COMPARATIVE STUDY OF THE OUTCOME OF ANTIBIOTIC COATED COLLAGEN GRANULES VS ANTIBIOTIC DRESSING IN CHRONIC ULCERS

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MAY 2020

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I hereby declare that the dissertation entitled **"COMPARATIVE STUDY OF THE OUTCOME OF ANTIBIOTIC COATED COLLAGEN GRANULES VS ANTIOBIOTIC DRESSING IN CHRONIC ULCERS**" is a bonafide and genuine research work carried out by me under the guidance of **Dr.V.SELVRAJ M.S.,DCH** Professor, Department of General Surgery, Madurai Medical College, Madurai. The Tamil Nadu Dr. M.G.R. Medical University, Chennai shall have the rights to preserve, use and disseminate this dissertation in print or electronic format for academic/research purpose.

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INTROUDCUTION

Wound Healing is a dynamic process involving soluble mediators, a variety of cells, and extracellular matrix. Wound result from precise disruption of tissue by the surgeon's knife (incision) to widespread damage of tissue (e.g. major trauma, burns). It also results from a contusion, hematoma, laceration or an abrasion. The continuity of the skin must be restored expeditiously because it plays a crucial role in maintaining homeostasis.

Wounds that are difficult to treat includes diabetic ulcers, venous ulcers, trophic ulcers, pressure sores and necrotizing fasciitis. An ideal dressing used in the wound management should be economical, easy to apply, readily available that will provide good pain relief, protect wound from infection, promote healing, keep moisture, be elastic, and non - antigenic and adhere well to the wound and waiting for spontaneous epithelisation and healthy granulation tissue.

Among newer type of wound dressings - Biological Dressings Like Collagen create the most physiological interface between the wound surface, environment and impermeable to bacteria. 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 remodelling are essential to the functional integrity of the wound.

Collagen granule dressing has better advantage over conventional dressing in terms of collagen formation with greater reduction in inflammatory cells during

healing days resulting in decreased days of healing, whereas conventional dressing has minimal collagen formation, high grade of inflammation during the healing days with maximum exudates formation resulting in increased days of healing. A collagen granule dressing has another advantage over conventional dressing in terms of non- immunogenic, non- pyrogenic, being natural, easy application, hypo allergic and pain free.

AIM OF THE STUDY

To compare the efficacy of antibiotic coated collagen granule dressings and conventional antibiotic dressing in chronic wounds in terms of

- Reduced wound healing time,

- Requirement of SSG,

- Size of the ulcer.

- **Design of study** : Prospective (case control) study
- **Period of study** : 1 year.
- **Selection of study** : Patients presenting with the ulcers of duration more than 6 weeks.
- **Data collection** : Data collected included patient's details, physical status and clinical profile.
- **Methods** : Randomized
- **Participants** : OPD or casualty patients presenting with Chronic ulcers.

INCLUSION CRITERIA

All non-healing chronic ulcers are included like diabetic ulcers, traumatic ulcers, pressure sores, amputation stump ulcers, post-surgical wound gaping of at least 6 weeks duration.

EXCLUSION CRITERIA

1. Ulcers having bone exposed raw area.
2. Malignant ulcers, ulcers with reduced vascularity.
3. Patients with connective tissue disorders and immune system disorders.
4. Patients on immunosuppressive drugs, steroids, chemotherapy and radiotherapy.
5. Patients with any known allergy to the dressing materials.

MATERIALS AND METHODS

- Patients presenting with chronic ulcers in GRH, Madurai OPD and casualty will be selected in this study.
- Following consent, a questionnaire will be filled to record the patient`s demographic data, duration of disease and other treatment details.
- This is a prospective study comprising of chronic ulcer patients.
- Patients were categorised into 2 groups A (study group) and B (control group).
- Complete blood count, renal function tests, serum proteins and pus culture and sensitivity will be sent.
- All the patients will be started on empirical intravenous antibiotic and changed after obtaining the culture report.
- One group received collagen granule dressing and the other one received the conventional antibiotic dressing with metronidazole and povidone iodine-soaked gauzes.
- In study group A after giving a saline wash collagen granules are applied and the wound dressing done.

- In control group after giving thorough wound wash antibiotic dressing is done with povidone iodine and metronidazole.
- Wound will be inspected after 3 days.
- Wound surface area will be measured before and after the application of collagen granules dressing and documented.
- Wound surface area will be measured with the help of a paper with multiple squares each having a surface area of 1 sq. cm.
- Wound surface area will be noted down in the proforma.

Wounds will be assessed for:

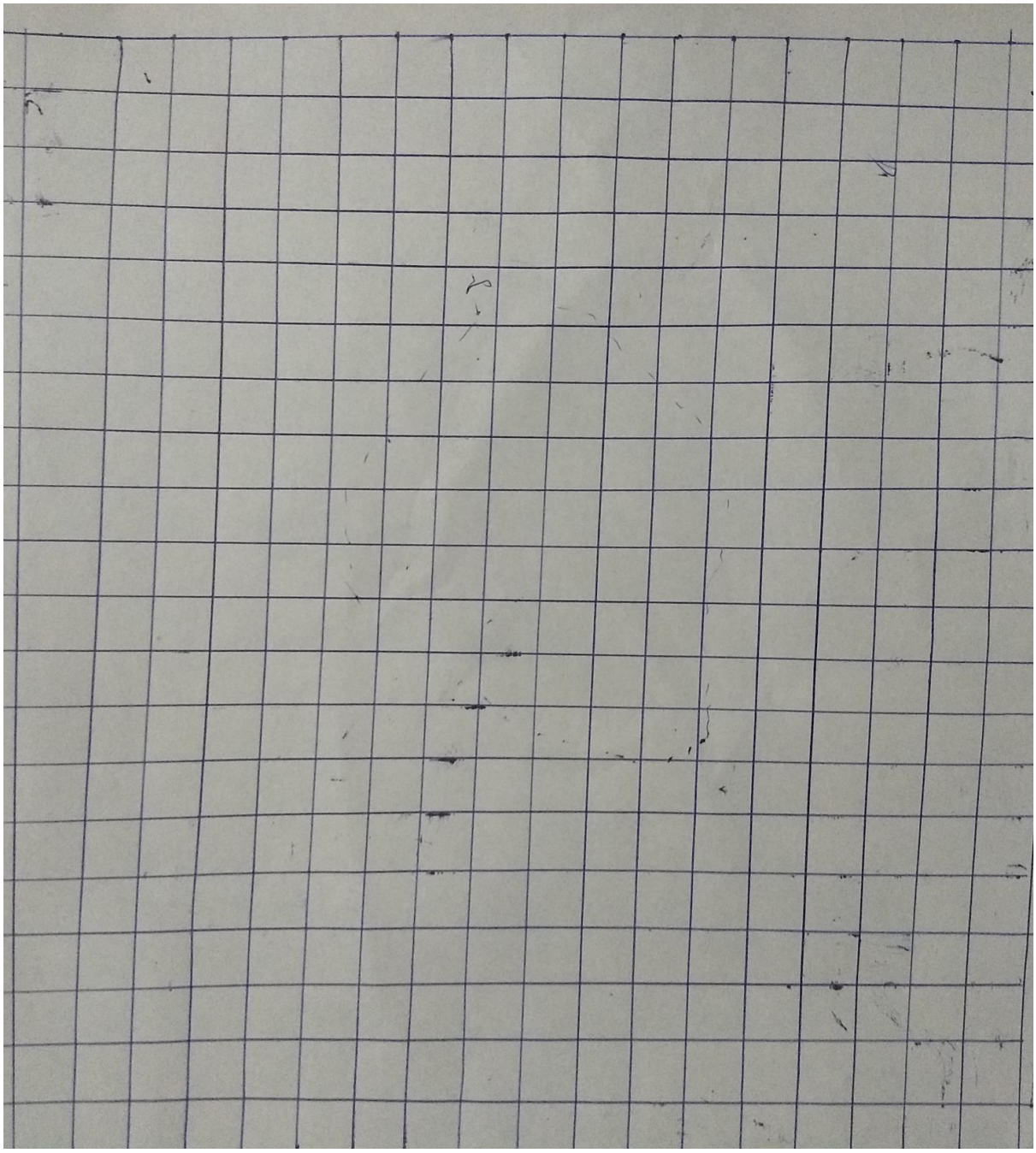
- reduction in surface area

- decreased time duration between the first debridement and skin cover with grafting.

- decreased need for skin grafting in small wounds.

- reduced hospital stays.

Figure 1: Wound surface area assessment



- Each box corresponds to 1 square cm.

- Wound surface area will be measured before and after each dressing.

REVIEW OF LITERATURE

HISTORICAL BACKGROUND OF WOUND HEALING

- The treatment and healing of wounds are the oldest topics discussed in the medical literature and probably earliest problems of human race.
- Early surgeons like Ambrose, Pare, John Hunter, & Sir James Paget have given some scientific knowledge to their handling of wounds, particularly those resulted from war.
- Halsted was intensely interested in wound healing process.
- In the early 1900's Carrel & his associates made investigations with the scientific approach to wound healing. Later Carrel (1916), Harvey & Howe's (1930), studied incised wounds & contributed to the knowledge of wound healing.
- There is a saying; "If there were no regeneration, there would be no life; if everything regenerated, then, there would be no death".
- The earliest medical writings deal extensively with wound care. Seven of the 48 case reports included in the Edwin Smith Papyrus (1700 BC) describe wounds and their management.
- Empirically, in Egypt, Greece, India and Europe, the physicians developed gentle methods of treating wounds by removing foreign bodies, suturing, covering wounds with clean materials, and protecting injured tissues from corrosive agents

- More than 4000 years ago, the theory of the "three healing gestures" was formed, with earliest writing recorded on a clay tablet from 2200 BC.

  The tablet describes the three gestures as:

- wound washing
- plasters over the wound
- application of bandage over the wound
- These gestures evolving into varying forms of today's same basic themes. The Greeks belief of dry healing came from Hippocrates, at a time when the only function of dressings was thought to be the protection of the wound from injury.
- During the fourteenth century, with the widespread use of gunpowder and the increasing frequency of bullet wounds, there was an increased need for surgeons assuming an aggressive posture, which was often done at the expense of aseptic precautions. Examples included applications of burning oil, scalding water, wine, turpentine, feathers, sugar, clay, bismuth, milk of magnesia to wounds. However, none of these have proven efficacy leased on sound scientific studies.
- The modern era of gentle wound care started in the mid-sixteenth century, when Ambroise Pare, the great French army surgeon, who during the Battle of Villaine, applied milder agents like digestive

solution of egg yolk, rose oil, honey and turpentine to amputation stumps with dramatic results.

- John Hunter, William Stewart Halsted, Alexis Carrel and many other great clinical biologists demonstrated that minimizing tissue injury produces rapid and effective healing leading to the "minimal interference" concept of wound care. If the surgeon can remove all impediments, normal wound healing process will produce the best possible result.
- Joseph Lister advocated cleanliness in the hospital, the frequent use of soap and water on wounds and carbolic acid dressings of contaminated wounds. Later Semmelweis, Ehrlich, Fleming, and Florey also realized that bacteria were pathogens. Control of bacteria by asepsis, antiseptics and antimicrobials heralded a new era in wound management.
- Finally it is apt to say that advances of the previous decades are only a prelude to the changes in wound care management that will occur in the coming decades.

PHASES OF NORMAL WOUND HEALING

Acute wounds are a common health problem. Typically, acute wound healing is a well-organized process leading to predictable tissue repair where platelets, keratinocytes, immune surveillance cells, microvascular cells, and fibroblasts play key roles in the restoration of tissue integrity. The wound repair process can be divided into 4 temporarily and spatially overlapping phases: coagulation, inflammation, formation of granulation tissue (proliferative phase), and remodelling or scar formation phase (figure 1).

