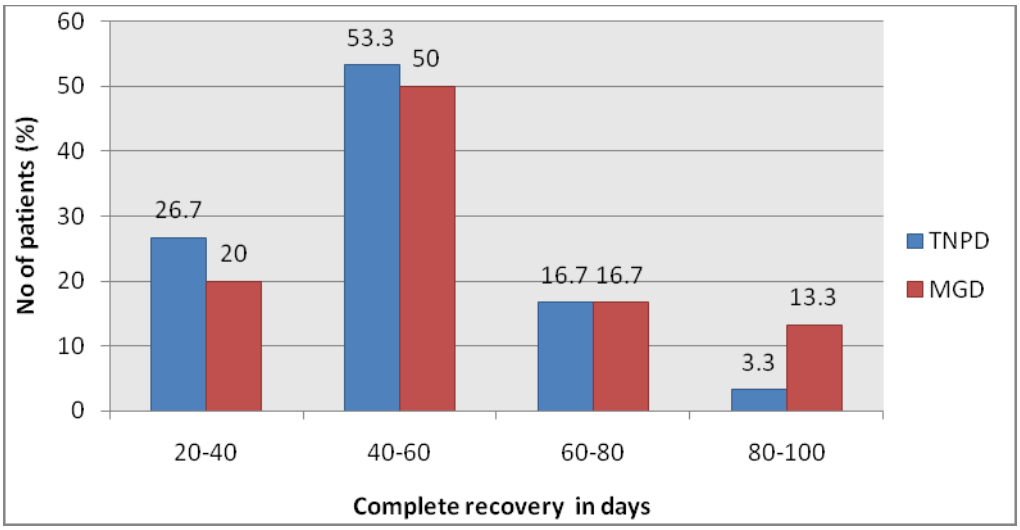
Among 30 patients in each group, 15 patients in TNPD group and 9 patients in MGD group underwent wound closure by STSG .Graft uptake in TNPD group were 80-100 % in 9 patients and 60-80 % in 6 patients, where as Graft uptake in MGD group were 80-100 % in 2 patients and 60-80 % in 7 patients.

DISTRIBUTION OF PATIENTS ACCORDING TO COMPLETE RECOVERY IN DAYS

TABLE.NO 15 :Frequency and Percentage distribution of patients according to Complete recovery in days

Complete recovery in days	Dressing				Total	Test
	TNPD	Percentage	MGD	Percentage		
20-40	08	26.7	06	20.0	14	Z value = 2.23
40-60	16	53.3	15	50.0	31	p-value 0.002
60-80	05	16.7	05	16.7	10	
80-100	01	3.3	04	13.3	05	
Total	30	100	30	100	60	

GRAPH NO 13: Percentage distribution of patients according to complete recovery in days



8(26.7%) of patients in TNPD group had recovery in 20-40 days , 16(53.3%) of patients in 40-60 days, 5(16.7%) of patients in 60-80 days, 1(3.3%) of patients in 80-100 days, while 6(20%) of patients in MGD group had recovery in 20-40 days , 15(50%) of patients in 40-60 days, 5(16.7%) of patients in 60-80 days and 4(13.3%) of patients in 80-100 days .

The mean recovery in TNPD Group was 49.1days (standard deviation of 11.94) and that on MGD Group was 56.56 days (standard deviation of 18.36). This difference was found to be statistically significant (p value = 0.002).

DISTRIBUTION OF PATIENTS ACCORDING TO FOLLOW UP AT FIRST WEEK

TABLE.NO 16 : Frequency and Percentage distribution of patients according to Follow up at first week

Follow up	Dressing					p-value
	TNPD	Percentage	MGD	Percentage	Total	
Good(G)	24	80.0	23	76.6	47	0.754
Satisfactory(S)	06	20.0	07	23.4	13	
Total	30	100	30	100	60	

GRAPH NO 14: Percentage distribution of patients according to follow up at first week

The patients in both the groups were followed up for 1 week post discharge. The wound were assessed at follow up after 7 days of discharge and were termed as good or satisfication depending on the status of wound. In TNPD Group 24 (80%) of the patients had a good uneventful recovery, 06 (20 %) had a satisfactory recovery, Whereas in MGD Group 23(76.6 %) had a good recovery, 7 (23.4 %) had a satisfactory recovery

DISCUSSION

The role of negative pressure dressing in healing of diabetic foot ulcers has been proposed as a novel method of manipulating the chronic wound environment in a way that it reduces bacterial burden and chronic interstitial wound fluid, increases vascularity and cytokine expression and to an extent mechanically exploiting the viscoelasticity of periwound tissues. VAC is generally well-tolerated and with few contraindications or complications, is fast becoming a mainstay of current wound care. Hence we planned to use NPWT for the treatment and fast healing of diabetic foot ulcers.

The demographical profile was statistically studied and found comparable with no much significant difference between the groups. The mean age of patients in TNPD group was 61.3years (Standard deviation of 11.6) and in MGD group was 58.1 years (Standard deviation of 12.9) which was comparable to the multicenter randomized controlled trial enrolling 342 patients done by Blume et al. who had a mean age of 58 years [14]. In a study done by Joseph et al mean age was 52.41 years in vacuum group and 53.2 years in control group[50]. In a study done by Nain et al. mean age of patients in study group was 61.33 ± 7.63 years and in control group was 55.40 years. [17]

The sex distribution in both TNPD group and MGD group were 73.3% males and 26.7 % female which was comparable to Blume et al study who had predominantly 78.5 % male[14]. Study done by Nain et al. had 79 % males[17].

