"A COMPARATIVE STUDY OF THE EFFECT OF PIROXICAM VERSUS DICLOFENAC ON WOUND HEALING IN CLEAN ABDOMINAL WOUNDS" A ONE YEAR RANDOMISED CONTROL TRIAL AT THE KLES DR PRABHAKAR KORE HOSPITALS, BELGAUM

By

Dr. CHANDRASHEKARREDDY J. MADINUR

(REG.NO. BH0109002)

Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. S.
in
GENERAL SURGERY

Under the Guidance of

Dr. A. S. GODHI MS, FICS
Vice Principal and Professor

DEPARTMENT OF SURGERY,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELGAUM, KARNATAKA

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Date:

Place: **Dr. CHANDRASHEKARREDDY J. MADINUR**
REG. NO. BH0109002

KLE UNIVERSITY, BELGAUM, KARNATAKA

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Date:

Place:

Dr. A. S. GODHI **MS,FICS**
Vice Principal and Professor,
Department of Surgery,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

KLE UNIVERSITY, BELGAUM, KARNATAKA

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Dr. V. M. UPPIN $_{MS}$
Professor and Head,
Department of Surgery,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

Date:
Place: Belgaum

Dr. V. D. PATIL $_{MD,DCH}$
Principal,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

Date:
Place: Belgaum

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Date :

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Dr. CHANDRASHEKARREDDY J. MADINUR
(REG. NO. BH0109002)

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Date:

Place: Belgaum

Dr. CHANDRASHEKARREDDY J. M.
REG No. BH0109002

LIST OF ABBREVIATIONS USED

5-HT	-	5-hydroxytryptamine
BP	-	Blood pressure
CBC	-	Complete blood count
COX-1	-	Cyclooxygenase-1
COX-2	-	Cyclooxygenase-2
dl	-	Decilitre
DMARDs	-	Disease modifying anti rheumatic drugs
DNA	-	Deoxyribo nucleic acid
DOA	-	Date of admission
DOD	-	Date of discharge
ECG	-	Echocardiogram
ECM	-	Extracellular matrix
EGF	-	Epidermal growth factor
FBL	-	Fecal blood loss
FBS	-	Fasting blood sugar
GAGs	-	Glycosaminoglycans
GC	-	Glucocorticoids
gm	-	Gram
HIF-1	-	Hypoxia-inducible factor-1
i.e.	-	That is
IGF-1	-	Insulin like growth factor 1
IP/OPD No	-	In patient / Out Patient Department Number
LFT	-	Liver function tests
MDGF	-	Macrophage derived growth factor

mg	-	Milligram
ml	-	Millilitre
MMPs	-	Matrix metaloproteineases
MOA	-	Mechanisms of action
NMDA	-	N-methyl-D-aspartate
NSAIDs	-	Non-steroidal anti-inflammatory drugs
PDGF	-	Platelet-derived growth factor
pH	-	Power of hydrogen
PMN	-	Polymorphonuclear leucocyte
PO2	-	Partial pressure of oxygen
POD	-	Post-operative day
PPARgamma	-	Peroxisome proliferator activated receptor gamma
RBS	-	Random blood sugar
RNA	-	Ribonucleic acid
Sr.	-	Serum
TEMP	-	Temperature
TGF-b	-	Transforming growth factor beta
USG	-	Ultrasonography
VEGF	-	Vascular endothelial growth factor

ABSTRACT

Background and Objectives

The primary function of the skin is to serve as a protective barrier against the environment. The process of wound healing constitutes an array of interrelated and concomitant events. Understanding these processes and various factors affecting these processes continue to expand. The present study was undertaken to compare and evaluate the effect of piroxicam versus diclofenac on wound healing in clean abdominal wounds.

Methodology

The present one year randomized controlled trial was conducted on all the patients undergoing appendicectomies for uncomplicated appendicitis and uncomplicated inguinal hernia repairs in the Department of Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of January 2010 to December 2010. Based on the thumb rule a total of 60 patients divided into two groups of 30 each were studied. Based on the computer generated randomization patients were allocated to two groups that is group A (Inj. Piroxicam) and Group B (Inj. Diclofenac).

Results

In the present study, males outnumbered females with male to female ratio between of 1.72 to 2:1. The mean age in group A was 30.9 ± 7.86 years and in group B it was 30.3 ± 7.97 years. Both the groups that is Group A and B were graded under grade I (Good wound healing) from the POD 3 onwards. Overall

the individual score and total scores had no influence of the final grading (outcome) of the wound.

Conclusion and interpretation

Overall, better results were seen on wound healing in patients who received Inj piroxicam with significantly less post operative redness and oedema. However, this did not have significant difference in the final outcome of the grading of the wound.

Keywords

Diclofenac sodium; Piroxicam; Wound healing;

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INTRODUCTION

The primary function of the skin is to serve as a protective barrier against the environment. Loss of the integrity of large portions of the skin as a result of injury or illness may lead to major disability or even death.[1]

The wound healing is a complex process that can be divided into inflammatory reaction, proliferation and maturation of newly formed tissue. The inflammatory phase involves vascular and cellular events and is best characterized by edema, erythema and marked increase of blood supply. During proliferative phase there is formation of the epithelium with concomitant growth of granulation tissue and new blood vessels (angiogenesis). Angiogenesis seems to be strictly coordinated and regulated by multiple growth factors and cytokines released at the wound site. Once the tissue within the wound is formed the maturation phase begins. The synthesis of collagens and other extracellular matrix components increases tensile strength of the wound. Thus, the final result of the process of healing is the formation of tissue which tries to replicate the normal, uninjured skin.[2]

This process can go awry and produce an exuberance of fibroblastic proliferation with a resultant hypertrophic scar, which by definition is confined to the wound site. Further exuberance can result in keloid formation, where scar production extends beyond the area of the original insult. Conversely, insufficient healing can result in atrophic scar formation.