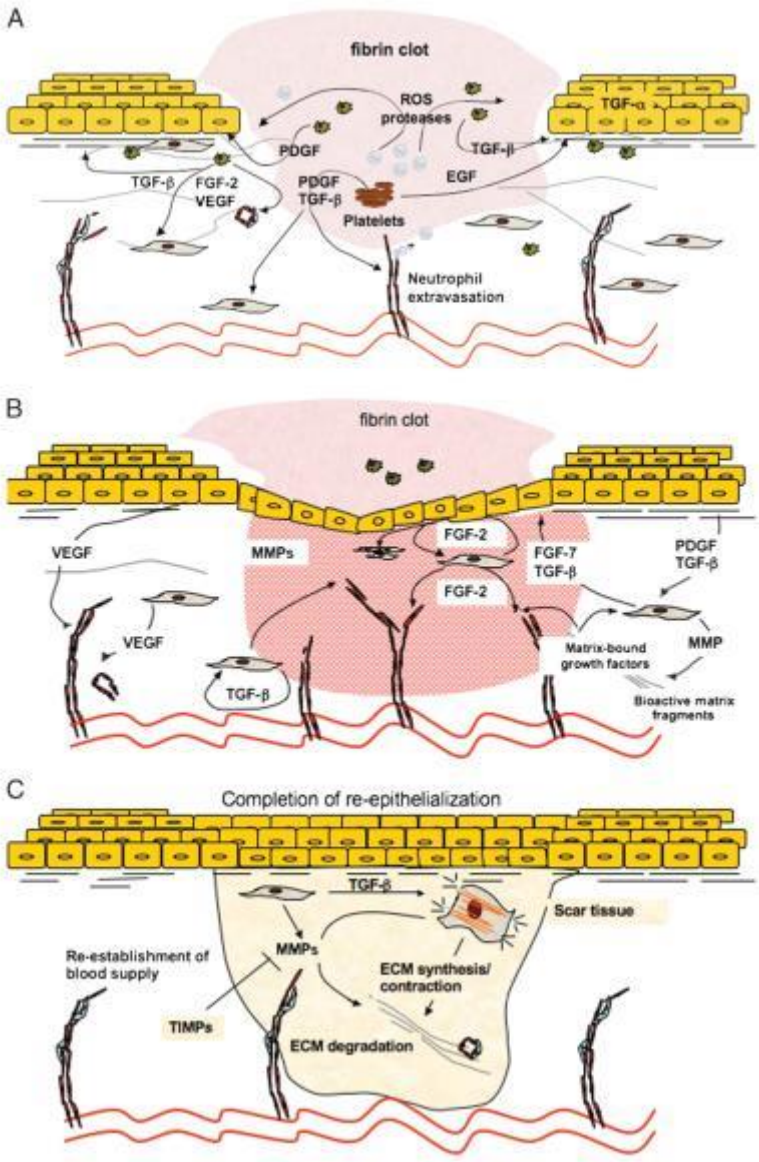


Figure 2

MECHANISMS OF NORMAL WOUND HEALING:

Normal wound healing processes can be divided into 4 overlapping phases: coagulation (not shown), inflammatory phase (A), proliferative phase/granulation tissue formation (B), and remodelling phase (C).

COAGULATION/INFLAMMATORY PHASE:

Immediately after injury, platelets adhere to damaged blood vessels, initiate a release reaction, and begin a haemostatic reaction, giving rise to a blood-clotting cascade that prevents excessive bleeding and provides provisional protection for the wounded area (FIGURE 1). As has been well studied, blood platelets release well over a dozen growth factors, cytokines, and other survival or apoptosis-inducing agents. Key components of the platelet release reaction include platelet-derived growth factor (PDGF) and transforming growth factors A1 and 2 (TGF-A1 and TGF-2), which attract inflammatory cells, such as leukocytes, neutrophils, and macrophages. As leukocytes are phagocytic cells, they release reactive oxygen species (ROS) that are antimicrobial and proteases that clear the wound of foreign bodies and bacteria. Resolution of the inflammatory phase is accompanied by apoptosis of inflammatory cells, which occurs gradually within a few days after wounding. The mechanism for resolution of inflammation is currently unknown. However, studies suggest that anti-inflammatory cytokines, such as TGF-A1 and interleukin 1, and bioactive lipids, such as cyclopentenone prostaglandin, lipoxins, and resolvins, take part in this process. The exact role of these entities during inflammatory phase resolution is under investigation.

PROLIFERATIVE PHASE: GRNULATION TISSUE FORMATION

As the inflammatory phase subsides, the proliferative phase of repair begins. At this stage, growth factors produced by remaining inflammatory cells and migrating epidermal and dermal cells act in autocrine, paracrine, and juxtacrine fashion to induce and maintain cellular proliferation while initiating cellular migration; all these events are required for the formation of granulation tissue while supporting epithelialization. As dermal and epidermal cells migrate and proliferate within the wound bed, there is a frank requirement for an adequate blood supply for nutrient delivery, gas, and metabolite exchange. Therefore, for wound healing to progress normally, a robust angiogenic response must be initiated and sustained.

Wound healing angiogenesis begins immediately after injury when local hypoxia, secondary to injury-induced blood vessel disruption, occurs. This event fosters the production of proangiogenic factors. Vascular endothelial growth factor (VEGF), fibroblast growth factor 2 (FGF-2), and PDGF, initially released by platelets and then by resident cells within the wound bed, are all central mediators of injury-induced angiogenic induction. In response, endothelial cells degrade basement membrane, migrate toward the wound site, proliferate, and form cell-cell contacts and eventually new blood vessels. More recently, it has been revealed that endothelial progenitor cells (EPCs) are also required for wound revascularization. Normally, EPCs reside in the bone marrow and are recruited

into the circulation in response to injury. Subsequently, EPCs are engrafted into the remodeling microvasculature, taking residence adjacent to endothelial cells bordering the injury site. Endothelial progenitor cell mobilization is mediated by nitric oxide, VEGF, and matrix metalloproteinases (MMP), particularly MMP-9; EPC engraftment and possibly differentiation occur in response to stomal cell–derived factor 1 and, as has become apparent more recently, insulin like growth factor (IGF). Although more research needs to be done to further elucidate the mechanisms of EPC recruitment and homing, it is clear that these progenitor cells are necessary for normal wound healing– associated neovasculogenesis and injury repair. In fact, key signalling intermediates responsible for coordinating/regulating wound healing angiogenesis and vasculogenesis may be dysfunctional during diabetes. Indeed, diabetic patients prone to the development of chronic wounds may exhibit deficiencies in either EPC bone marrow release or peripheral tissue homing and engraftment. Thus, therapies aimed at correcting EPC-linked deficiencies may prove beneficial for treating diabetes-induced chronic wounds.

MATRIX REMODELLING AND SCAR FORMATION:

Reestablishment of a normal blood supply provides a favourable microenvironment for epidermal and dermal cell migration and proliferation. In turn, this leads to wound re-epithelialization and restoration of epidermal integrity. Fibroblasts proliferate within the wound and synthesize extra-cellular matrix (ECM) forming granulation tissue perfused with newly formed blood vessels. Simultaneously, provisional matrix mainly consisting of collagen III, fibrin, fibronectin, and hyaluronic acid is progressively substituted with ECM mainly containing collagen I. Next, wound contraction and matrix remodelling occur. Contraction is mainly achieved by differentiated fibroblasts or myofibroblasts that, in response to TGF-A, tissue tension, and the presence of certain matrix proteins (such as ED-A fibronectin and tenascin C), acquire smooth muscle actin–containing stress fibres. Fibroblast-induced contractile forces are then transmitted to the ECM via cytoskeleton-associated and ECM receptor–dependent mechanocoupling focal adhesion complexes, that is, integrin receptors. Another mechanism leading to wound contraction is fibroblast motility with consequent matrix reorganization. This dynamic and reciprocal process involves slow cycles of ECM synthesis and degradation both occurring in a stromal- or fibroblastic cell–dependent manner. Here, matrix-remodelling enzymes, particularly MMPs, play important roles in remodelling the local matrix microenvironment in support of several healing responses, including cellular

migration, proliferation, and angiogenic induction. Finally, apoptosis of fibroblastic cells occurs, leading to the formation of a relatively acellular scar tissue whose tensile strength is comparable with unwounded skin.

Although the importance of apoptosis in granulation tissue remodelling and scar formation is widely accepted, the triggers of apoptosis are not well understood. It has been suggested that TGF-A, tumour necrosis factor, and surprisingly FGF-2 (that normally is considered a stimulator of cell proliferation) can lead to an increase in the number of apoptotic cells during the final phase of healing. Inability of dermal cells, particularly myofibroblasts to undergo timely apoptosis, has been linked to wound healing pathologies, including the hypertrophic scar and keloid formation. Clinicians' improved understanding of the role of apoptosis in normal and pathological wound healing may initiate novel approaches for their treatment and/or prevention.

CHRONIC WOUNDS:

The majority of the chronic wounds begin as minor traumatic injuries. penetrating injuries, insect bites, or even simple scratches of dry skin that would normally heal within a few days/weeks can lead to formation of a nonhealing wound in patients with underlying pathologies, such as diabetes-induced and nondiabetic neuropathies.

Chronic wounds can be classified into vascular ulcers (e.g., venous and arterial ulcers), diabetic ulcers, and pressure ulcers. Some common features shared by each of these include a prolonged or excessive inflammatory phase, persistent infections, formation of drug-resistant microbial biofilms, and the inability of dermal and/or epidermal cells to respond to reparative stimuli. In aggregate, these pathophysiologic phenomena result in the failure of these wounds to heal. The underlying pathologies, however, deviate in different types of chronic wounds.

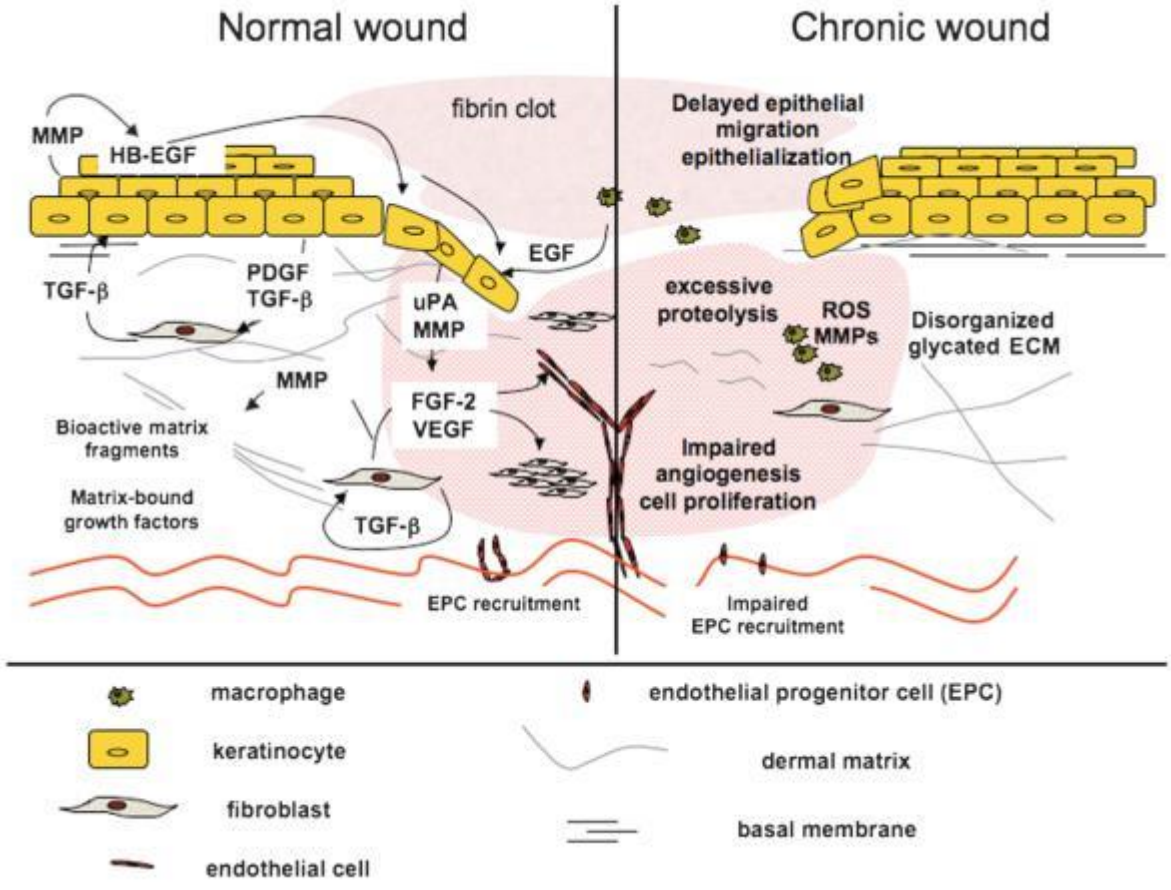


Figure 3

Normal Versus Chronic Wound Healing:

Microenvironment within a normal wound bed (left) is characterized by the presence of numerous growth factors, a well-organized ECM, and responsive cell populations. Matrix synthesis, here, exceeds its degradation, and MMP activity is regulated by the presence of MMP inhibitors (TIMPs). Angiogenesis and neovascularization of normal wounds proceed in a timely manner via well-regulated sprouting of existing blood vessels and recruitment of endothelial progenitor cells (EPC), respectively.