Application of negative pressure over wound bed allows the arterioles to dilate, so increasing the effectiveness of local circulation, promoting angiogenesis,

which assists in the proliferation of granulation tissue. It was found that the patients on NPWD therapy had earlier appearance of granulation tissue. As the ulcers were compared for rate of formation of granulation tissue on the 7th, 14th, 21st, and the 28th day, the ulcers in the TNPD group showed evidence of granulation tissue on an earlier date than the MGD group.

Rate of granulation tissue formation in our study was 46.6% in TNPD group when compared to MGD group which was 3.3% on 14 th day and 83.3% in TNPD group when compared to MGD group which was 42.3% on 28 th day which was comparable to the study done by Joseph, et al who had 81.56% of granulation tissue formation in vacuum group and 54.3% in control group after 2 week [50].In a similar study done by Tauro,et al. had 71.43 % granulation tissue formation in vacuum group and 52.85% in control group[51] .A multicenter randomized controlled trial enrolling 342 patients done by Blume et al showed a 95% of granulation tissue formation[14]. When compared to similar study done by Nain et al.showed 75% of granulation tissue formation in vacuum group as compared to 30% in the control group by the end of 2nd week and this was also found to be statistically significant ($P<0.05$)[17].

We observed that patients of TNPD group showed rapid clearance of bacterial load as compared to MGD group. The decrease in the bacterial load could have been attributed to the antibiotic regimes administered during the study. Hence we were unable to eliminate this bias. However, In TNPD group culture showed no growth of organism on most of occasions after 2nd week . In MGD group Staphylococcus Aureus was the most common organism found on culture , when compared to study done by Nain et al. patients of vacuum group showed rapid clearance of bacterial load as compared to control group[17]. This was suggested by 40% of the cultures in study group having no growth by 3rd week as compared to 20% in control group. S.

aureus was found to be most prominent in vacuum group whereas cultures from control group mostly showed mixed growth and Acinetobacter .Study done by Moues et al had observed that nonfermentative Gram-negative bacilli showed a significant decrease in vacuum-assisted closure-treated wounds, whereas S. aureus showed a significant increase in VAC-treated wounds.

The endpoints were wound healed by secondary intension . or a wound ready for secondary suturing or skin grafting which ever was earlier.Both the groups had received similar treatment for the closure of wound, the most common mode of wound closure being STSG in TNPD group. It was also observed that the failure rate was higher in patients of control group as compared to TNPD group.Our study correlates with the study conducted by David Armstrong et al. who had observed that NPWT delivered by VAC device was safe and effective treatment for complex diabetic foot wounds and could lead to higher proportion of healed wounds, faster healing rates and potentially fewer re-amputations than standard care[19].

The graft uptake in TNPD group was 85.3 % and in MGD Group was 73%. Enhanced vascularity, reduced wound edema, reduced bacterial growth in the former group all favor better uptake of the graft, when compared with Peter A. Blume et al Graft uptake in vacuum group was 43.2% and in control group was 28.9% [14] .When compared with study done by Joseph et al graft uptake in vacuum group was 85.3 % and control group was 56.43% [50] .

A mean duration of hospital stay in the TNPD group was 29.4 days (Standard deviation of 15.8) as compared to 23.3 days (Standard deviation of 15.5) in MGD group which was found statistically not significant. When compared with Peter A. Blume et al 66.6 days in study group and 78.1 days in control group[14]. Study done by

Joseph et al hospital stay in vacuum group was 86.4 days and control group was 70.4 days [50].

The mean recovery i,e complete wound closure in TNPD group was 49.1 days (Standard deviation of 11.94) and that on MGD group was 56.56 days (Standard deviation of 18.36). Enhanced rates of wound healing, better wound conditions all favoring healing were seen in the TNPD group, thus a shorter duration of wound closure when compared to the latter group, However when compared with study done by Mc Callon et al. observed satisfactory healing in VAC group in 22.8 ± 17.4 days, compared to 42.8 ± 32.5 days in control group and study done by Blume et al. showed 100% ulcer closure in 96 days (95% CI 75.0–114.0) for Negative pressure wound therapy and not determinable for Advanced moist wound therapy ($P = 0.001$)[14] . Nain et al showed the time status of wound closure was comparable in both the groups ($P>0.10$), the study group showed faster rate of wound closure as compared to control group [17]. Post discharge follow up shows good result In TNPD group when compared with MGD group.