It is postulated that, NSAIDs by their anti inflammatory action may impair wound healing[3] which may explain why they have been used to only a limited extent to relieve pain. If they are to have maximal effect they must be started before the operation.[4]

Inhibition of matrix metaloproteineases (MMPs) promotes early wound healing by increase in the tissue permeability around the wound.[5] Piroxicam is a known NSAID. Which is known to inhibit matrix metaloproteineases.[5,6] Hence unlike other NSAIDs, Piroxicam is likely to promote wound healing. However there is limited data to support this hypothesis.

Hence the present study was undertaken to compare and evaluate the effect of piroxicam versus diclofenac on wound healing in clean abdominal wounds.

OBJECTIVES

The objective of this study was to evaluate and compare the effect of piroxicam versus diclofenac on wound healing in clean abdominal wounds.

REVIEW OF LITERATURE

Historical aspects[7]

The earliest recording of a 'wound healing man' is in a cave drawing in Spain dating back about 20-30,000 years. From the earliest recorded history it is clear that the Assyrians knew about healing, not just from an observational point of view but also in terms of practical management.

The Egyptians also had experience in wound healing and several treatises on healing have been recorded. The Egyptians also used antiseptics. They used the copper pigment malachite as both an eye adornment and an antiseptic. The Egyptians also knew of the value of sugar and honey. A mould can grow on sugar but no organism grows in a concentrated solution. A honey or sugary salve can improve healing and reduce surface contamination, and act as a topical nutrient. Antiseptics used in open wounds are probably not always necessary and some antiseptics are actually quite toxic.

Soon after the Egyptians, Sushruta Samhita by Sushruta, professed knowledge about methods of skin suture and the details of techniques to incise an abscess in Indian context. For practice, a bag of warm butter was used to simulate the feel of the knife going in and the pus coming out.

The Sushruta scripts also include a description of how insects have been applied in the healing of wounds. The earliest type of clip was based on the mandibles of certain ants. It describes how wounds in connection with the bowels caused so much juice that they were difficult to close. The mandibles from a

certain ‘soldier ant’ were used to close these types of wounds. This technique is also found in Asia, Africa and South America.

The father of medicine, Hippocrates, who lived nearly 2500 years ago, wrote several accounts on wound healing and was aware of the importance of infection in relation to wound healing. He understood the concepts of primary and secondary wound healing, using antiseptics such as wine. The effect has been much disputed but cannot be due only to the alcohol in the wine. When taking the same concentration of alcohol the effect has been shown to be limited. Hippocrates pointed to the significant role of compression in the treatment of patients with leg ulcers.

For centuries only limited information existed on wound healing. During the 15th century the anatomy was described in greater detail by the surgeon Andreas Vesalius. As a result surgical expertise became more acknowledged, although it was still carried out by barber surgeons. In England the association of Barber Surgeons was constituted which laid the grounds for a surgical speciality.

From the early history of wound healing it is apparent that Celsus in De Medicina, recognized the cardinal signs of inflammation. John Hunter, considered one of the fathers of surgery, recognized that it is not possible to operate without inflammation. Actually it was thought that the pus had to be present in order for the wound to heal.

Ignaz Semmelweis, a Hungarian obstetrician who lived in Vienna discovered that “if you went from the post-mortem room to the delivery room, but washed your hands in between using chloride of lime, the maternal mortality

was reduced". By introducing obligatory hand washing the mortality rate fell from over 10% to 1% in two years.

Sadly Semmelweis published his work too late and it did not receive the attention it deserved. Lord Lister introduced antiseptics containing carbolic acid and realized that by using antiseptics compound fractures could heal and amputation be avoided. The idea of cleansing wounds was further developed by Alexander Fleming who discovered that penicillin could treat infections.

Certain antiseptics can cause a negative effect on new as well as old tissue, and today antiseptics are rarely used in the treatment of open wounds. Alexander Fleming suggested in 1920 that the value of the antiseptic (antimicrobial) effect of antiseptics should be weighed against their toxicity in tissues.

Contemporary surgery is based on the discovery of these surgeons. In the early 1800s Ephraim McDowell performed the first elective abdominal operation on a large ovarian cyst. By the 1920s major elective surgery was common with general anaesthesia and the surgeons using gloves but no masks. From these artisans came the aphorism of 'cut well, sew well, get well'. Since then, research has produced many results and significant improvements have been made. Several experimental methods were used for wound healing research, some are crude and others relatively sophisticated.

Wound healing

Wound healing is a complex and dynamic process of restoring cellular structures and tissue layers. The various stages of wound healing have been widely investigated over the years and several major events associated with healing have been discussed in the literature.[8,9,10] Wound healing is a multistep process that involves a multitude of cells and events. Initial stages of wound healing involve the formation of a blood clot and inflammation. The inflammatory response is followed by proliferation and migration of dermal and epidermal cells, and matrix synthesis, in order to fill the wound gap and to reestablish the skin barrier.[11,12] Finally, tissue remodeling and differentiation enable recovery and restoration of skin aesthetics.[11,13] The consensus in the literature is that the stepwise process of wound healing first strives toward immediate filling of the gap, followed by re-epithelialization and reestablishment of the skin barrier.[14]