Finally, unlike their chronic counterparts, acute wounds are generally characterized by low bacterial burden. Chronic wounds (right) often have high incidence of bacterial biofilms, leading to persistent inflammation, excessive proteolysis, and degradation of critical growth factors, receptors, and/or ECM. Cells residing within these wounds are unable to proliferate and/or migrate effectively perhaps because of the absence of functional receptors or appropriate promigratory matrix substrates. Impaired angiogenesis and neovascularization, both hallmarks of chronic wounds, result in insufficient oxygen and nutrient supply for the cells residing within the wound bed, which leads to further wound bed mutilation and impaired healing.

VENOUS ULCERS:

Venous ulcers display profound pathological changes that arise secondary to venous valvular incompetence in the deep and superficial veins. This, in turn, leads to a constant blood backflow resulting in an increase in venous pressure. Pressure-induced changes in blood vessel wall permeability then lead to leakage of fibrin and other plasma components into the perivascular space. Accumulation of fibrin has direct and negative effects on wound healing. It down-regulates collagen synthesis, leads to formation of pericapillary fibrin cuffs that create a barrier for normal vessel function, and traps blood-derived growth factors, In the 1980s and 1990s, the cuffs were considered as continuous obstructions preventing free blood-dermis oxygen exchange. Recently, however, using confocal

microscopy, it has been demonstrated that fibrin deposits surrounding dermal veins are patch like and discontinuous. These findings question the barrier role of fibrin cuffs and suggests the presence of yet other unknown factors contributing to low oxygen tension found in venous ulcers and surrounding tissues. Identification of these factors may reveal novel targets for therapeutic interventions and treatment of venous ulcers.

ARTERIAL ULCERS:

Arterial ulcers are less common than chronic venous wounds. They occur because of arterial insufficiency caused by atherosclerosis or embolism that can lead to narrowing of arterial lumen and ischemia, which prevents timely healing of minor traumatic injuries. Unlike venous ulcers, which generally arise between the knee and the ankle, arterial leg wounds may present at any spot distal to arterial perfusion such as a tip of a toe. Unlike venous ulcers that often can be improved with therapeutic compression, chronic wounds linked to arterial insufficiency can be treated successfully only after the restoration of arterial function via revascularization. Current options for limb revascularization are rather limited and include reconstructive surgery (angioplasty) or pharmaceutical interventions. Because failure of wound revascularization almost inevitably leads to limb amputation in arterial ulcer sufferers, novel techniques allowing for restoration of blood supply to the wound bed, including stem cell therapies, are now under investigation.

PRESSURE ULCERS:

Pressure ulcers develop as a result of prolonged unrelieved pressure and shearing force applied to skin and the underlying muscle tissue leading to a decrease in oxygen tension, ischemia reperfusion injury, and tissue necrosis. Pressure ulcers are common in patients with compromised mobility and decreased sensory perception (neuropathies) and are exacerbated in individuals with arterial and venous insufficiencies described above.

DIBAETES MELLITUS:

Complications of aging and diabetes can lead to and exacerbate vascular pathologies related to both arterial and venous insufficiencies and worsen pressure ulcers. Other abnormalities leading to development of chronic wounds in diabetic patients (also called diabetic ulcers) include neuropathy, often linked to vascular impairment, deficiencies in muscle metabolism, and a number of microvascular pathologies often caused by hyperglycaemia. Macroscopic pathologies seen in chronic, particularly diabetic, wounds often are linked to cellular phenotypic abnormalities, including low mitogenic potential and inability to respond to environmental cues. Thus, a better understanding of these cellular changes may aid in the development of better treatment options.

Although all of the wounds described previously may have different origins, each wound is characterized by a chronically inflamed wound bed and a failure to heal. Excessive recruitment of inflammatory cells to the wound bed

often triggered by infection and cell extravasation is facilitated by disproportionate expression of vascular cell adhesion molecule 1 and interstitial cell adhesion molecule 1 by resident endothelial cells. Inflammatory cells accumulated inside the chronic wound produce various ROS that damage structural elements of the ECM and cell membranes and lead to premature cell senescence. In addition to these direct negative effects, ROS together with proinflammatory cytokines induce production of serine proteinases and MMPs that degrade and inactivate components of the ECM and growth factors necessary for normal cell function. Inactivation of proteinase inhibitors by proteolytic degradation augments this process. Therefore, although the production of growth factors is often increased in chronic compared with acute wounds, their quantity and bio-availability are significantly decreased.

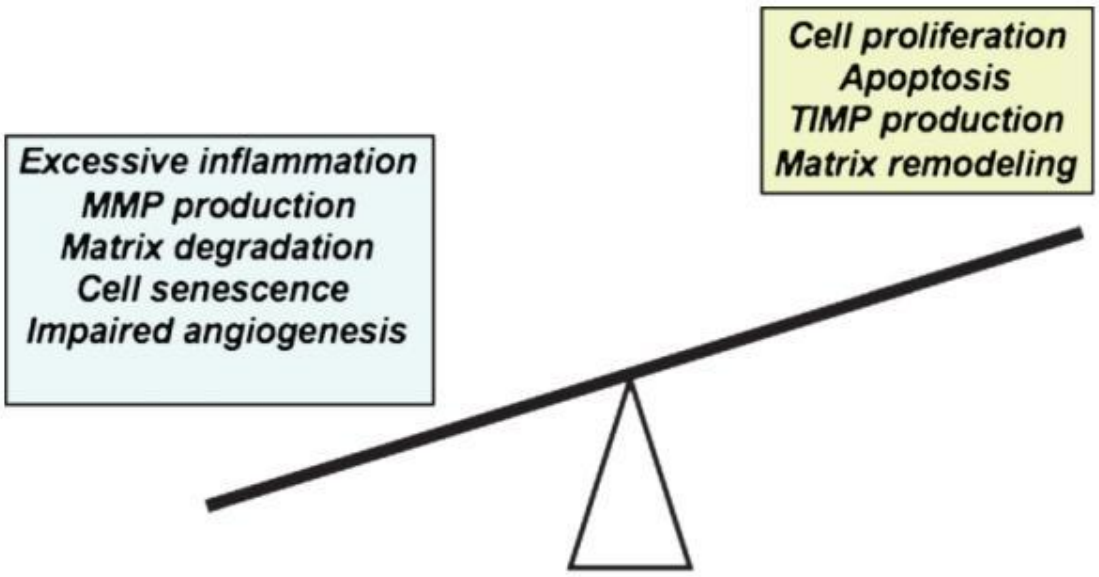


Figure 4

Physiologic imbalance: a key feature of chronic wounds:

Inflammation, MMP production, matrix degradation, and cell senescence/apoptosis are all elevated in chronic wounds. These processes cannot be overcome because of insufficient levels of cell proliferation, ECM synthesis, production of TIMPs, and impaired angiogenesis/ neovascularization. This imbalance leads to inability of chronic wounds to heal.

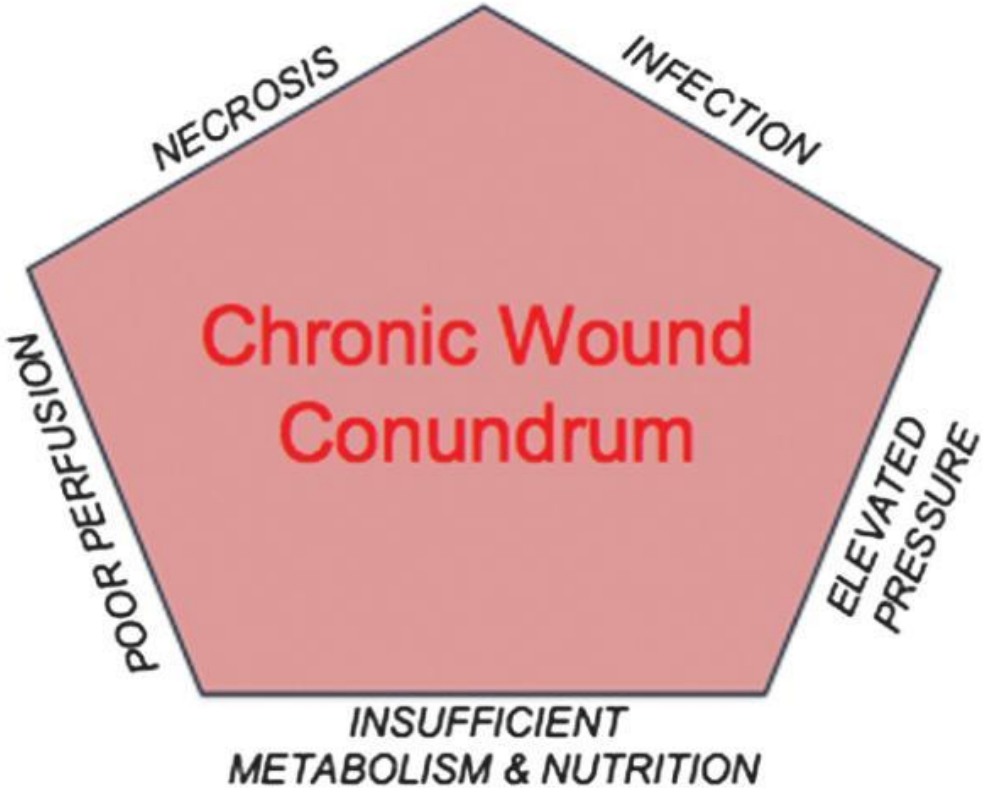


FIGURE 5

Chronic Wound Conundrum:

Diagrammatic representation of those physiologic functions that are perturbed or disequilibrated during chronic wound healing.

PHENOTYPIC ABNORMALITIES IN CHRONIC WOUND CELLS:

- ***Low density growth factor receptors and low mitogenic potential***

The phenotypic abnormalities of epidermis- and dermis-derived cells residing in chronic wounds include lower density of growth factor receptors and lower mitogenic potential preventing them from responding properly to environmental cues. For instance, fibroblasts, isolated from patients with chronic diabetic, chronic nondiabetic wounds, or patients with venous insufficiency, have lower mitogenic response to PDGF-AB, IGF, bFGF, and epidermal growth factor applied separately or in combination. These findings are likely due to a decrease in receptor density. Furthermore, fibroblasts isolated from leptin receptor–deficient diabetic mice, as well as derived from patients with chronic venous insufficiency, have reduced motility, compared with normal fibroblasts. These cellular abnormalities impede the formation of granulation tissue and ECM deposition, leading to formation of nonhealing wounds.

- ***Impaired keratinocytes***

Keratinocytes derived from chronic ulcers have also been reported to possess a "chronic wound–associated" phenotype. Overexpressing the proliferation marker Ki67, these cells up-regulate expression of several cell cycle–associated genes, such as CDC2 and cyclin B1, suggesting a hyperproliferative status. However, these chronic wound–derived keratinocytes exhibit impaired migratory potential. The mechanisms of this impairment are not completely

understood but have been linked to decreased production of laminin 332 (formerly known as laminin 5), which is an important epithelial ECM component and substrate for injury-induced keratinocyte migration. In addition, these cells possess an increased activation of A-catenin/c-myc pathway and do not express markers of differentiation, particularly keratin 10 and keratin 2.