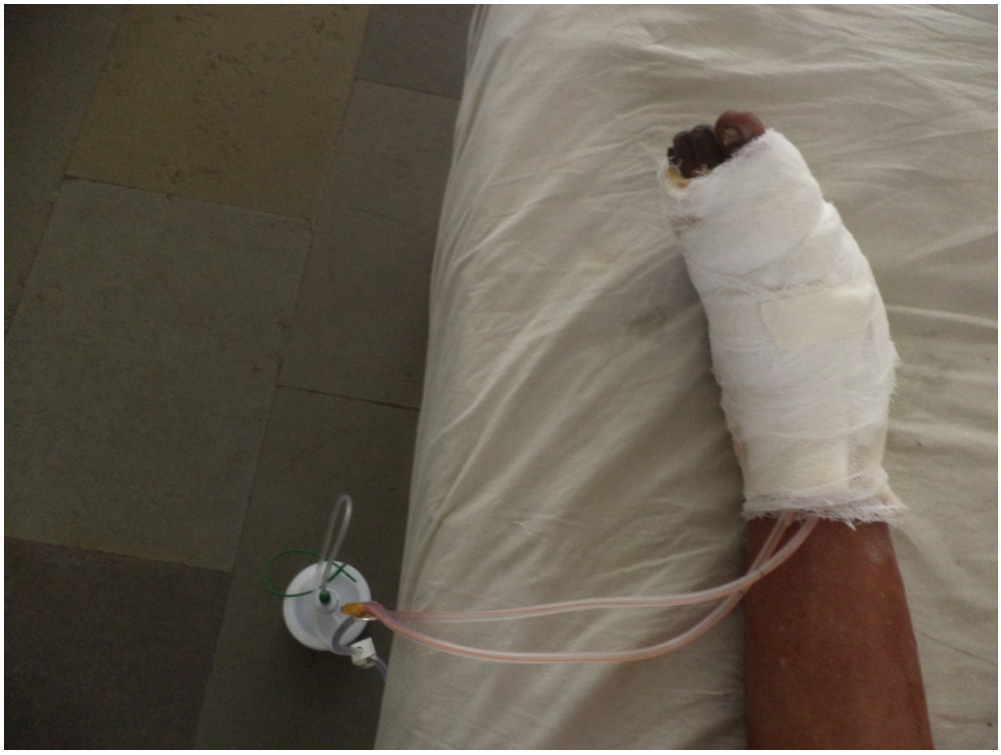


FIGURE 2 :APPLICATION OF NEGATIVE PRESSURE DRESSING

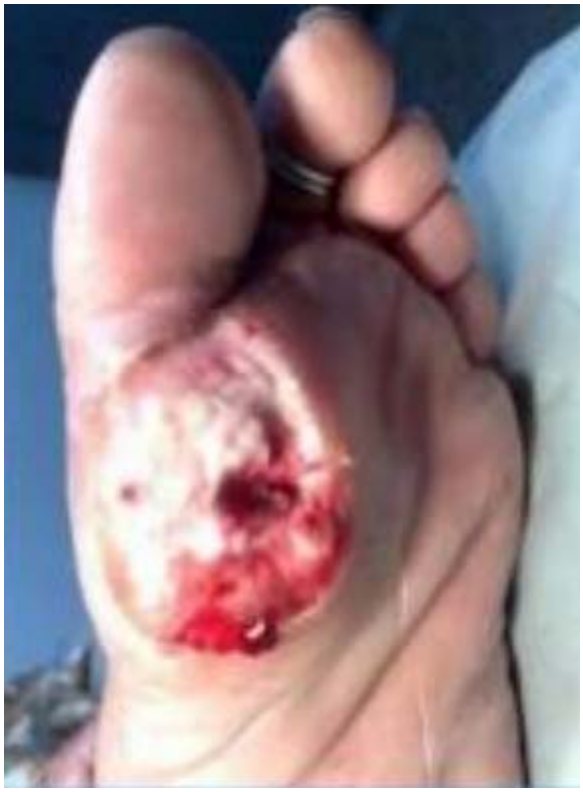


FIGURE 3 : ULCER ON 14 DAY AFTER APPLICATION OF TOPICAL NEGATIVE PRESSURE THERAPY

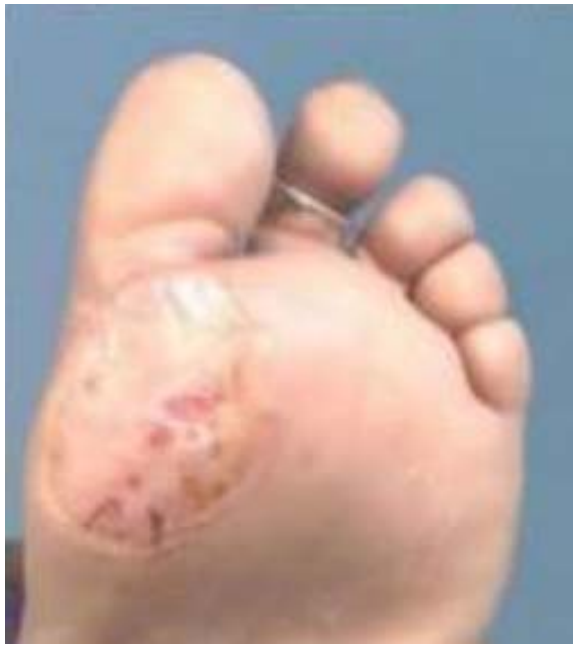


FIGURE 4 : HEALING BY SECONDARY INTENSION AFTER NEGATIVE PRESSURE THERAPY OF PATIENT AS SHOWN IN FIGURE 3

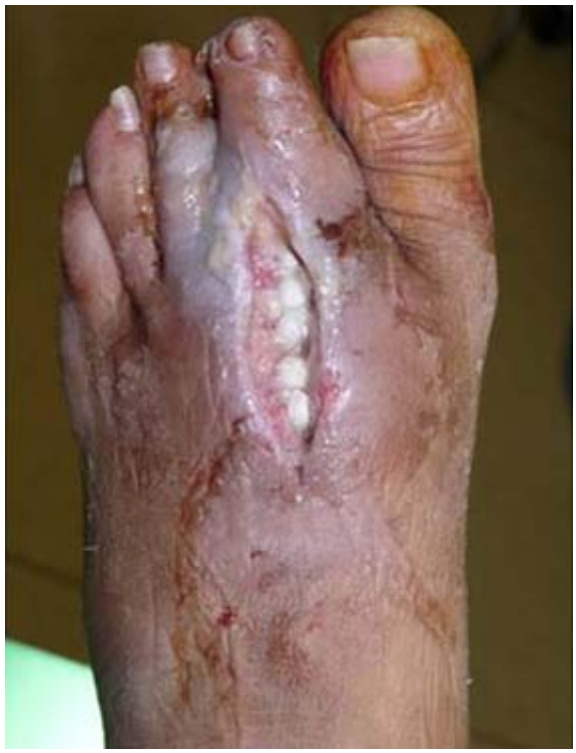


FIGURE 5 : POST INCISION AND DRAINAGE WOUND FOR ABSCESS OVER DORSUM OF FOOT

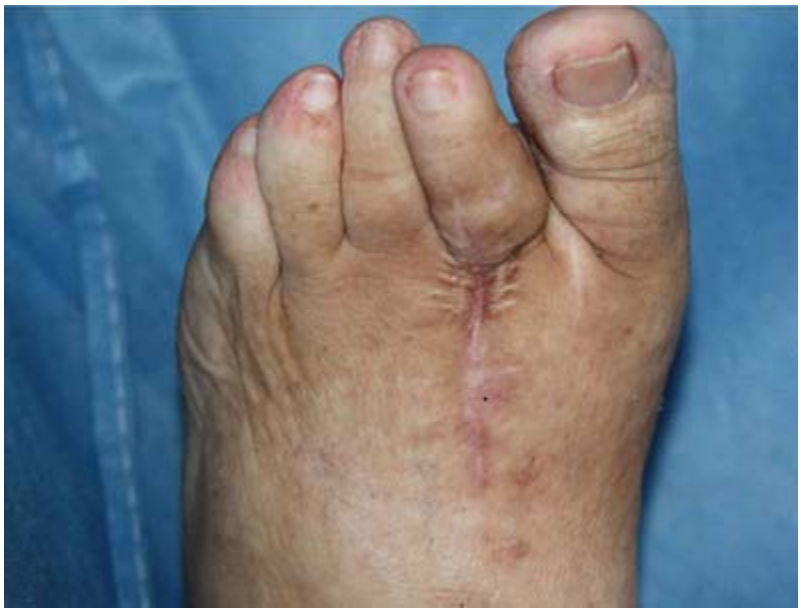


FIGURE 6 : HEALED WOUND AFTER SECONDARY SUTURING

FIGURE 7 : GRANULATION TISSUE APPERANCE AFTER 14 DAYS

FIGURE 8 : GRANULATION TISSUE APPERANCE AFTER 21 DAYS

FIGURE 9 : GRANULATION TISSUE APPERANCE AFTER 28 DAYS

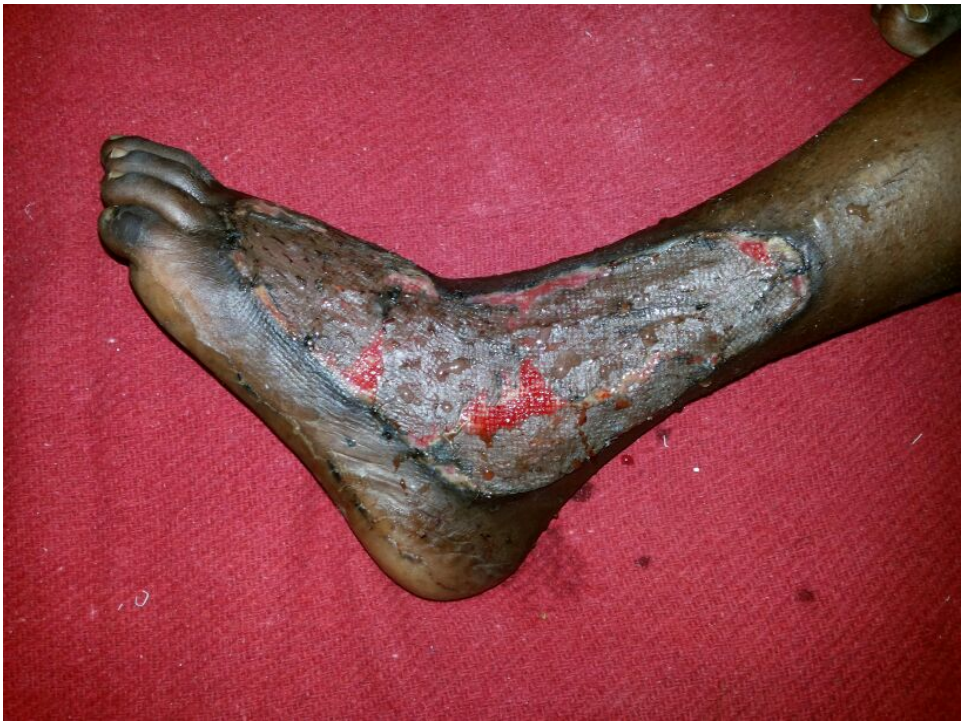


FIGURE 10 : WOUND AFTER PARTIAL THICKNESS SKIN GRAFT OF PATIENT SHOWN IN FIGURE 9

LIMITATIONS OF THE STUDY

The most important limitation of the present study is its sample size. A randomized controlled comparative study with a much larger population may help to further substantiate the findings or reveal variations which were not observed in the present study.

The financial burden on the patient is not analyzed in this study as this can be influenced by various factors other than the cost of the dressing.

Post operative parameters like wound contraction, pain and residual raw ulcer area were not included in the present study, which if included, might have given a much better analysis of the efficacy of topical negative pressure moist dressings as compared to conventional moist dressings.