Monitoring throughout the wound-healing process enabled a longitudinal assessment of the discrete steps that occur over a time continuum. Evaluation of individual components allowed us to study the contribution of overlapping, but distinct steps to the overall process of wound healing. Furthermore, methods have been developed which enable an accurate assessment of the equilibrium in normal wound healing, the changes which lead to impaired wound healing, and the influence of treatments. The insights gained from this type of assessment facilitate the development of novel therapies and delineate their specific contribution to the progression of discrete healing steps as well as to the continuum of the wound-healing process in a time- and stage-specific manner.[15]

Tremendous advancements have been made in understanding the processes of wound healing. The cell types and the order in which they appear in the wound have been established; many growth factors and their functions have been elucidated.[16]

Despite the advances in understanding the science of wound healing, many more steps have yet to be discovered and elucidated. The frontier of this field includes the prevention of hypertrophic scar and keloid formation and, ultimately, any visual remnant of the wound.

An incision created by a scalpel, trauma resulting from a bullet, or tissue death caused by a myocardial infarction all undergo a similar and predictable reparative process. Understanding how the body repairs damaged tissue and what factors influence the wound healing process helps the surgeon predict the outcome from surgery.

Tissue injury is common thread to every medical speciality. Wound healing in any tissue follows a predictable sequence of events. A broad understanding of the sequence of events, cells involved, relative time table, and molecular signaling can allow for improvements in would healing.

Although seemingly basic in concept, advances in molecular science have allowed modern medicine to understand the complex interplay between the cells involved in the phases of wound healing. As greater understanding of the growth factors involved in wound healing emerges, future patient care may include scarless wound healing and transplant of tissues engineered from stem cells.

Physiology of wound healing

Phases of wound healing

Knowledge of the phases of wound healing allows the practitioner to counsel patients effectively and treat wounds appropriately. The typical wound, after primary closure, may take over a year to fully mature; the appearance of the scar may dramatically change during this time. Thus, all wounds should be at least 1 year old before scar revision is considered.

The wound healing process has three phases. 1. Inflammatory phase; 2. Proliferative phase; and 3. Remodeling phase.[17] The inflammatory phase is characterized by hemostasis and inflammation. Collagen exposed during wound formation activates the clotting cascade (both the intrinsic and extrinsic pathways), initiating the inflammatory phase. After injury, the damaged cell membranes release thromboxane A2 and prostaglandin 2-alpha, which produce vasoconstriction. This initial response helps to limit hemorrhage. After a short period, capillary vasodilatation occurs secondary to local histamine release, and the cells of inflammation are able to migrate to the wound bed. The timeline for cell migration in a normal wound healing process is predictable.

Following tissue injury via an incision, the initial response is usually bleeding. The cascade of vasoconstriction and coagulation commences with clotted blood immediately impregnating the wound, leading to hemostasis, and with dehydration, a scab forms. An influx of inflammatory cells follows, with the release of cellular substances and mediators. Angiogenesis and re-epithelization occur and the deposition of new cellular and extracellular components ensues.

Inflammatory phase

The inflammatory phase begins at the time of injury and lasts 2-4 days. The phase begins with hemostasis and formation of the platelet plug. Platelets upon activation also secrete soluble modulators of wound healing and release their granular contents. These include chemotactic and growth factors such as platelet derived growth factor (PDGF), proteases and vasoactive substances such as serotonin and histamine.Platelets release PDGF and transforming growth factor beta (TGF-b) from their alpha granules to attract neutrophils and macrophages. Neutrophils fight potential bacterial contamination of the wound and activate cytokine secretion to activate dermal and epidermal processes.[9] Macrophages are the most important mediators of wound healing which continue to emit growth factors to attract fibroblasts and usher in the next phase of wound healing. If inflammation increases beyond a certain level, it will lead to healing impairment, destruction of the early migratory effect and an arrest of the healing process.[13] Furthermore, sustained chronic inflammatory response leads to extracellular matrix (ECM) collapse and formation of necrotic centers.

Proliferative phase

The proliferative phase begins on approximately day 3; it overlaps with the inflammatory phase. This phase consists of different subphases. These subphases do not happen in discrete time frames but constitute an overall and ongoing process. The subphases are "fibroplasia, matrix deposition, angiogenesis and re-epithelialization".[18]

In days five to seven, fibroblasts have migrated into the wound, laying down new collagen of the subtypes I and III. Early in normal wound healing, type III collagen predominates but is later replaced by type I collagen.

Tropocollagen is the precursor of all collagen types and is transformed within the cell's rough endoplasmic reticulum, where proline and lysine are hydroxylated. Disulfide bonds are established, allowing three tropocollagen strands to form a triple left-handed triple helix, termed procollagen. As the procollagen is secreted into the extracellular space, peptidases in the cell wall cleave terminal peptide chains, creating true collagen fibrils.

The wound is suffused with glycosaminoglycans (GAGs) and fibronectin produced by fibroblasts. These GAGs include heparan sulfate, hyaluronic acid, chondroitin sulfate, and keratan sulfate. Proteoglycans are GAGs that are bonded covalently to a protein core and contribute to matrix deposition.

Angiogenesis is the product of parent vessel offshoots. The formation of new vasculature requires extracellular matrix and basement membrane degradation followed by migration, mitosis, and maturation of endothelial cells. Basic fibroblastic growth factor and vascular endothelial growth factor (VEGF) are believed to modulate angiogenesis.

Re-epithelization occurs with the migration of cells from the periphery of the wound and adnexal structures. This process commences with the spreading of cells within 24 hours. Division of peripheral cells occurs in hours 48 to 72, resulting in a thin epithelial cell layer, which bridges the wound. Epidermal growth factors are believed to play a key role in this aspect of wound healing.