- ***Growth factors dysregulation***

Finally, several genes encoding a variety of growth factors are down- or up-regulated; for example, VEGF, epiregulin, and TGF-A2 expression are decreased, whereas PDGF and platelet-derived endothelial growth factor encoding genes are up-regulated. Decreased growth factor production directly confirms the impaired state of the keratinocytes residing within a chronic wound and inability to fully participate in repair processes, whereas up-regulation of key growth factor genes enables a sustained proliferative capacity, suggesting that this could be an "entry point" for therapeutic intervention.

Mitogenic stimuli together with activators of keratinocyte differentiation, such as recently described hyperforin, may be able to induce phenotypic changes and transform the chronic wound keratinocytes into competent cells necessary for epithelialization. Similarly, modern transduction techniques could be used to improve growth factor responsiveness of cells residing in chronic wounds by increasing the density of growth factor receptors.

PERTURBATIONS IN THE ECM MICROENVIRONMENT THAT CONTRIBUTE TO SUSTAINING WOUND CHRONICITY:

The microenvironment of the chronic wound bed is heralded by a matrix. It is known, however, that deposition of a number of matrix components is different in chronic as compared with acute wounds.

- Chronic wounds are characterized by prolonged or insufficient expression of fibronectin, chondroitin sulphate, and tenascin, which gives rise to impaired cellular proliferation and migration.
- Reduced production of laminin 332—a basement membrane component that serves as a chemotactic substrate for postinjury keratinocyte motility was found to be one of the reasons for impaired reepithelialisation and wound healing.
- Changes of the ECM, including posttranslational modification of key structural components, can also negatively influence cellular responses to injury.
- Matrix glycation is often seen in diabetic patients and is likely to be responsible for or linked to premature cell senescence, apoptosis, inhibition of cell proliferation, migration, and angiogenic sprout formation.
- Glycation adds to matrix instability and disrupts matrix assembly and interactions between collagen and its binding partners, including heparan sulphate proteoglycans.

- High glucose has also been shown to stimulate MMP production by fibroblasts, macrophages, and endothelial cells, thus contributing to a "vicious" cycle of matrix degradation detrimental for cell survival and therefore wound healing.
- Matrix instability that occurs because of glycation and insufficient intermolecular cross-linking seen under hypoxic conditions and excessive matrix degradation by MMPs are also detrimental to the healing process.
- Matrix instability prevents normal cell-matrix interactions necessary for cell survival and function and, ultimately, injury repair. Therefore, inhibition of matrix degradation, addition of exogenous matrices, and induction of matrix synthesis by resident cells all provide therapeutic opportunities.

BIOFILMS AND CHRONIC WOUND BED:

Infection is an extrinsic factor that causes delay of wound healing, contributing to wound chronicity, morbidity, and mortality. High bacterial counts of greater than 10^5 viable bacteria or any number of A-haemolytic streptococci are considered detrimental. Bacterial toxins (as well as live bacteria) induce excessive inflammatory responses and tissue damage that can lead to abscess, cellulites, osteomyelitis, or limb loss (diabetic patients). Furthermore, recruited inflammatory cells, as well as bacteria, produce a number of proteases (including

MMPs), which degrade the ECM and growth factors present within the wound bed. Bacteria that colonize chronic wounds often form polymicrobial communities called biofilms. These complex structures are composed of microbial cells embedded in secreted polymer matrix, which provides optimal environment for bacterial cell survival, enabling their escape from host immune surveillance/defence and resistance to antibiotic treatment. Although biofilms are prevalent in chronic wounds and significantly delay re-epithelialization in animal models, it remains unclear precisely how they delay healing. Increased bacterial survival and enhanced production of virulence factors are likely explanations. Nonetheless, it is possible that extracellular biofilm components possess or display a toxic phenotype for host cell functionality and therefore impede healing. Recently, it has been demonstrated that hindering biofilm formation by RNAIII-inhibiting peptide reverses wound-healing delays induced by bacterial biofilms. Better understanding of the precise mechanisms by which bacterial biofilms delay repair processes together with optimizing methods for biofilm detection and prevention may enhance opportunities for chronic wound beds to actively heal

DRESSINGS

Most wounds do not require extensive debridement, yet the principles must always be remembered. Dressings are used to serve the following purposes.

- Contain wound drainage.
- Debride a wound
- Protect an area from trauma
- Protect an area from contamination
- Promote proper wound healing

The basic equipment necessary for bedside wound care are:

1. Sterile debridement set containing

- Sharp scissors
- Blunt ended needle wound probe
- Smooth forceps

2. Sterile toenail clippers

3. Sterile gauze dressings

4. Tube gauge, paper tape, culture tubes

5. Medicines - Povidone iodine 2.5% - Bactericidal

- Dakin's solution (chlorazene 0.25%)
- Bacitracin ointment - antibacterial

- Vaseline gauze
- Normal saline

Dakin's solution: is a chlorine releasing agent that is both bactericidal and active in loosening necrotic tissue to aid in local debridement. Dakin's also helps to control fetid odours from severely infected wounds.

Routine Foot Dressings:

- Moisten gauze with appropriate solution and pack the wound gently.
- Fashion a heel cup from cut, folded and taped abdominal pad.
- Fluff two 4 inch gauze sponges over toes.
- Secure the primary dressing, including heel cup by using a spiral roller by wrapping in a figure of eight fashion.
- Apply paper tape to secure the roller gauze.

Casts / Splints:

A cast or splint may be applied to immobilize a limb after a skin graft or to protect the incision and reduce contractures after a below knee amputation. Applying a rigid plaster cast or splint to any neuropathic extremity can be hazardous and may cause pressure sores.

Amputation Stump Dressings:

The dressing applied to any amputation stump is fashioned to meet the needs of the wound. Since most amputation wounds do not have drains, the dressing is put on more for wound protection than to collect and contain blood and secretions. A first trans metatarsal amputation dressing is a bulky standard foot dressing. A posterior splint may be applied to prevent plantar flexion and thus avoid tension on the delicate suture line. A below knee amputation (BKA) requires an extra bulky initial.

Dressing to contain the initial expected bleeding. Below knee amputations are managed with a posterior splint that extends from the crease of the buttocks to beyond the end of the stump. A well-padded knee immobilizer is the splint of choice. Knee flexion is a natural pain-relieving action or reflex that, if allowed to occur, can lead to serious contracture. It is customary to have a patient with a BKA measured for a prosthesis on the 3rd or 4th post op day. Depending on the progression of stump healing, a patella bearing prosthesis may be fitted and patient begins mobilization eight to ten days postoperatively.

The initial dressing for an Above Knee Amputation (AKA) is bulky and similar to the BKA dressing. Splints are not used for AKA despite the tendency for patients to hold up and flex the painful thigh. The stump usually

falls down with muscle fatigue, thus decreasing the tendency for a hip contracture.

Skin graft dressings are usually applied in accordance with the surgeon's preference. Mesh grafts are the most common split thickness skin graft. The mesh graft has proved to be the most successful because the open mesh allows adequate wound drainage.

Bed rest is the first thing in the care of a diabetic foot lesion. Bed rest must be absolute and continuous. A patient with diminished circulation who has a painful ischemic foot lesion may be helped by having the head of the bed elevated to 6-8 inches. This elevation allows gravity flow of blood to the feet and is known as arterial position or Reverse Trendelenburg position.

Non-Surgical Modalities to Enhance Healing:

1. Growth Factors

Greater understanding of the healing process at the cellular level has resulted in the use of growth factors like becaplermin, recombinant platelet-derived growth factor, are produced through recombinant DNA technology. According to a study by Steed et al, debridement enhances the effectiveness of becaplermin in healing chronic neuropathic ulcers.

2. Human Skin Equivalents

Modern human skin replacement dates back to the 1960s, when advances in tissue culture technologies led to the cultivation of human epidermal cells. These were obtained via biopsy of the tissue and treated with trypsin so that the dermis gets separated from epidermis.

The keratinocytes were then grown in vitro to produce sheets of autologous epidermal tissue. These sheets were fragile, delicate to handle, and provided only 50 percent to 60 percent permanent take. New tissue required two to three weeks growth time, and lacked a dermal component, vital in skin grafting.

More dermis grafted means less wound contracture and scarring, more tensile strength and better cosmetic results. Refinements in the development of a matrix led to the development of Dermagraft, a living, metabolically active, immunologically inert dermal tissue.

Dermagraft contains normal dermal matrix proteins and cytokines, and is composed of cultural neonatal fibroblasts grown on a polyglycolic acid bioabsorbable mesh. As the tissue grows it produces extracellular proteins and closely resembles human skin. In two studies by Gentzkow et al and one by Pollak et al, patients were enrolled with full-thickness diabetic ulcers that had adequate perfusion. Pooled data showed that 51 percent of those who received a weekly application of Dermagraft for 12 weeks achieved complete healing, vs. 31.7 percent in the control group.

Apligraf, another living tissue equivalent, was approved by the Food and Drug Administration in 1998 for venous leg ulcers. Apligraf consists of bovine Collagen matrix containing fibroblasts and connected to a layer of stratified epithelium. The result is a sheet of tissue with both dermal and epidermal layers, metabolically and biochemically comparable to human skin. The dermo epidermal junction is flatter, however, and there are no melanocytes, Langerhans cells, lymphocytes or hair follicles present.

In a study by Falanga et al, 293 patients with non-healing venous ulcers received either compression therapy or Apligraf. At six months, 63 percent of the patients receiving Apligraf healed vs. 49 percent in the control group and did I so more quickly - than the control group - 61 vs. 181 days to closure.

3. Miscellaneous Topical Agent:

Collagen: Collagen is critical in the proliferative phase of wound healing. Exogenous sources of collagen primarily purified bovine extracts, are available as gels, particles, and in an alginate dressing. Exogenous collagen provides additional protein for tissue repair. As a foreign agent it might also revert the chronic wound to an inflammatory phase, "jump-starting" the healing process.

Donaghue et al evaluated the alginate dressing (Fibracol, Johnson and Johnson, Arlington, Texas) in the treatment of diabetic foot ulcers. Seventy-five patients were randomly assigned to either a collagen-alginate dressing or gauze group. At the end of the study, the mean reduction in wound size was 80.6 percent for the collagen-alginate group and 61.1 percent for the gauze group. Complete healing was achieved in 48 percent of the collagen-alginate group and 36 percent in the gauze group.

Hyaluronic Acid: Hyaluronic acid is involved in the structure and organization of the extracellular matrix and is associated with increased mitotic activity. It is a highmolecular weight polysaccharide synthesized in the plasma membrane of fibroblasts and other cells. The ability of injured fetal tissues, which are high in Hyaluronic acid, to heal without scarring has prompted extensive research

Beta Glucan: It is a major cell-wall carbohydrate extracted from such grains as oats and barley. The biological activity of beta glucan results from its ability to bind macrophage beta-glucan receptors and promote macrophage stimulation.

Beta glucan products enhance the activities of not only macrophages but also neutrophils, natural killer cells, T cells and B cells. Beta glucan is thought to increase macrophage infiltration, speeding the onset of fibroplasia and fibrogenesis, stimulation of increased tissue granulation, and enhanced reepithelialisation. Beta glucan is available as either BCG matrix or Glucan II.

Both are available in multifilament mesh dressings; BCG matrix is also impregnated with collagen.

Silver Arglaes: Silver compounds are powerful antimicrobials, useful in promoting healing. Arglaes is an inorganic phosphate similar to other compounds such as silver nitrate, silver oxide and silver chloride. It consists of fused sodium and calcium phosphates with small amounts of silver in the presence of water, these materials release free silver ions.