SUMMARY

- Increased rate of formation of granulation tissue was seen in the topical negative pressure group when compared to the moist gauze dressings group.
- Better graft uptake was seen in the Topical Negative Pressure Group when compared to the moist gauze dressings group.
- Shorter duration of complete recovery was seen in the Topical Negative Pressure Dressing Group.
- Follow up observations revealed that topical negative pressure dressing group suffered lesser post skin grafting complications like wound contractures, residual raw area and pain compared to the moist gauze dressings group.
- The application of Topical Negative Pressure was found to be totally safe, free of any complication and easy to apply to the wounds.

CONCLUSION

In this study it was found that the application of Topical Negative Pressure increased the rate of formation of granulation tissue and had better graft uptake than the patients who underwent a moist gauze dressings for their ulcers. The patients in the study group had better patient compliance and had a shorter duration of complete recovery when compared to the control group. Thus, topical negative pressure moist wound dressing can be considered as a superior option in the management of diabetic foot ulcers. But further studies with larger population will be needed in the future before topical negative pressure dressing can be added to the wide spectrum of treatment modalities available in the management of diabetic foot.

BIBLIOGRAPHY

1. Ramachandran A, Das AK, Joshi SR, Yajnik CS, Shah S, Prasanna Kumar KM. Current status of diabetes in India and need for novel therapeutic agents. Supplement to JAPI 2010;58:7-9.
2. Pendsey SP. Understanding diabetic foot. Int J Diabetes Dev Ctries 2010; 30:75- 79.
3. Calhoun, Jason H, Overgaard C, Melinda BS, Dowling, James JF. "Diabetic Foot Ulcers and Infections: Current Concepts" Clinical Management Extra Diabetic Foot Ulcers 2000; 15:31-42.
4. Nain PS, Uppal SK, Garg R, Bajaj K, Garg S. Role of Negative Pressure Wound Therapy in Healing of Diabetic Foot Ulcers. Journal of Surgical Technique and Case Report Jan-Jun 2011 ; 3 :17-22 .
5. Nather A, Chionh SB, Han YY, Chan PL, Nambiar A. Effectiveness of Vacuum-assisted Closure (VAC) Therapy in the Healing of Chronic Diabetic Foot Ulcers. Ann Acad Med Singapore 2010;39:353–8.
6. Ethridge RT, Leong M, Phillips LG; Wound healing. In : Townsend CM, Beauchamp RD, Evers BM, Mattox KL, editors. Sabiston Textbook of surgery, 18th edn. Philadelphia : Elsevier ; 2008. p. 213
7. Seed , David L. "Foundations of good ulcer care". Am J of surg 1998; 176: 20S-25S.
8. WHO Prevention and control of diabetes mellitus, report of an Intercountry workshop , Dhaka Bangladesh 27-30 April 1998, SEA/NCD/40.
9. International Diabetes Federation. Time to Act: Diabetes and Foot Care.Brussels: International Diabetes Federation, 2005.

10. Laing, Patric. The development and complications of diabetic foot ulcers. Am J of surg 1998; 11S-19S.
11. Phillips, Pat, Evans, Angela, Popplewell, Phil et al . "Diabetic Foot Ulcers A Guide to Treatment" 2000; 1: 117- 123
12. Robson MC. Wound infection. A failure of wound healing caused by an imbalance of bacteria. Surg Clinics of North America 1997; 77 :637-50.
13. Van Gils, Carl C. et al. Amputation prevention by vascular surgery and podiatry collaboration in high risk diabetic and non diabetic patients .Diabetes care 1999; 22 : 678-683.
14. Blume PA, Walters J, Payne W, Ayala J, Lantis J. Comparison of negative pressure wound therapy using vacuum assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcer. Diabetic Care 2008;31 :631-636.
15. Nather A, Chionh SB, Han AY, Chan PL, Nambiar A. Effectiveness of vacuum assisted closure therapy in the healing of chronic diabetic foot ulcers. Ann Acad Med Singapore 2010;39:353-358.
16. Sepulveda G, Espindola M, Maureira M, Sepulveda E, Fernandez I, Olivnc. Negative-pressure wound therapy versus standard wound dressing in the treatment of standrd wound dressing. Cir Esp 2009;86 :171-177.
17. Nain PS, Uppal SK, Garg R, Bajaj K, Garg S. Role of negative pressure wound therapy in healing of diabetic foot ulcers. J Surg Tech 2011;3:17-22.
18. Venturi, Mark L; Attinger, Christopher E; Mesbahi, Ali N; Hess, Christopher L; Graw, Katherine S . Et al. Mechanisms and Clinical Applications of the Vacuum-Assisted Closure (VAC) Device. A Review. Wound healing 2005; 6 : 185-194.