This succession of subphases can last up to 4 weeks in the clean and uncontaminated wound.

Phase of Remodeling

After the third week, the wound undergoes constant alterations, known as remodeling, which can last for years after the initial injury occurred. Collagen is degraded and deposited in an equilibrium-producing fashion, resulting in no change in the amount of collagen present in the wound. The collagen deposition in normal wound healing reaches a peak by the third week after the wound is created. Contraction of the wound is an ongoing process resulting in part from the proliferation of the specialized fibroblasts termed myofibroblasts, which resemble contractile smooth muscle cells. Wound contraction occurs to a greater extent with secondary healing than with primary healing. Maximal tensile strength of the wound is achieved by the 12th week, and the ultimate resultant scar has only 80% of the tensile strength of the original skin that it has replaced.

The timetable for wound healing can be quite variable. Chronic wounds can stall in the inflammatory phase because of poor perfusion, poor nutrition, or a myriad of other factors causing excessive buildup of exudates in the wound base. These wounds tend to remain unhealed unless active and aggressive measures are undertaken to correct the underlying comorbidities while providing proper wound care.

Healing may also become exaggerated in keloid and hypertrophic scar formation. Excessive type III collagen formation in the proliferative phase causes an overgrowth of scar tissue in these wounds. The etiology is multidimensional.

Individuals with darkly pigmented skin are genetically prone to keloid formation. Certain areas of the body, such as the sternum and shoulder, are more prone to hypertrophic scar formation.

Phases can also be blunted as in the fetus, which has a decreased inflammatory phase and heals without scar. Experiments evaluating fetus wound healing have found a higher level of TGF-b3 than in adults.[19] This is thought to antagonize the effects of TGF-b2 and TGF-b1 found to be upregulated in keloids and hypertrophic scars. Thus, a greater understanding of the growth factors in fetus healing may lead to novel therapy for scarless wound healing and treatment of keloid and hypertrophic scars. Human trials are currently underway.[19]

Collagen types and locations are as follows:

- Type I - Located in all connective tissue except hyaline cartilage and basement membranes
- Type II - Located in hyaline cartilage
- Type III - Located in distensible connective tissue (blood vessels)
- Type IV - Located in basement membranes
- Type V - Located in all tissues
- Type VI - Located in all tissues
- Type VII - Located in the dermal-epidermal junction
- Type VIII - Located in the Descement membrane
- Type IX - Located in hyaline cartilage
- Type X - Located in hypertrophic cartilage and hyaline cartilage

Types of wound healing

Although various types of wound healing have been described, the ultimate outcome of any healing process is repair of a tissue defect. The three types of wound healing are primary, secondary, and tertiary. Primary healing occurs on primary closure of a wound within hours of its creation. Secondary healing occurs in wounds which are not primarily closed; the wound closes spontaneously by contraction and re-epithelialization. Tertiary wound healing occurs after delayed primary closure following initial debridement of the wound for an extended period and then formal closure with suturing or by skin grafting. A fourth type is healing that occurs in wounds that are only partial skin thickness.[20]

In all these types of wound healing the interaction of cellular and extracellular constituents are similar.

Primary wound healing

Primary wound healing or healing by first intention occurs on suturing a full-thickness surgical incision within hours of wounding. This surgical insult results in the mortality of a minimal number of cellular constituents.

Delayed primary wound healing

If the wound edges are not approximated immediately, delayed primary wound healing can take place. This type of healing may be desired in the case of contaminated wounds. By the fourth day, phagocytosis of contaminated tissues is well underway, and the processes of epithelization, collagen deposition, and

maturation are occurring. Foreign materials are walled off by macrophages that may metamorphose into epithelioid cells, which are encircled by mononuclear leukocytes, forming granulomas. Usually the wound is closed surgically at this juncture, and if the "cleansing" of the wound is incomplete, chronic inflammation can ensue, resulting in prominent scarring.

Secondary wound healing

A third type of healing is known as secondary healing or healing by secondary intention. In this type of healing, a full-thickness wound is allowed to spontaneously close and heal. Secondary healing results in an inflammatory response that is more intense than with primary wound healing. In addition, a larger quantity of granulation tissue is fabricated. Secondary healing results in pronounced contraction of wounds. Fibroblastic differentiation into myofibroblasts, which resemble contractile smooth muscle, is believed to contribute to wound contraction. The myofibroblasts are maximally present in the wound from the 10^{th} to 21^{st} days.

Healing in partial thickness skin wounds:

Epithelization is the process by which epithelial cells migrate and replicate via mitosis and traverse the wound. This occurs as part of the phases of wound healing, which are discussed in Sequence of Events in Wound Healing. In wounds that are partial thickness, involving only the epidermis and superficial dermis, epithelization is the predominant method by which healing occurs. Wound contracture is not a common component of this process if only the epidermis or epidermis and superficial dermis are involved.

Conditions that affect wound healing can make all the difference in various wounds, ranging from an inconspicuous wound after plastic surgery to an amputation or even death. When approaching an injured patient, the following list can guide the thought process of the physician or caretaker in optimizing healing conditions.