4. Pharmaceuticals:

Oxandrolone: Oxandrolone is an anabolic steroid with a high anabolic and low androgenic ratio, and has anticatabolic, protein-sparing properties. Exogenous anabolic agents clubbed with nutritional intervention can result

in a threefold to fourfold higher rate of protein synthesis than with nutritional interventions alone.

Demling and De Santi studied eight patients with non-healing wounds and a 10 percent or greater loss of body weight. Nutrition was optimized over four weeks, without significant effect on weight gain or healing. Adding oxandrolone resulted in gains of approximately 4 pounds per week across 12 weeks. During this time, five wounds closed completely and three others were 75 percent closed.

5. Devices

Vacuum Assisted Closure (VAC): Argenta and Morykwas determined that intermittent negative pressure at 125 mmHg promoted wound healing by improving blood flow, granulation tissue growth rates and nutrient flow while reducing bacterial levels. Based on these findings, Kinetic Concepts (San Antonio, Texas) developed the VAC system. The VAC consists of a wound dressing (a charcoal - impregnated sponge - like material) connected by tubing to a wound canister, with a pump that creates negative pressure. A transparent drape or film over the dressing establishes the seal needed to create a vacuum. The pump can be adjusted for various levels of intermittent or continuous pressure. Exudate is collected in the cainster. The VAC also is said to reduce edema.15

Radiant Heat Bandage: Heat therapy has long been employed, especially for musculoskeletal conditions, but it has not been widely used as a wound healing modality. Heat increases local blood flow, subcutaneous oxygen tenson which improve healing mechanisms. In clinical studies by Santilli and Robinson on patients with venous leg ulcers, those who used radiant heat bandage devices reported significant decreases in both wound size and pain across two weeks with no adverse effects.16

Topical Hyperbaric Oxygen Therapy:

The therapy is based on achieving an atmospheric pressure of 1.02 to 1.03 atmos, which is thought to stimulate fibroblast, growth, collagen formation and neoangiogenesis. This provides a lethal environment for anaerobes, often a normal part of the diabetic foot's flora. Topical hyperbaric oxygen 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 and a half hours.

In a study of Landau, 50 patients with diabetic ulcers were treated with topical hyperbaric therapy, alone or with a low-energy laser. On average, 25 treatments were performed over three months. Forty-three of the 50 patients experienced resolution of their ulcers.

Classification of Dressings:

Wound dressings have evolved over the years on the principles of providing protection to wound raw surface, absorbing exudates, controlling infection and promoting granulation tissue formation and creating ideal environment for healing.

There are two major categories in dressings:

1. **Short term application:** we should replace these dressings frequently

2. **Long term or skin substitutes**:

    Temporary: these are applied till complete healing. Used in partial thickness wounds

    Semi-Permanent: these are used till autografting. Used over full thickness wounds.

They are classified as conventional, synthetic, biological, based on material used for preparation. Each further divided into:

- **Primary Dressing :** Which is in physical contact to the wound bed.
- **Secondary Dressing :** Primary dressings are covered with these dressings.
- **Island Dressing :** at the central region there is absorbent part, adhesive part surrounds the central portion.

A. Conventional Dressings:

Fabric materials like gauze are used, but these allows moisture to evaporate and dries the desiccated wound bed.Also causes exogenous bacteria to enter the wound. Some used paraffin soaked dressings. This also led to development of usage of antibacterial agents like polymixin,carbolic acid in combination with dressings.

B. Synthetic Dressings:

1. Films: these are polymer sheets with adhesive coated on one side. Polyurethane, polyethylene, dimethyl aminoethyl methacrylate, polytetra fluoroethylene are commonly used in superficial wounds. But causes accumulation of wound fluid, due to impermeability to water vapour and gases, and lack of absorbing capacity. Thus, leading to leakage and entry of exogenous bacteria.

2. Foams and sprays: Polymers of polyvinyl alcohol and polyurethane are converted to foam solutions and are used for dressings. They are better than film dressings. They provide thermal insulation and keep the surface moist. They are permeable to gas. They are non-adherent also. Silastic foam and lyofoam are examples. Spray dressings are co polymers of certain compounds, eg: hydroxyl vinyl chloride acetate modified maleic acid ester is polymerised to form Aeroplast.

3. **Composite dressings:** This dressing consists of more than one layer. Durability and elasticity maintained by outer layer. And inner layer maintains the adherence.

They are classified as:

a. **Hydrocolloid dressings:** These contain mixture of gelling agents and elastomeric adhesive. Commonly used absorptive agent is Carboxymethyl cellulose.

b. **Hydrogel sheets:** These are hydrophilic polymers made into sheets of 3 dimensional networks. Polyethylene oxide, polyacrylamide and polyvinyl pyrrolidine are usually used in thermal burns because of their cooling ability.

Eg: Vigilon.

c. **Hydrogel Amorphous:** They are similar to hydrogel, but there isn't any crosslinking between the polymers. Collagen or complex carbohydrates are present in small amounts. They give moisture to dry wound eschar and also promotes autolytic debridement

d. **Super Absorbents:** examples are Combiderm, Convatec.

e. **Gels:** examples are HEMA, Hydran, Geliperm etc.

Above mentioned dressing is usually act as a temporary covering. In large burns injuries these are combined with alternative wound closure techniques.

C. Biological Dressings:

They are obtained naturally from tissues and are combined with collagen lipid and elastin in various formulations. Their main advantages over synthetic dressings are:

1. Prevent dehydration of wound by restoring a water vapour barrier.
2. Lessen heat loss by evaporation
3. Exudative loss of protein and electrolytes are reduced.
4. Contamination of wound by organism are prevented.
5. Change of dressings are less painful.
6. Joint mobility is maintained.
7. Wound debridement can be done.
8. Autografting made easy by creating good granulation.
9. Reduce the healing time and
10. Healing quality is improved and contraction of tissues are decreased.

Other Biological dressings which are used are allografts,embryonic membranes, skin of foetus/neonate, fibrin, grafts from cultured epidermis/dermal matrix, bovine collagen is reconstituted to films. Heterografts from pigs and dogs are also used.

COLLAGEN

Proteins are natural polymers and make up almost 15% of the human body. The building blocks of all proteins are amino acids. Collagen is the major protein of the extracellular matrix (ECM) and is the most abundant protein found in mammals, comprising 25% of the total protein and 70% to 80% of skin (dry weight). Collagen acts as a structural scaffold in tissues. The central feature of all collagen molecules is their stiff, triple-stranded helical structure. Types I, II, and III are the main types of collagen found in connective tissue and constitute 90% of all collagen in the body. Function of collagen in wound healing. Previously, collagens were thought to function only as a structural support; however, it is now evident that collagen and collagen-derived fragments control many cellular functions, including cell shape and differentiation, migration, and synthesis of a number of proteins.

ROLE OF COLLAGEN IN WOUND HEALING:

- Type I collagen is the most abundant structural component of the dermal matrix; migrating keratinocytes likely interact with this protein. Collagenase (via formation of gelatin) may aid in dissociating keratinocytes from collagen-rich matrix and thereby promote efficient migration over the dermal and provisional matrices. Cellular functions are regulated by the ECM. The information provided by ECM macromolecules is processed and transduced into the cells by specialized cell surface receptors. Evidence demonstrates that the receptors play a major function in contraction of wounds, migration of epithelial cells, collagen deposition, and induction of matrix-degrading collagenase. Although keratinocytes will adhere to denatured collagen (gelatin), collagenase production is not turned on in response to this substrate. Keratinocytes have been known to recognize and migrate on Type I collagen substratum, resulting in enhanced collagenase production.
- Collagen plays a key role in each phase of wound healing.
- Platelets aggregate around exposed collagen. Platelets then secrete factors, which interact with and stimulate the intrinsic clotting cascade, which strengthens the platelet aggregate into a stable haemostatic “plug.” Blood platelets also release αa-granules, which release a variety of growth factors (GFs) and cytokines, such as platelet derived GF (PDGF), insulin-like GF (IGF-1), epidermal GF (EGF), and transforming GF-beta (TGF-b), which

"call" a variety of inflammatory cells (neutrophils, eosinophils, and monocytes) to the wound site and initiate the inflammatory phase. Inflammation (duration = days).

- TNF-α and IL-1bβ are key pro-inflammatory cytokines, which directly influence deposition of collagen in the wound by inducing synthesis of collagen via fibroblasts and down regulation of tissue inhibitors of matrix metalloproteinases (TIMPs). Inflammatory cells also secrete growth factors including TGF-b, TGF-b, bHB-EGF, and bFGF. [12] These GFs continue to stimulate migration of fibroblasts, epithelial cells and vascular endothelial cells into the wound. As a result, the cellularity of the wound increases. This begins the proliferative phase. Proliferation (duration = weeks).
- Cleavage products resulting from collagen degradation stimulate fibroblast proliferation. Fibroblasts secrete a variety of GFs (IGF-1, bFGF, TGF-b, PDGF, and KGF), which guide the formation of the ECM.
- The collagen cleavage products also stimulate vascular endothelial cell proliferation. These cells secrete a variety of GFs (VEGF, βFGF, PDGF), which promote angiogenesis. With a vascularized ECM, granulation is achieved.
- Collagen cleavage products also stimulate keratinocyte migration and proliferation. Keratinocytes secrete a variety of GFs and cytokines, such as TGF-b, TGF-b, and IL-1. As keratinocytes migrate from the edge of the

wound across the newly formed granulation tissue, re-epithelization is achieved. Remodelling (duration = 1+year).

- A balance is reached between the synthesis of new components of the scar matrix and their degradation by MMPs, such as collagenase, gelatinase, and stromelysin.
- Fibroblasts are the major cell type that synthesizes collagen, elastin, and proteoglycans. They are also the major source of MMPs and TIMPs. In addition, they secrete lysyl oxidase, which cross-links components of the ECM. Angiogenesis ceases and the density of capillaries in the wound site decreases as the scar matures.
- The result is the creation of a stronger scar, though the skin only regains almost 75% of its original tensile strength.

THE ROLE OF MMPS IN WOUND HEALING:

Wound bed preparation (WBP) can be described as the management of the wound to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures.

The 4 basic aspects of WBP can be represented by the acronym:

TIME. T = tissue (nonviable or deficient);

I = infection or inflammation;

M = moisture control;

E = epidermal margin.

Focusing on the "E" in TIME, collagen dressings possess properties, which lend themselves to creating a wound environment favourable to the migration of cells from the epidermal margin across granulation tissue, encouraging wound closure.

- Due to a number of potential stimuli (local tissue ischemia, bioburden, necrotic tissue, repeated trauma, etc.), the wound has stalled in the inflammatory phase contributing to the chronicity of the wound.
- As a result of the aforementioned pro-inflammatory stimuli, the wound is overstimulated and inflammatory cells, such as macrophages, are present in higher numbers and are more active.

- In addition, the cells, such as fibroblasts and endothelial cells, are senescent and unable to function properly as they would in an acute wound.
- With the overabundance of macrophages, there is an overabundance of key pro-inflammatory cytokines, such as TNF-b and IL-1b, secreted by the macrophages.
- These pro-inflammatory cytokines signal the fibroblasts to secrete MMPs, but due to the overabundance of pro-inflammatory cytokines the fibroblasts secrete elevated levels of MMPs.
- At this level, MMPs not only degrade nonviable collagen, but also viable collagen laid down by the fibroblasts themselves.
- Additionally, the fibroblasts are unable to secrete tissue inhibitors of MMPs (TIMPs) at an adequate level to control the activity of the MMPs.
- In addition, cells in a chronic wound tend to be senescent, thus unable to communicate with other cells and unable to function properly.
- One result of this is a lack of endothelial cell activity slowing the formation of blood vessels. Without an adequate blood supply, tissue can die and as a result, there is an increase in wound size.
- All of the aforementioned phenomena impede the formation of viable granulation tissue and thus inhibit re-epithelialization (i.e. wound closure).

- One of the key contributors to wound chronicity is an overabundance (and/or activity) of MMPs in the wound; the ability to inhibit or deactivate a number of excess MMPs may help create an environment more conducive to the formation of granulation tissue, and eventual wound closure.