19. David G Armstrong, Lawrence A Lavery. Negative pressure wound therapy after partial diabetic foot amputation : a multicentre randomized controlled trial. Lancet 2005; 366 : 1704 -1710.
20. Barbul A . Wound healing . In : Brunicards FC,Anderson DK,Billars TR,Dunn OZ, Hunter JG,Pollock RE , editors. Schwartz's principles of surgery, 8th edn. America :Mc Graw-Hill companies ; 2005. P. 223-224.
21. Drake RL, Vogl W, Mitchell A. Foot. Grays anatomy for students , 1st edn. Philadelphia : Elsevier ; 2005. p. 557-572.
22. Drake RL, Vogl W, Mitchell A. Foot. Grays anatomy for students , 1st edn. Philadelphia : Elsevier ; 2005. p. 573-579.
23. Barbul A . Wound healing . In : Brunicards FC, Anderson DK, Billars TR,Dunn OZ, Hunter JG, Pollock RE , editors. Schwartz's principles of surgery, 8th edn. America :Mc Graw-Hill companies ; 2005. P. 224-230.
24. Edmonds M.E, P.J.Watkins . " The Diabetic foot" in International textbook of diabetes mellitus. K.G.M.Alberti, p.Zimmet, R.A.Defronzo, 2nd edn , West Sussex, England: Johnwiley & sons.1997, p. 1657-1669.
25. Andros G, Lavery L . Diabetic foot ulcers . In : Cronenwett JL, Johnston WK, editors. Rutherfords vascular surgery, 7th edn. China :Elsevier ; 2010. p. 1735-1740.
26. Grunberg A,Davier H, Blair J. Diabetic gangrene. British Medical Journal 1951; 24: 1254-1257.
27. Laing P: "The development and complications of diabetic foot ulcers". Am J of surg 1998 ; 2A : 11S-19S.
28. Raj Mani et al editors. Chronic Wound Healing: Clinical Measurement and Basic Science. 1st ed. London: WB Saunders and Company; 2000.

29. Edmonds ME ,Foster AM, Sanders LJ ;The normal foot . A Practicle manual of diabetic foot care ,Massachusetts : Blackwell ; 2004. p. 19-141.
30. N. Katsilambros, E. Dounis, P. Tsapogas and N. Tentolouris. Anatomical risk factors for diabetic foot ulceration; Atlas of the Diabetic Foot :John Wiley & Sons 2003. p. 50-56.
31. Wagner FW. The dysvascular foot: a system for diagnosis and treatment. Foot Ankle 1981; 2: 64–122.
32. Edmonds, M.E., P.J.Watkins . The Diabetic foot, chapter-87 in International textbook of diabetes mellitus. K.G.M.Alberti, Zimmet, R.A.Defronzo, 2nd Edn, Vol.2, West Sussex, England: Johnwiley & sons.1997, p.1657-1669.
33. Golinko et al. Operative debridment of diabetic foot ulcers.J Am Coll Surg 2008;207:1-6.
34. Barie SP . Surgical infection and antibiotic use. In : Townsend CM, Beauchamp RD, Evers BM, Mattox KL, editors. Sabiston Textbook of surgery, 19th edn. Philadelphia : Elsevier ; 2012. p. 257.
35. Armstrong et al. It's Not What You Put On, but What You Take Off:Techniques for Debriding and Off-Loading the Diabetic Foot Wound . Clinical Infectious Diseases 2004; 39:S92–9.
36. Saad AZM, Khoo TL, Halim AS. Wound Bed Preparation for Chronic Diabetic Foot Ulcers. ISRN Endocrinology 2013;1-9.
37. Hilton JR, Williams DT, Beuker, Miller DR, Harding GR . Wound Dressings in Diabetic Foot Disease. Clinical Infectious Diseases 2004; 39:S100–104.
38. Brem, Harold M.D.; Sheehan, Peter M.D.; Rosenberg, Harvey J. B.A.; Schneider, Jillian S. M.S.; Boulton, Andrew J. M. M.D. Evidence-Based

Protocol for Diabetic Foot Ulcers reconstructive wound healing supplement. original articles: reconstructive June 2006; volume 117 : p. 193S-209S.

39. Edmonds ME ,Foster AM, Sanders LJ. The normal foot . A Practicle manual of diabetic foot care ,Massachusetts : Blackwell ; 2004. p.39.
40. Berendt AR . Counterpoint: Hyperbaric Oxygen for Diabetic Foot Wounds Is Not Effective. Clinical Infectious Diseases 2006; 43:193–8.
41. Alexiadou K, Doupis J. Management of Diabetic Foot Ulcers. Diabetes Ther 2012; 3: 8.
42. Alexiadou K, Doupis J. Management of Diabetic Foot Ulcers. Diabetes Ther 2012; 3:4:9-15.
43. Argenta LC, Morykwas MJ. Vacuum-assisted closure: a new method for wound control and treatment: clinical experience. Annals of Plastic Surg 1997; 38 : 563-577.
44. Fleischmann W, Strecker W, Bombelli M, Kinzl L. Vacuum sealing as treatment of soft tissue damage in open fractures. Unfallchirurg 1993; 96 : 488-92.
45. Mullner T, Mrkonjic L, Kwasny O, Vecsei V. The use of negative pressure to promote the healing of tissue defects: a clinical trial using vacuum sealing technique. Br J Plast Surg 1997; 50 : 194-99.
46. Morykwas MJ, Argenta LC, Shelton-Brown EI, et al. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. Ann Plast Surg 1997; 38: 553-562.
47. Falanga V. Growth factors and chronic wounds : The need to understand the microenvironment. J Dermatol 1992; 19: 667-72.

48. Gwan-Nulla DN, Casal RS. Toxic shock syndrome associated with the use of the vacuum assisted closure device. Ann Plast Surg 2001; 47: 552-4.

49. Farquharson M, Moran B; Surgery of bone and amputations . Farquaharsons Textbook of operative general surgery, 9th edn. Great Britan: Hodde education ; 2005. p.64-68.

50. Joseph E, Hamori CA, Bergman S, Roaf E, Swann NF, Gasper WA. A prospective randomized trial of vacuum-assisted closure versus standard therapy of chronic non-healing wounds. Wounds 2000; 12 : 60–67.