Factors affecting wound healing

Local factors affecting wound healing

Infection

Infection is defined as having quantitative bacterial counts of 10^5 colony forming units per gram of tissue. It is the most common local cause for prolonged healing. All wounds are contaminated postoperatively by resident bacterial flora, however clinical infection occurs when a critical number of pathogenic organisms are present. Bacteria prolong healing by activating the alternate complement pathway and detrimentally exaggerating and prolonging the inflammatory phase of wound healing. They also elaborate toxins and proteases that can be damaging to cells. Finally, they compete for oxygen and nutrients in the wound milieu. Lactic acid is produced in this hypoxic state, that further stimulates the release of damaging proteolytic enzyme.[21]

Formation of excessive devitalised tissue, increased tension in the wound, hematoma and seromas, foreign bodies in the wound, all these factors predispose to bacterial infection. All these can be avoided by proper surgical techniques.[22]

Surgical Technique

The rough handling of tissue or the use of inappropriately bulky instrumentation can lead to crushed skin edges and subsequent devitalization of tissue, leading to increase in inflammatory reaction and risk of secondary infection with increased scarring.[22]

Wound closed with inappropriately reactive suture material may increase the chances of a foreign body reaction and subsequent infection. Skin sutures tied too tightly may lead to tissue ischaemia and predispose to infection.[22]

Hematoma Formation

Excessive bleeding and the formation of a hematoma within the wound not only can mechanically disrupt the wound closure but also can serve as an excellent culture medium for micro organisms.[22]

Foreign body reaction

A foreign body in the wound serves as an appropriate surface for the activation of the alternate complement pathway and the generation of a prolonged inflammatory response, which interferes with the subsequent stages of wound repair. Wounds containing foreign materials are characterised by low pH and low PO2. These factors significantly slow down wound repair.[22]

Tissue ischemia

Tissues cannot heal without the cells, oxygen, and nutrients that the cardiovascular system delivers.[21] Local factors such as foreign bodies, infection

or strangulating sutures significantly slow healing by producing tissue ischemia. Local hypoxia is detrimental to cellular proliferation, resistance to infection and collagen production. The cumulative effect is delayed healing.[22]

Topical medications and dressings

Occlusive or semiocclusive dressings promote faster reepithelization.[23] They may also alter certain aspects of dermal repair. They also provide the moist environment needed for optimal wound repair, they may also help to prevent bacterial invasion and wound infection.[24] Numerous dressings are available in the market. Many claim that they need to be changed less often than other dressings. This may be true for a clean wound. However, there is no substitute for frequent dressing changes in a grossly contaminated or recently debrided infected wound. Other basic principles apply. The wound should be kept moist (but not wet) at all times. Desiccated tissue is dead tissue and must be sharply debrided. With the advent of negative pressure wound dressing, healing of chronic wounds can be greatly improved.[22]

Currently, cytokines have a limited role in clinical practice. The only currently available commercial product proven to be efficacious in randomized, double-blind studies is platelet-derived growth factor (PDGF), available as recombinant human PDGF-BB. In multiple studies, recombinant human PDGF-BB has been demonstrated to reduce healing time and improve the incidence of complete wound healing in stage III and IV ulcers.[25] Many other cytokines currently under in vitro study include transforming growth factor beta (TGF-b), epidermal growth factor (EGF), and insulin like growth factor 1 (IGF-1).

Proper wound healing involves a complex interaction of cells and cytokines working in concert. In recent years, more chemical mediators integral to this process have been identified. The sequential steps and specific processes have not been fully differentiated. When examining the process of wound healing, one should identify the major steps and know the important mediators.

Local medicaments applied to the wound may affect wound repairs. Even the bases in which these agents are compounded may accelerate or diminish the rates of epithelization. Triamcinolone acetonide ointment (0.1%) nitrofurazone, benzoyl peroxidase cream, silver sulfadiazine, neosporin ointment are examples of the drugs that affect epidermal migration.

Systemic factors affecting wound healing

1.Deficiency states

a. Metabolism: Aberrant carbohydrate and fat metabolism slows wound repair. Glucose may be unavailable or fail to enter cell properly. Insulin may act as a fibroblast growth factor and its deficiency leads to suppression of collagen deposition in the wound.[26]

b. Vitamins: Vitamin supplementation has not been proven to increase wound healing unless a specific deficiency exists.[27] Vitamin A is an exception to this rule.Vitamin A deficiency has been associated with slowed reepithelization, decreased collagen synthesis and stability and an increased susceptibility to infection.

Vitamin C (Ascorbic acid) is an essential cofactor during collagen biosynthesis. In scurvy, the collagen formed is unhydroxylated, relatively unstable and subject to collagenolysis.

Vitamin K deficiency results in a deficiency in the production of vitamin K dependent clotting factors (factors II, VII, IX and X) resulting in bleeding diathesis, hematoma formation which exert detrimental effects on wound healing.

c. Proteins: When assessing nutritional status, certain serum nutritional markers can be helpful. Albumin is a good marker of overall long-term nutritional status over the last month; ideally, it should be at least 3.5 g/dL to optimize wound healing. Prealbumin is a marker of more recent nutritional status and should be maintained above 17 mg/dL. Caloric needs of the severely injured patient can exceed 35 kcal/kg/d. Protein intake of 0.8-2 g/kg/d should be assured and adjusted according to the stage of healing and injury. This is particularly true for burn patients who require multiple debridements and grafting.

Negative nitrogen balance and relative protein deficiency may occur after major trauma or during sepsis. Fibroplasia and all aspects of matrix formation are delayed, wound remodelling is also impaired. Cellular and humoral immune responses are blunted and bacterial phagocytosis and killing are defective. Protein deficiency may lead to an increased propensity for infection.

d. Trace elements and minerals: These are required as cofactors for various enzymes during wound healing. These include zinc, copper, iron, manganese etc. Zinc deficiency however is more important clinically, as it is a constituent of multiple important metalloenzymes including collagenase and deoxyribonucleic

acid (DNA) and ribonucleic acid (RNA) polymerases. Its deficiency results in impaired immune responses, decreased protein and collagen synthesis, decreased lysyl oxidase activity and interfere with vitamin A transport.