COLLAGEN BASED WOUND DRESSINGS:

There are a number of different collagen dressings available, which employ a variety of carriers/combining agents such as gels, pastes, polymers, oxidized regenerated cellulose (ORC), and ethylene diamine tetraacetic acid (EDTA). The collagen within these products tends to be derived from bovine, porcine, equine, or avian sources, which is purified in order to render it nonantigenic. The collagen in a given collagen dressing can vary in concentration and type. Certain collagen dressings are comprised of Type I (native) collagen; whereas, other collagen dressings contain denatured collagen as well. A given collagen dressing may contain ingredients, such as alginates and cellulose derivatives that can enhance absorbency, flexibility, and comfort, and help maintain a moist wound environment. Collagen dressings have a variety of pore sizes and surface areas, as well. All of these attributes are meant to enhance the wound management aspects of the dressings. Many collagen dressings contain an antimicrobial agent to control pathogens within the wound. Collagen dressings typically require a secondary dressing.

COLLAGEN GRANULES

Figure 6

Figure 7

They are primarily a type 1 collagen in lyophilised particle form with Mupirocin USP 2% and Metronidazole IP 1% of specified volumes. It is gamma sterilised and supplied in convenient cold blister packs. Should be stored dry in at least 25 deg celcius and do not freeze. Shelf life is 2 years.

Figure 8: A diabetic foot wound after debridement

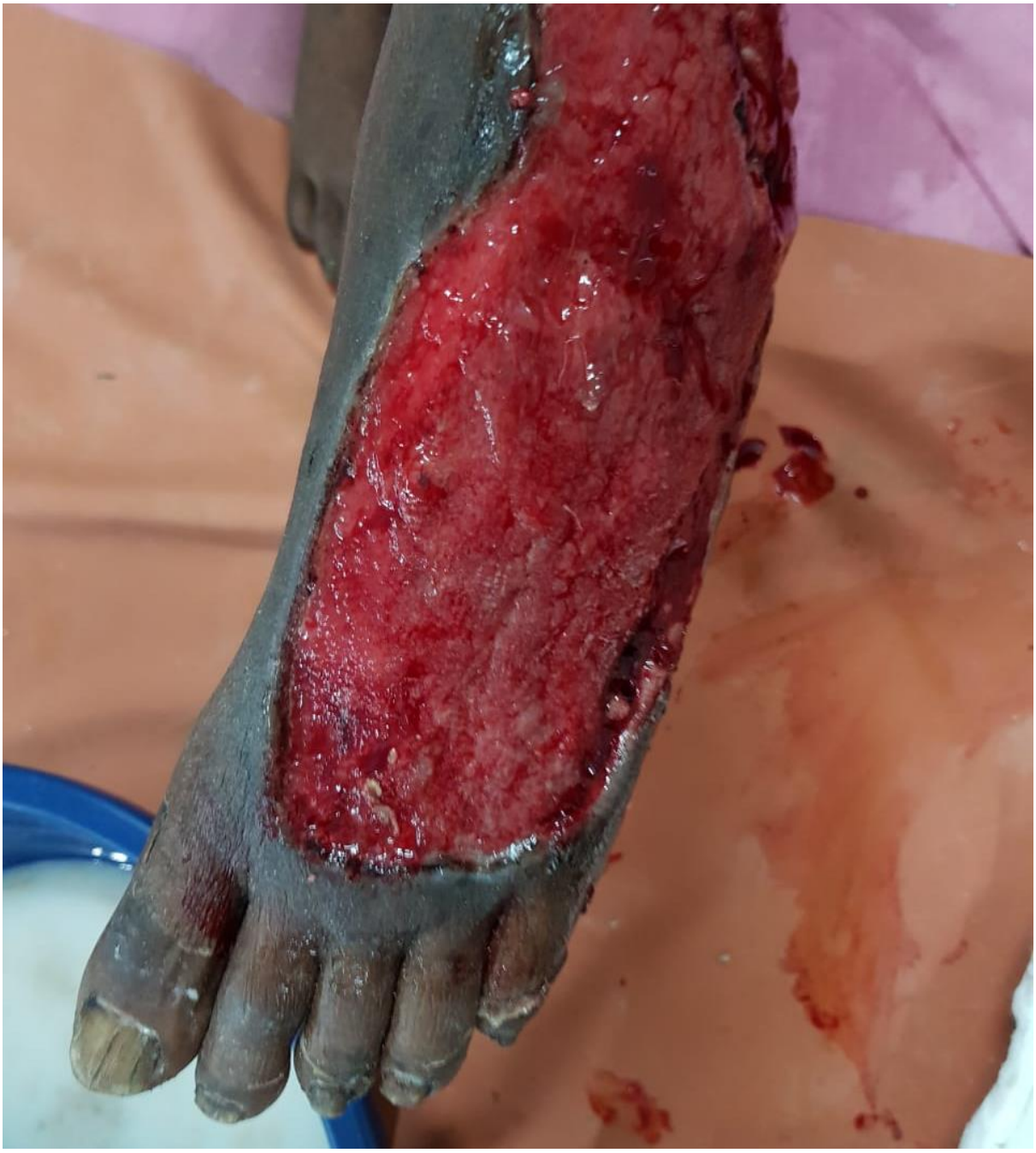


Figure 9: Wound after collagen granules application

Figure 10: Wound after SSG application

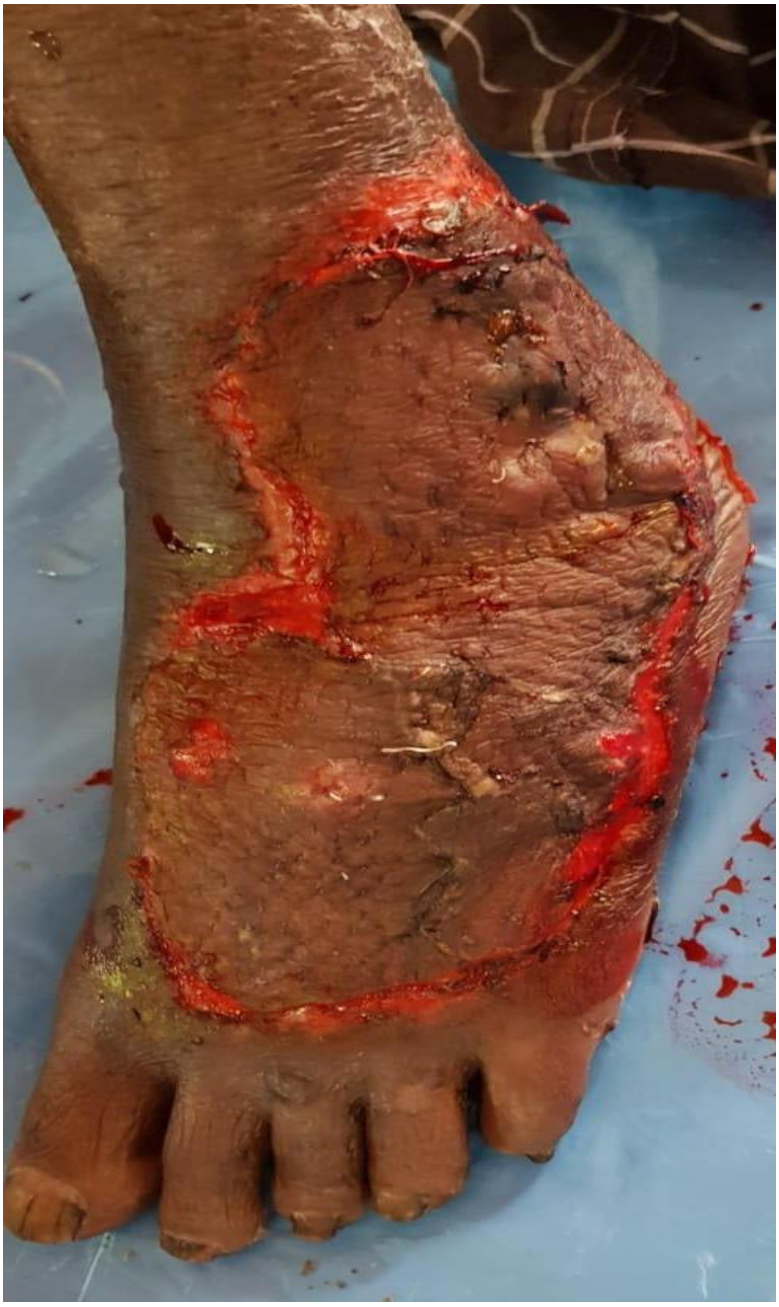


Figure 11: wound after ssg uptake

RESULTS

The present study comprising of 60 cases of chronic wounds was studied during a period of May 2018 To May 2019. Both outpatient and inpatients were diagnosed and included in the study. Patients were categorised into two groups based on the collagen application and normal dressing. Above mentioned parameters were assessed and the results were estimated.

Figure12: depicting the gender distribution among the case and control group

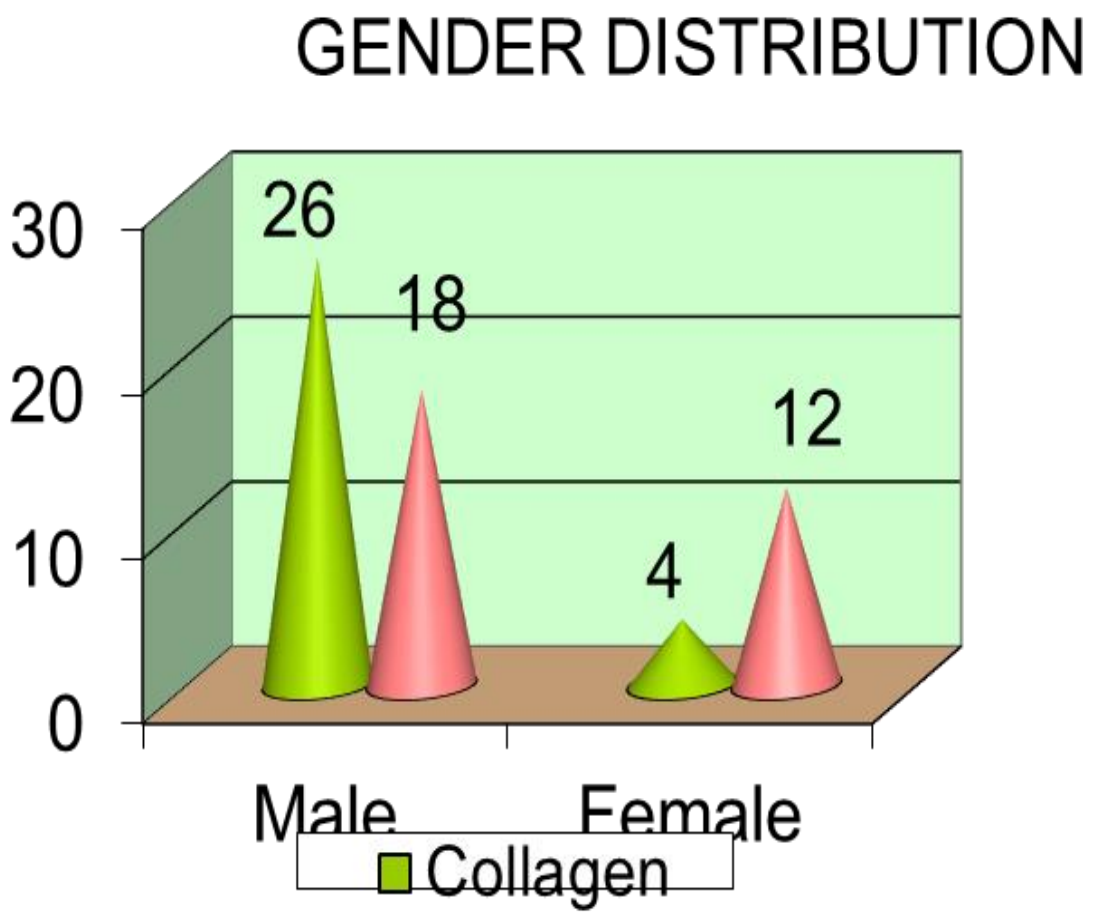


Figure 13: bar diagram demonstrating the age distribution among the case and control groups.