51. Tauro LF, Ravikrishnan J, Satish Rao BS, Shenoy HD, Shetty SR, Menezes LT. A comparative study of the efficacy of topical negative pressure moist dressings and conventional moist dressings in chronic wounds. Indian J of Plastic Surgery 2007; 40:133-40.

ANNEXURES

SAMPLE INFORMED CONSENT FORM
BLDEU'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, BIJAPUR- 586103

TITLE OF THE PROJECT - COMPARATIVE STUDY OF NEGATIVE PRESSURE WOUND THERAPY USING VACUUM ASSISTED CLOSURE WITH MOIST GUAZE DRESSING IN THE TREATMENT OF DIABETIC FOOT ULCERS.

PRINCIPAL INVESTIGATOR - DR. RAJ AHEMED

GUIDE - Dr. MANJUNATH.S.KOTENNAVAR
M.S. (GENERAL SURGERY)
PROFESSOR
DEPARTMENT OF SURGERY

Purpose of research:

I have been informed that this study is comparison of Negative Pressure Wound Therapy using vacuum closure dressing with Moist Guaze dressing. I have also been given a free choice of participation in this study. This study will help in proper understanding, regarding treatment outcome of Diabetic Foot Ulcers

Risk and discomforts:

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.

Benefits:

I understand that my participation in this study will have no direct benefits to me other than the potential benefits of diagnosis & treatment which is planned to reduce my pain. The major potential benefit is to find out which treatment is more effective.

Alternatives:

I understand that the two modes of treatment being studied are standard ways of treating my problem that is Diabetic foot ulcers.

Confidentiality:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code-key connecting name to numbers will be kept in a separate location.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

In the study understand the effectiveness of negative pressure wound therapy using vacuum assisted closure in comparison with moist guaze dressing is to be studied their relevant designated authority and the industrial sponsor are permitted to

have access to my medical record and to the data produced by this study for audit purposes however they are required to maintain confidentiality.

Request for more information:

I understand that I may ask more questions about the study at anytime. Dr. Raj Ahemed is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation.

If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.

Refusal or withdrawal of participation:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that Dr. Raj Ahemed may terminate my participation in the study after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or physical therapist, if this is appropriate.

Injury Statement:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study I am not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks and benefits to the best of my ability in patient's own language.

_____	_____	_____
Dr. Raj Ahemed	Dr. Manjunath S. Kotennavar	Date
(Investigator)	(Guide)	

Study subject consent statement

I confirm that Dr. Raj Ahemed has explained to me the purpose of research, the study procedures that I will undergo, and the possible risks and discomforts as well as benefits that I may experience in my own language. I have read and I understand this consent form. Therefore, I agree to give consent to participate as a subject in this research project.

_____ _____

Participant / Guardian Date

_____ _____

Witness to signature Date

SCHEME OF CASE TAKING:

Name:	CASE NO:
Age:	IP NO:
Sex:	DOA:
Religion:	DOD:
Occupation:	
Residence:	

Chief complaints with History of presenting illness

Past History:

- Diabetes mellitus
- Hypertension
- History of any drug intake

Personal History :	Diet	Appetite
	Sleep	Habit

Family History:

General Physical Examination

Vitals

PR:

BP:

RR:

Temp:

Local Examination

- Inspection:
  - Site
  - Size
  - Shape
  - Surrounding skin
  - Foot deformity

- Palpation

  - Sensation
  - Pulsation

Clinical diabetic foot Grading

Other Systemic Examination

- Respiratory System.
- Cardiovascular System.
- Central Nervous System
- Per Abdomen Examination.

Investigations

1) Blood: Hb% TC DC
   ESR BT CT
2) Urine: Albumin Sugar Microscopy Ketone bodies.

3) HIV: HBSAg:

4) Random blood sugar:
   Fasting blood Sugar Post prandial blood sugar.
5) Blood Urea Serum creatinine

6) Pus culture and sensitivity

7) Colour Doppler

8) X-ray foot – AP and Oblique view.

9) ECG.
10) Echocadiography whenever necessary.

Final Digonsis

Follow up :

1st Week
2nd Week
3rd Week
4th Week

Comments:

ETHICAL CLEARANCE CERTIFICATE

Ethical Committee BIJAPUR-586103 OUT WARD No 27/2011 Date 21-10-11 B.L.D.E. Shri B. M. PATIL Medical College

B.L.D.E. UNIVERSITY'S

SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 20-10-2011 *at* 10-30 am *to scrutinize the Synopsis/Research projects of postgraduate/undergraduate student/Faculty members of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis/Research project has been accorded Ethical Clearance.*

Title "Comparative study of negative pressure wound therapy using vacuum assisted closure with gauze dressing in the treatment of diabetic foot ulcers"

Name of P.G./U.G. student/Faculty member Dr. Raj Ahmed
Dept of Surgery.

Name of Guide/Co-investigator Dr. M.S. Kotennavar Assoc Prof. Surgery.