2. *Aging*

Physiologic aging diminishes virtually all phases of wound healing. Disease status associated with accelerated aging (such as Werner's syndrome) may be characterized by recalcitrant cutaneous ulcerations and impaired healing.[22]

The mechanism behind lack of scarring in fetal wounds are unknown, but probably relate to the control of collagen fibrillogenesis. The role of collagen in the fetal wound matrix is controversial. A study[28] found that collagen was deposited in fetal wounds much more rapidly than in adults. Collagen deposition occurred in a normal dermal and mesenchymal pattern in second and early third trimester in fetal lambs. These findings are consistent with the observation that fetal wounds heal faster and without scar formation.[22]

3. *Disease states*

Some of the most important diseases leading to impaired wound healing are listed here.[21]

Hereditary[22]

- Ehlers-Danlos syndrome, Prolidase deficiency

Coagulation disorders[22]

- Hemophilia

- Von Willebrand's disease
- Factor XIII deficiency
- Hypofibrinogenemia
- Werner's syndrome
- Vascular disorders
- Congestive heart failure, Atherosclerosis, Vasculitis
- Venous stasis
- Lymphoedema

Metabolic[22]

- Chronic renal failure
- Diabetes mellitus
- Malnutrition
- Cushing's syndrome
- Hyperthyroidism
- Immunologic deficiency states may impair healing by predisposing the wound to infection and diminishing the inflammatory phase of wound healing.

Others[22]

- Chronic pulmonary disease
- Chronic liver disease (cirrhosis)
- Malignancy
- Myelofibrosis and other chronic hematologic disorders associated with thrombocytopenia

Drugs affecting Wound Healing

Some of the drugs causing impaired wound healing are;[21]

- Glucocorticoids
- Anticoagulants
- Antineoplastic drugs
- Cyclosporin A
- Colchicine
- Penicillamine
- Zinc sulfate (high doses)
- Beta amino propionitrile

Glucocorticoids

Systemic glucocorticoids (GC), which are frequently used as anti-inflammatory agents, are well-known to inhibit wound repair *via* global anti-inflammatory effects and suppression of cellular wound responses, including fibroblast proliferation and collagen synthesis. Corticosteroids affect the inflammatory process by stabilizing lysosomes within neutrophils, inducing antiinflammatory proteins, and inhibiting cytokine release and chemotaxis.[29,30] Systemic steroids cause wounds to heal with incomplete granulation tissue and reduced wound contraction.[31] Glucocorticoids also inhibit production of hypoxia-inducible factor-1 (HIF-1), a key transcriptional factor in healing wounds.[32] Beyond effects on repair itself, systemic corticosteroids may increase the risk of wound infection. By reducing neutrophil chemotaxis, the host may be more susceptible to bacterial infection.[33] Collagen production, angiogenesis, and

reepithelization in dermal wounds may also be impaired.[34] In addition, fibroblast dysfunction occurs with the use of corticosteroids, which decreases wound tensile strength, an important component of the remodeling phase.[35,36] The clinical consequences of these effects include dehiscence of incision site, wound infection, and delayed open-wound healing.[37]

One of the earliest reports on the effect of corticosteroids on wound healing in humans was made in 1965.[38] This investigator retrospectively examined the charts of 38 surgical patients who took corticosteroids preoperatively. Arbitrarily, he divided patients into groups according to the length of time they had received corticosteroids. Patients taking corticosteroids for at least 1 week were considered to be receiving "long-term" therapy. Most of the patients underwent splenectomy. The investigator found that 29% of all patients who received preoperative corticosteroids had complications (complete or partial disruption or prolonged discharge) with wound healing. No statistical analysis was performed, however. The investigator stated that there was no difference in complication rates based on the length of preoperative corticosteroid administration, but he did not account for confounding factors. This study represents one of the first known studies showing a link between corticosteroid administration and impaired surgical wound healing.

In another retrospective analysis in humans, authors analyzed the postoperative complication rate in patients with rheumatoid arthritis who underwent orthopedic surgery.[39] Of 111 total subjects, 49 had used corticosteroids (prednisolone 2.5-15 mg/day or its equivalent) within the previous 2 years. The authors found no difference between the times to complete wound

healing in patients with rheumatoid arthritis compared with controls (16.6 B1 7.5 vs 15.2 B1 7.9 days, $p>0.10$). Compared with patients who did not receive corticosteroids, no difference was noted in wound healing among patients receiving corticosteroids (rates not given, $p>0.10$). However, the authors found that patients who had taken corticosteroids for more than 3 years took longer to heal after surgery (20.3 B1 11 vs 15.2 B1 4.9 days, $p<0.05$). Although these findings appear to be of clinical importance, it is difficult to assess the non significance of the primary end point (days to complete wound healing) since no power analysis was done earlier.

Finally, in a retrospective study, authors reviewed the rates of fusion in 26 patients with rheumatoid arthritis who had either compression arthrodesis or internal fixation of the ankle.[40] Each group of patients was similar with regard to age and sex, and all of the patients had disease involvement in other joints. The authors found that four of seven ankles that failed to fuse were associated with infection. These patients were taking dosages of prednisone ranging from 6.5-40 mg/day (mean 17 mg/day), whereas patients who experienced failed fusion without infection were only taking an average of 6 mg/day. Although the study is limited by its small population, it is possible that higher dosages of prednisone may be a risk factor for failed fusion.