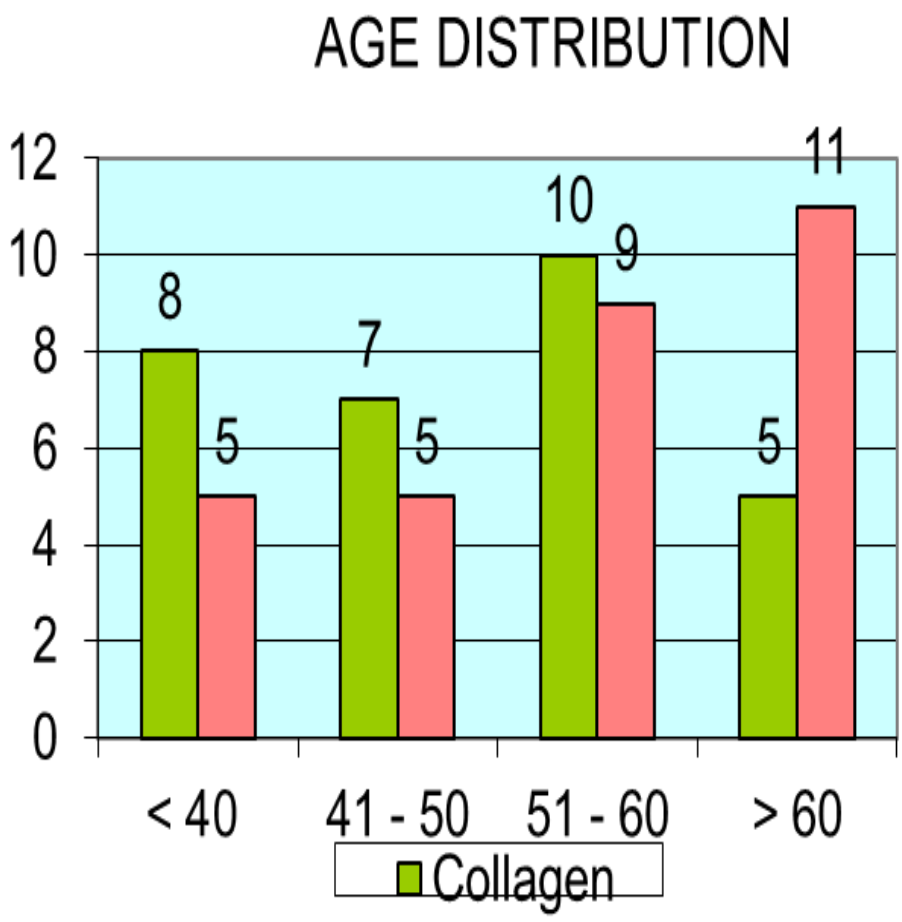


Figure 14: mean wound surface area before applying collagen dressing and conventional antibiotic dressing

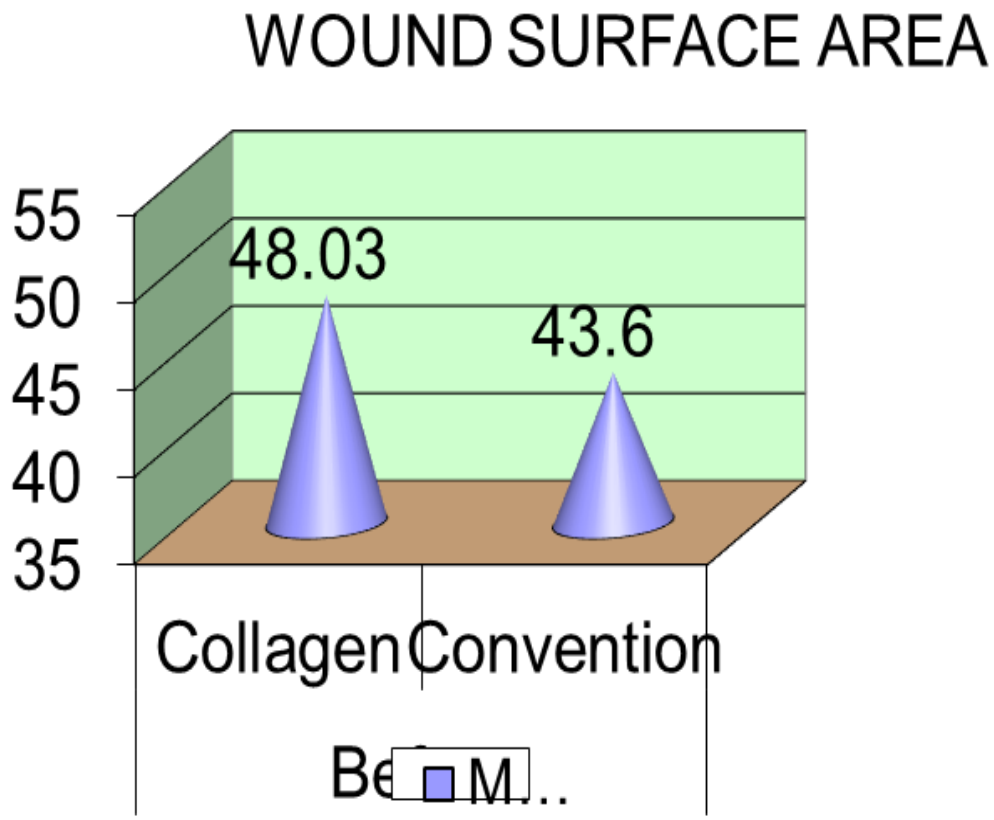


Figure 15: Mean wound surface area after regular dressings with collagen and conventional antibiotic dressing.

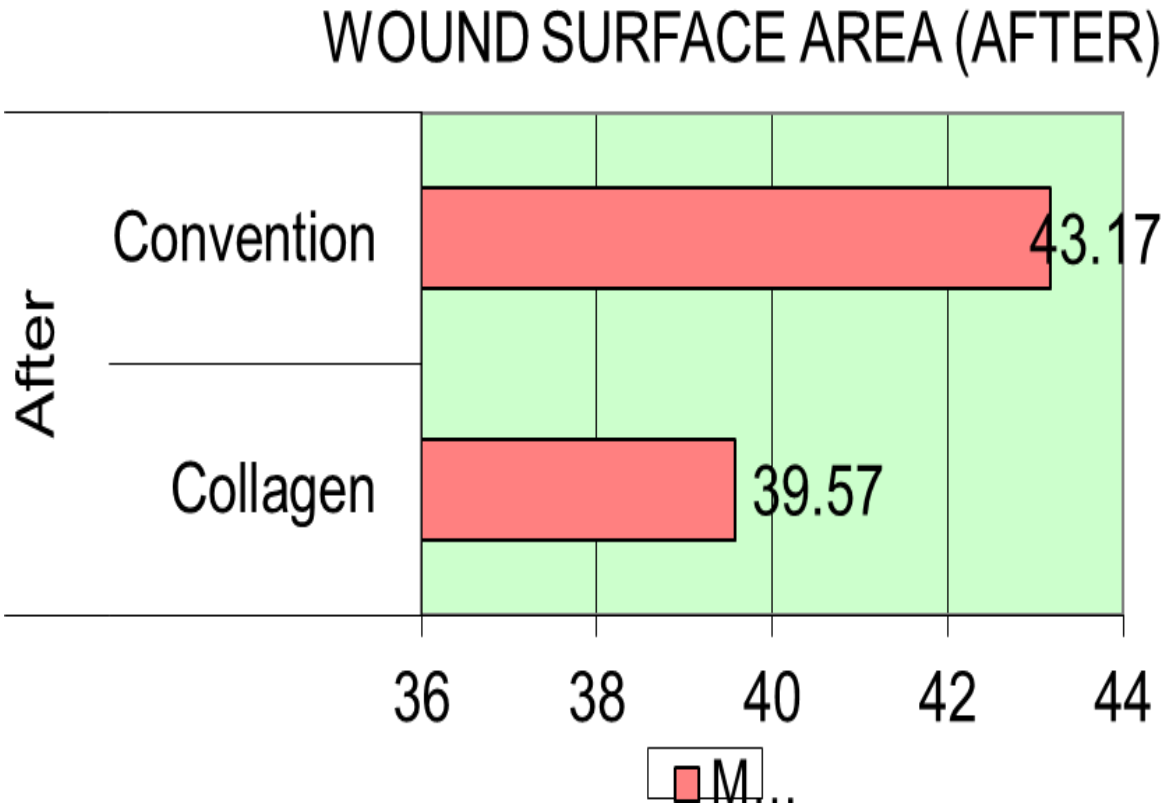


Figure 16: bar diagram depicting the mean hospital stay of both case and control group

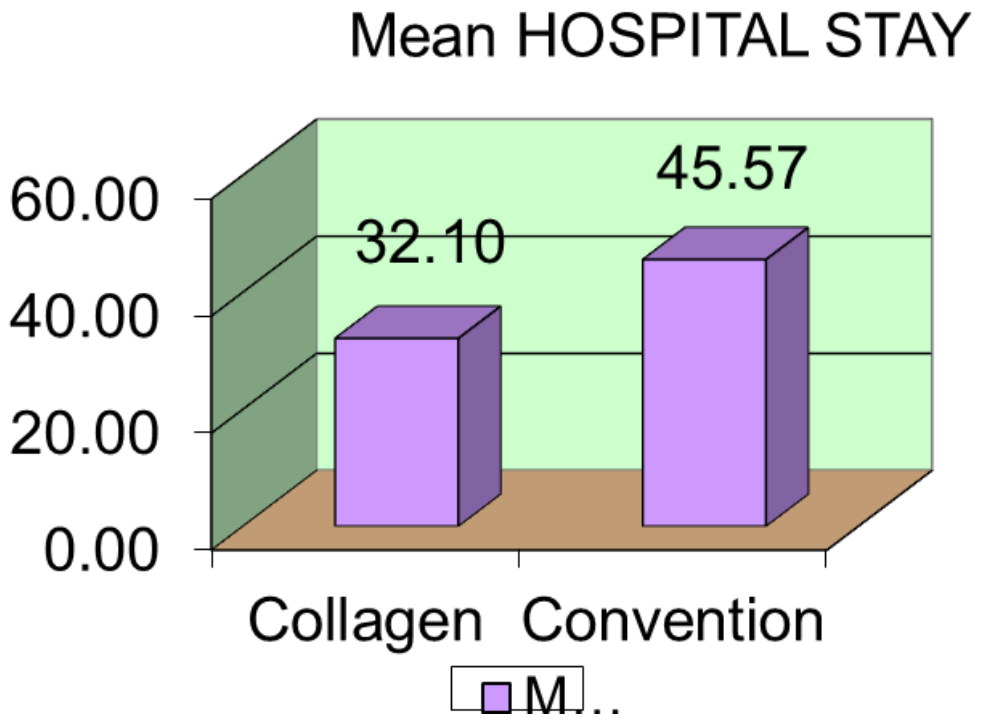


Figure 18: showing the decrease in wound surface area in case group who received the collagen granule dressing. Mean wound surface area in case group is 48.03 cm^2 before application of dressings and 39.57 after application of dressings. This indicates significant reduction in the wound surface area.

Wound surface area (cm^2)	Collagen dressing	
	Before	After
Mean	48.03	39.57
SD	17.31	14.97
p' value	0.047 Significant	

Figure 19: Showing the reduction in the duration of mean hospital stay among the case group who received the collagen dressing than the conventional dressing. The mean hospital stay for case group is 32.10 days and among the control group is 45.57 days. There is a significant decrease in the mean hospital stay.

Hospital stay(days)	Collagen	Convention
Mean	32.10	45.57
SD	5.52	7.05
p' value	<0.001 significant	

Figure 20: showing the significant decrease in the number of dressings required before application of SSG to the wound. The mean number of dressings for collagen group is 5.40 and for the conventional dressing group is 8.20 and there is a significant decrease in the no of dressings required.