DR.M.S.BIRADAR,
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.
Chairman
Ethical Committee
BLDEA'S Shri. B.M. Patil
Medical College
Bijapur-586103

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

KEY TO THE MASTER CHART

IP. NO	: In Patient Number
DOA	: Date Of Admission
DOD	: Date Of Discharge
TNPD	: Topical Negative Pressure Dressing
MGD	: Moist Gauze Dressings
U	: Ulcer
A	: Abscess
C	: Cellulites
G	: Gangrene
P Aeruginosa	: Pseudomonas Aeruginosa
P vulgaris	: Proteus vulgaris
S aureus	: Staphylococcus aureus
S Pyogene	: Streptococcus Pyogenes
SIH	: Secondary Intention Healing
SS	: Secondary Suturing
STSG	: Split Thickness Skin Graft
G	: Good
S	: Satisfactory

Master Chart Group - II (MOIST GAUZE DRE

Sl. No	NAME	AGE IN YEARS	SEX	IP NO	DOA	DOD	DAYS	MODE OF PRESENTATION	DURATION OF DIABETES	BACTERIA GROWN ON CULTURE	GRANUL C
											7 d
1	Gurubasappa	55	M	171	03/01/12	21/01/12	19	U	12 yr	Sterile	5
2	Veerapakashppa	63	M	649	09/01/12	27/01/12	19	A	14 yr	S Aureus	15
3	Shivamma	70	F	3243	08/02/12	27/02/12	20	U	3 yr	Sterile	30
4	Nandabasappa	75	M	3670	14/02/12	24/02/12	11	A	ND	E Coli	5
5	Shivabasappa	65	M	5950	14/03/12	28/03/12	14	C	ND	S Aureus	30
6	Mallikarjun	45	M	9450	05/04/13	18/04/13	14	C	3 yr	Klebsiella	20
7	Shrimanth	55	M	11132	21/04/13	30/04/13	10	A	ND	S Aureus	5
8	Basavaraj M	59	M	159339	12/05/12	19/07/12	68	U	5 yr	P Aeruginosa	5
9	Shivanagouda	66	M	13438	19/06/12	07/07/12	19	U	15 yr	S Aureus	5
10	Prakash	22	M	14138	27/06/12	01/09/12	65	NF	5 yr	S Aureus	5
11	Laxmibai	56	F	14118	27/06/12	03/07/12	8	U	25 yr	Sterile	20
12	Suresh B	49	M	15241	11/07/12	14/08/12	34	U	3 yr	S Aureus	5
13	Shankargouda	60	M	15930	27/07/12	11/09/12	22	C	7 yr	P Aeruginosa	5
14	Yamannawwa	59	F	21726	26/09/12	05/10/12	10	U	12 yr	Sterile	15
15	Ramachandra	70	M	18132	16/08/12	16/09/12	30	U	10 yr	Sterile	20
16	Mahadevappa	42	M	18388	19/08/12	26/08/12	8	U	5 yr	Sterile	15
17	Sonabai	45	F	23816	19/10/12	30/10/12	12	U	10 yr	Sterile	30
18	Mudugouda	70	M	22602	06/10/12	22/11/12	37	NF	ND	Sterile	10
19	Boramma	60	F	23478	16/10/12	06/11/12	20	NF	10 yr	E Coli	5

20	Mallappa T	50	M	23816	19/10/12	30/10/12	12	C	10 yr	E Coli	5
21	Bhimappa	75	M	24666	30/10/12	09/11/12	10	U	15 yr	S Aureus	10
22	Monappa	60	M	848	09/01/13	23/01/13	15	U	4 yr	Sterile	5
23	Rajakumar	34	M	2272	25/01/13	11/03/13	44	C	2 yr	P Aeruginosa	5
24	Sarojani	50	F	3603	08/02/13	18/03/13	40	U	4 yr	S Aureus	20
25	Shantaram	75	M	4838	21/02/13	12/03/13	22	NF	20 yr	P Aeruginosa	30
26	Bhimanagouda	80	M	7062	13/03/13	23/03/13	11	A	3 yr	Sterile	20
27	Maheboobi	50	F	7134	14/03/13	30/03/13	17	NF	7 yr	Klebsiella	5
28	Shantabai	55	F	11635	27/04/13	03/07/13	67	C	12 yr	S Aureus	5
29	Nijaguni	58	M	11083	20/04/13	17/05/13	28	A	6 yr	S Aureus	5
30	Kadarsab	70	M	11329	23/04/13	01/05/13	9	U	5 Mth	S Aureus	5

SSING)

.ATION TISSUE FILL UP (%))F WOUND IN DAYS			WOUND CLOSURE BY	PERCENTAGE OF GRAFT UPTAKE	DURATION OF COMPLET RECOVERY IN DAYS	FOLLOW UP AT 1ST WEEK
14 d	21 d	28 d				
10	30	50	STSG	60	89	G
25	50	60	SIH	-	60	G
50	65	80	SIH	-	40	G
15	25	40	SIH	-	52	G
60	70	85	SIH	-	54	G
50	90	-	STSG	75	32	G
25	50	75	STSG	80	46	S
15	40	50	SS	-	78	G
20	40	70	SIH	-	50	G
15	30	40	SS	-	84	G
40	85	-	SIH	-	46	G
15	30	55	SIH	-	50	S
10	25	30	SIH	-	78	G
35	50	60	STSG	60	52	G
45	60	80	SS	-	50	G
35	60	85	SS	-	60	S
60	90	95	SIH	-	36	G
20	30	50	SIH	-	66	S
25	50	75	STSG	75	60	G

5	10	30	STSG	90	56	G
30	90	-	STSG	85	46	G
35	70	90	SIH	-	37	S
30	45	65	SS	-	58	G
45	60	70	SIH	-	22	G
70	90	-	STSG	60	30	G
50	70	80	STSG	75	44	S
10	10	15	SS	-	92	G
10	15	30	SIH	-	76	G
10	15	20	SIH	-	86	G
20	45	50	SIH	-	67	S