While systemic corticosteroids inhibit wound repair, topical application produces quite different effects. Topical low-dosage corticosteroid treatment of chronic wounds has been found to accelerate wound healing, reduce pain and exudate, and suppress hypergranulation tissue formation in 79% of cases. While

these positive effects are striking, careful monitoring is necessary to avoid a potential increased risk of infection with prolonged use.[41]

Mycophenolate Mofetil, Tacrolimus, Sirolimus, and Cyclosporine

There is an emerging role for the use of other immunosuppressant drugs in the treatment of inflammatory disease states such as inflammatory bowel disease and rheumatoid arthritis. Tacrolimus was found to be useful in the treatment of DMARD-resistant rheumatoid arthritis, and its congener, sirolimus, has also shown similar promise.[42-44] Cyclosporine may be used for patients with inflammatory bowel disease and refractory fistulas; it has also been studied for use in patients with rheumatoid arthritis who have failed initial therapy.[45,46] Mycophenolate mofetil also may be a treatment option for rheumatoid arthritis.[47] Although these agents are traditionally used as immuno-suppressants after organ transplantation, their scope appears to be evolving to include treatment of other conditions such as rheumatoid arthritis and inflammatory bowel disease. Regardless of the clinical setting, practitioners should be mindful of their effects on wound healing in the perioperative period.

One group conducted a retrospective analysis of 158 adult patients undergoing kidney transplantation and receiving immunosuppression with either mycophenolate mofetil or sirolimus.[48] They showed that sirolimus was an independent risk factor for postoperative surgical complications and superficial healing problems. These results were confirmed in a prospective trial that showed an increase in superficial wound infections in patients receiving a sirolimus-based immunosuppressive regimen.[49] Similar results were found in rats that underwent

sigmoidostomy and received either mycophenolate mofetil or placebo.[50] A significant decrease in healing and mechanical stability was found in the group that received mycophenolate mofetil. These findings underscore the importance of further research to determine the optimal time to resume therapy in the postoperative period in order to optimize healing and prevent disease flare-ups.

Many medications, such as those which interfere with clot formation or platelet function, or inflammatory responses and cell proliferation have the capacity to affect wound healing. Here we review only the commonly used medications that have a significant impact on healing, including glucocorticoid steroids, non-steroidal antiinflammatory drugs, and chemotherapeutic drugs.

Chemotherapeutic Drugs

Most chemotherapeutic drugs are designed to inhibit cellular metabolism, rapid cell division, and angiogenesis and thus inhibit many of the pathways that are critical to appropriate wound repair. These medications inhibit DNA, RNA, or protein synthesis, resulting in decreased fibroplasia and neovascularization of wounds.[31,51] Chemotherapeutic drugs delay cell migration into the wound, decrease early wound matrix formation, lower collagen production, impair proliferation of fibroblasts, and inhibit contraction of wounds.[31] In addition, these agents weaken the immune functions of the patients, and thereby impede the inflammatory phase of healing and increase the risk of wound infection. Chemotherapy induces neutropenia, anemia, and thrombocytopenia, thus leaving wounds vulnerable to infection, causing less oxygen delivery to the wound, and also making patients vulnerable to excessive bleeding at the wound site.

Impaired wound healing due to chemotherapeutic drugs such as adriamycin is most common when the drugs are administered pre-operatively or within 3 weeks post-operatively.[52] Additionally, low post-operative albumin levels, low post-operative hemoglobin, advanced stage of disease, and electrocautery use have all been reported as risk factors for the development of wound complications.[53]

A newer generation of tumor chemotherapeutics is the angiogenesis inhibitors, such as bevacizumab, which is an antibody fragment that neutralizes VEGF. These therapies work in conjunction with traditional chemotherapeutics to limit the blood supply to tumors, reducing their ability to grow. Wound-healing complications, including an increase in wound dehiscence, have been described in patients on angiogenesis inhibitors.[54] A caveat is that most patients on angiogenesis inhibitors are also on traditional chemotherapeutics, making it difficult to sort out whether angiogenesis inhibitors alone would perturb repair.[55,56] Nevertheless, current recommendations include discontinuation of angiogenesis inhibitors well in advance of any surgical procedures.

Nonsteroidal Antiinflammatory Drugs and Wound Healing

Nonselective NSAIDs are reversible inhibitors of both COX-1 and COX-2, with each NSAID inhibiting the COX enzymes at varying degrees.[57] Inhibition of both COX-1 and COX-2 results in decreased production of eicosanoids such as prostaglandins and leukotrienes. Deficiency of prostaglandins results in decreased permeability of endothelial cells[58] and inhibition of hyaluronic acid production, which is needed in the proliferative phase of healing.[59,60] These drugs also inhibit

the production of thromboxane A_2, which decreases platelet aggregation, thus predisposing the patient to hematoma formation and persistent bleeding. Animal studies have shown that the interruption in the balance between prostaglandin and thromboxane A_2 can impair angiogenesis and wound healing.[61,62]

Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen are widely used for the treatment of inflammation and rheumatoid arthritis and for pain management. Low-dosage aspirin, due to its anti-platelet function, is commonly used as a preventive therapeutic for cardiovascular disease, but not as an anti-inflammatory drug.[63] There are few data to suggest that short-term NSAIDs have a negative impact on healing. However, the question of whether long-term NSAIDs interfere with wound healing remains open. In animal models, systemic use of ibuprofen has demonstrated an anti-proliferative effect on wound healing, resulting in decreased numbers of fibroblasts, weakened breaking strength, reduced wound contraction, delayed epithelialization,[64,65,66] and impaired angiogenesis.[67] The effects of low-dose aspirin on healing are not completely clear. Clinical recommendations suggest that, to avoid anti-platelet effects, individuals should discontinue NSAIDs for a time period equal to 4 to 5 times the half-life of drugs before surgery. Thus, the majority of surgical patients do not have significant NSAID activity at the time of wound repair. The exception may be those cardiac patients who must be maintained on low-dose aspirin due to severe risk of cardiovascular events.[63] In terms of the topical application of NSAIDs on the surfaces of chronic wounds, the local use of ibuprofen- foam provides moist wound healing, reduces persistent and temporary wound pain, and benefits chronic venous leg ulcer healing.