Number of dressings	Collagen	Convention
Mean	5.40	8.20
SD	0.86	1.77
p' value	<0.001 significant	

Figure 21: Showing the decrease in the decrease in the duration between the first dressing and SSG application. The mean duration in the case group is 22.23 and the control group is 36.03, there is a significant decrease in the duration between the first dressing and the application of SSG

Difference between the duration of first dressing and SSG application	Collagen	Convention
Mean	22.23	36.13
SD	3.49	6.79
p' value	<0.001 significant	

DISCUSSION

- Collagen is a key component of a healing wound.
- Due to a number of potential stimuli (local tissue ischemia, bio burden, necrotic tissue) wounds can stall the inflammatory phase, contributing to the chronicity of the wound.
- One key component of chronic wounds is an elevated level of matrix metalloproteinases (MMP), at elevated levels MMPs not only degrade nonviable collagen but also feed on viable collagen.
- In addition, fibroblasts in a chronic wound may not secrete tissue inhibitors of MMPs (TIMPs) at an adequate level to control the activity of MMPs.
- These events prevent the formation of the scaffold needed for cell migration and ultimately prevent the formation of the extracellular matrix and granulation tissue.
- Collagen granules redress the grievances as following
    - It acts as a sacrificial substrate for MMPs, MMPs will act upon it.
    - Collagen breakdown products are chemotactic for a variety of cell types required for the formation of granulation tissue.
    - It has the ability to absorb wound exudates and maintain a moist wound environment.

- Since it contains antibiotics which will counteract the microorganisms.
- Provides matrix for tissue and vascular growth.
- Collagen granule dressings will maintain the wound microenvironment.

CONCLUSION

On the basis of the statistical analysis of our study we come to the conclusion that antibiotic coated collagen granule dressing is advantageous than conventional antibiotic dressing in terms of

- Decreased wound surface area
- Decreased number of dressings required before the application of skin grafting.
- Decreased duration between the first dressing and SSG application.
- Decreased duration of hospital stay.

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CONSENT FORM

ஆராய்ச்சிதகவல்அறிக்கை

மதுரைஅரசு இராசாசி மருத்துவமனையில் வரும் நோயாளிக்குள் ஒருஆராய்ச்சி இங்கு நடைபெற்றுவருகிறது. நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்கவிரும்பிகிறோம். உங்களை சில சிறப்புபரிசோதனைக்கு உட்படுத்தி அதன்தகவல்களை ஆராய்வோம்.அதனால் தங்களது நோயின் ஆய்வரிகையோ அல்லது சிகிச்சையோ பாதிப்பு ஏற்படாது என்பதை தெரிவித்து கொள்கிறேன் .முடிவுகளை வெளியிடும் போது அல்லது ஆராய்ச்சியின்போதோ தங்களது பெயரோ அல்லது அடையாளங்களோ வெளியிடமாட்டோம் என்பதை தெரிவித்து கொள்கிறோம். இந்தஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின்பேரில்தான் நடக்கும். மேலும் நீங்கள்எந்நேரமும் இந்த ஆராய்ச்சியில் இருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துகொள்கிறோம். இந்த சிறப்பு பரிசோதனைமுடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துகொள்கிறோம்.

ஆராய்ச்சியாளரின் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

PROFORMA

PATIENT DETAILS

Name :

Age :

Sex :

Ip No :

D.O.A. :

Diagnosis :

Duration of disease :

Comorbid illness :

Patient general condition

Body built :

Pallor :

Basic investigations

Blood Haemoglobin :

Paced cell volume :

RBS :

RFT : Bl. Urea

Sr. Creatinine

Total proteins : Albumin

Globulin

WOUND DETAILS

Site :

Size :

Shape :

Extent :

Margins :

Edges :

Floor :

Wound surface area :

COLLAGEN APPLICATION	WOUND SURFACE AREA (sq cm)	
	BEFORE	AFTER

Sl. No	name	Age	sex	Diagnosis	Comorbidities	wound surface area before collagen application	No of collagen granule dressings	Wound surface area after collagen application	After	SSG done	no of between first dressing and ssg	Hospital stay
1	Natarajan	38	M	Left Diabetic foot	Htn, Diabetic	36	5	31	31	yes	21	28
2	Manthaiyan	48	M	Chronic ulcer Rt foot	nil	64	6	60	51	yes	25	35
3	Sekar	57	M	Ulcer Rt foot	Diabetic	29	6	23	23	yes	25	37
4	Mohamed Jinnah	55	M	Traumatic ulcer Rt leg	nil	47	4	43	39	yes	15	24
5	Chinnaraj	28	M	Snake bite cellulitis Rt Hand	nil	49	6	44	41	yes	25	34
6	Paraman	65	M	Cellulitis with raw area Rt leg	Htn	73	7	62	62	yes	28	42
7	Subbaiya	65	M	Ulcer Lt foot	Diabetic	67	5	63	61	yes	21	28
8	Selvaraj	50	M	Raw area Lt foot	Diabetic	47	5	44	42	yes	21	32
9	Senthil Eswaran	27	M	Rt traumatic ulcer	nil	84	6	80	71	yes	24	32
10	Chinnan	60	M	Lt diabetic foot	Diabetic	33	4	28	27	yes	15	22
11	Rajakumar	40	M	Lt traumatic ulcer foot	nil	54	6	50	48	yes	24	32
12	Kanthavel	59	M	Rt bk amputee with stump ulcer	Diabetic	35	5	31	29	yes	21	42
13	Savithri	42	M	Rt raw area foot	Diabetic	22	5	19	19	yes	21	30
14	Rani	48	M	Raw area Lt foot	Htn	29	6	24	24	yes	24	32
15	Arifa beevi	63	F	Raw area Rt foot	Diabetic	49	5	43	37	yes	22	30
16	muthupandi	28	M	Rt traumatic ulcer	nil	84	6	74	74	yes	24	32
17	iyyavu	60	M	Lt diabetic foot	Diabetic	33	4	28	27	yes	15	22
18	Arun	40	M	Lt traumatic ulcer foot	nil	60	6	48	48	yes	24	34

19	Irulatchi	59	F	Rt bk amputee with stump ulcer	Diabetic	35	4	31	26	yes	21	40
20	Karuppasamy	42	M	Rt raw area foot	Diabetic	28	5	27	23	yes	22	31
21	Vellaisamy	47	M	Cellulitis with raw area Rt leg	Htn	29	6	24	24	yes	24	32
22	Pothumponnu	62	F	Raw area Rt foot	Diabetic	52	5	40	40	yes	22	30
23	Muthandi	38	M	Left Diabetic foot	Htn, Diabetic	36	6	29	29	yes	21	26
24	Ravi	48	M	Chronic ulcer Rt foot	Diabetic	64	5	48	48	yes	25	35
25	Gopi	56	M	Ulcer Rt foot	Diabetic	29	6	27	21	yes	25	37
26	Pradeep	55	M	Lt traumatic ulcer foot	nil	42	4	43	36	yes	15	24
27	Sankar	28	M	Snake bite cellulitis Rt Hand	Diabetic	49	6	41	41	yes	25	36
28	Amalan	67	M	Raw area Lt foot	Htn	68	7	62	54	yes	28	42
29	Xavier	60	M	Ulcer Lt foot	Diabetic	67	5	54	53	yes	21	28
30	Muthulakshmi	53	F	Raw area Lt foot	nil	47	6	42	38	yes	23	34

Sl. No	Name	Age	sex	Diagnosis	Comorbidites	Wound surface before conventional dressing	No of conventional dressings	Wound surface area after conventional dressing	SSG done	No of between SSG and first dressing	Hospital stay
1	Sakthi	21	M	Traumatic ulcer Rt thigh	nil	55	9	54	yes	36	45
2	madathiyammal	75	F	Chronic ulcer Lt foot	CKD, Htn	45	10	43	yes	42	51
3	Ainudeen	34	M	Ulcer Rt foot	Diabetic	24	7	24	yes	32	40
4	Rajendran	80	M	Ulcer Rt foot	Diabetic	36	6	35	yes	29	38
5	Petchiyammal	60	F	Raw area	Diabetic	44	8	44	yes	37	47
6	Jakkariya	46	M	Raw area Rt lower limb	Diabetic	112	12	110	yes	49	62
7	Nallamuthu	69	M	post neck dissection raw area	nil	24	5	24	yes	20	30
8	Ashok kumar	25	M	Raw area Rt leg	nil	38	7	37	yes	33	42
9	Moorthy Nayakkar	85	M	Raw area Lt foot	diabetic	47	9	47	yes	34	43
10	Gothandapani	60	M	Rt Ulcer foot	Diabetic	29	7	28	yes	31	42
11	Rajakesavan	60	M	Lt diabetic foot	Diabetic	56	10	54	yes	44	55
12	Jothi	60	F	Ulcer Rt foot	Diabetic	34	7	33	yes	34	42
13	Pothumponnu	72	F	Traumatic ulcer let foot	nil	47	9	46	yes	37	45
14	Seethalakshmi	70	F	Ulcer Lt foot	Diabetic	31	8	31	yes	38	46
15	Muthu lakshmi	48	F	Ulcer Rt foot	Diabetic	37	8	35	yes	38	47
16	Sanjeevi	66	M	Chronic ulcer Lt foot	CKD, Htn	45	8	43	yes	42	51
17	Samy	34	M	Raw area Rt leg	Diabetic	24	7	24	yes	32	42

18	V ivek	78	M	Ulcer Rt foot	Diabetic	36	6	35	yes	29	38
19	Geetha	56	F	Raw area	Diabetic	44	8	46	yes	37	47
20	Vadivel	42	M	Raw area Rt lower limb	Diabetic	108	10	106	yes	49	62
21	Irulandi	67	M	post neck dissection raw area	nil	24	5	24	yes	20	34
22	Ajithkumar	25	M	Raw area Rt leg	nil	38	8	38	yes	33	42
23	Karuppanan	81	M	Raw area Lt foot	diabetic	49	9	46	yes	34	43
24	Muthu	58	M	Lt diabetic foot	Diabetic	56	11	54	yes	46	55
25	Begam	48	F	Ulcer Rt foot	Diabetic	34	7	36	yes	34	42
26	Selvalakshmi	57	F	Traumatic ulcer let foot	nil	45	9	46	yes	37	45
27	Sarathkumar	68	M	Ulcer Lt foot	Diabetic	31	9	33	yes	38	48
28	Karuppayee	48	F	Ulcer Rt foot	nil	39	7	35	yes	40	44
29	Vellaiyammal	51	F	Raw area Lt foot	Diabetic	34	8	38	yes	38	48
30	Pappathi	73	F	Chronic ulcer Lt foot	CKD, Htn	42	12	46	yes	41	51

MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University,
Chennai, Tamil Nadu)

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr. Michael senraj J.
Course	:	PG in MS., General Surgery
Course of Study	:	2017-2020
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	Comparative study of the outcome of Antibiotic coated collagen Granules vs Antibiotic dressing in chronic ulcers
Ethical Committee as on	:	11.10.2018

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary Chairman Dean / Convenor

Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc (Hon)
CHAIRMAN
IEC - Madurai Medical College
Madurai

DEAN
Madurai Medical College
Madurai-20

22 OCT 2018

URKUND

Urkund Analysis Result

Analysed Document: COMPARATIVE STUDY OF THE OUTCOME OF ANTIBIOTIC COATED COLLAGEN GRANULES VS ANTIBIOTIC DRESSING IN CHRONIC ULCERS.docx (D58315652)
Submitted: 11/5/2019 5:51:00 PM
Submitted By: michaelsenraj@gmail.com
Significance: 8 %

Sources included in the report:

A PROSPECTIVE COMPARATIVE STUDY TO ASSESS THE EFFICACY OF PLATELET RICH PLASMA.docx (D51458192)
completed.docx (D42334458)
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https://www.ncbi.nlm.nih.gov/pubmed/25941895
https://healthdocbox.com/71916048-Cancer/Acute-and-impaired-wound-healing.html