The effect of NSAIDs on human tendon cell proliferation also has been evaluated. One group studied the effect of NSAIDs (diclofenac, aceclofenac, indomethacin, naproxen) in vitro on tendon cell proliferation and production of proteoglycans in 28 tendons (14 digital flexor tendons, 14 patella tendons).[68] The concentrations of NSAIDs used were similar to those that would be achieved in vivo with doses normally used in clinical practice. The concentration of prostaglandins was also evaluated by radioimmunoassay utilizing dextracoated charcoal to separate bound from free ^{3}H-prostaglandins. Cell proliferation and glycosaminoglycan synthesis in patellar tendon cultures were significantly inhibited by naproxen and indomethacin when compared with media controls. Conversely, no significant difference was found on tendon cell proliferation and glycosaminoglycan synthesis with the use of diclofenac and aceclofenac. The authors concluded that the use of some NSAIDs may inhibit tendon repair after injury. These findings may be due to differences in COX 2:COX 1 specificity, as diclofenac has a greater selectivity for COX-2 inhibition when compared with the other NSAIDs in the study.[57]

The safety of NSAID use was examined in a retrospective analysis of patients with osteoarthritis (mean age 60 yrs) who underwent surgery for primary total hip arthroplasty.[69] Patients were grouped as either taking NSAIDs before surgery (but not within 24 hrs) or not taking NSAIDs. The NSAIDs administered during this study were indomethacin, sulindac, tolmetin, ibuprofen, ketoprofen, naproxen, fenoprofen, meclofenamate, aspirin, and piroxicam. Patients were compared based on intraoperative fluid administration requirements, estimated blood loss, number of transfusions needed, postoperative complications, and

length of hospital stay. The authors found that 12% of patients taking NSAIDs had hypotensive or minor bleeding episodes postoperatively, whereas only 2% of patients not taking NSAIDs experienced either of these complications. Both groups had the same length of hospital stay (10 days), the same number of transfusions (2.2 units), and similar postoperative wound drainage (NSAID 483 ml vs no NSAID 548 ml, p=NS). The increased bleeding seen in patients who received NSAIDs may have been due to the inhibition of thromboxane A_2. The authors concluded that NSAIDs should be discontinued for a sufficient amount of time to allow for total drug elimination before surgery.

All studies reported are very small, and caution must be exercised when applying these data in the perioperative setting. Clinically significant differences may exist in soft tissue and tendon cell healing when nonselective NSAIDs are given during the postoperative period. It is recommend that, withholding nonselective NSAIDs for at least three to four half-lives before surgery involving tendons and soft tissue ensure removal from the systemic circulation.

DICLOFENAC

Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) taken to reduce inflammation and as an analgesic reducing pain in conditions such as arthritis or acute injury. It can also be used to reduce menstrual pain, dysmenorrhea. The name is derived from its chemical name: 2-(2,6-dichloranilino) phenylacetic acid.

Diclofenac is a potent anti-inflammatory and analgesic compound with good antipyretic and uricosuric properties. It is one of the most potent inhibitors

of prostaglandin synthetase known. It shows a favourable therapeutic ratio considering its efficacy, and proved superior to the reference drugs in terms of gastro-intestinal tolerability. All metabolites are clearly less potent than the parent compound.[70]

Diclofenac sodium is the active ingredient in a nonsteroidal anti-inflammatory drug designed by selection of appropriate physicochemical and steric properties. Its pharmacologic activity, specifically its effects in acute and subchronic inflammation, and its analgesic activity have been assessed in animal models. The tolerability of the compound as judged by several parameters (i.e., ratio between the acute lethal dose or the dose inducing gastrointestinal blood loss and the desired pharmacologic activity) is favorable in comparison with other nonsteroidal anti-inflammatory drugs. Diclofenac sodium acts by potent cyclo-oxygenase inhibition, reduction of arachidonic acid release, and enhancement of arachidonic acid uptake. It thereby results in a dual inhibitory effect on both the cyclo-oxygenase and lipoxygenase pathways.[71]

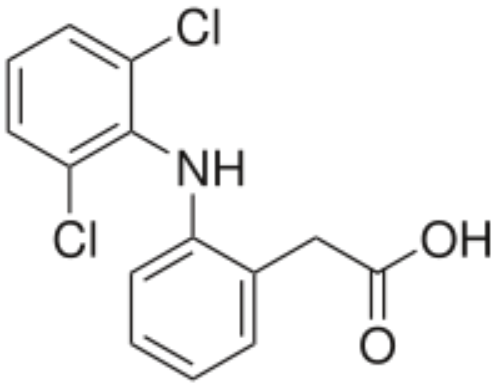


Figure 1. Chemical structure of diclofenac

Mechanism of action[71]

The exact mechanism of action is not entirely known, but it is thought that the primary mechanism responsible for its anti-inflammatory, antipyretic, and analgesic action is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX). It also appears to exhibit bacteriostatic activity by inhibiting bacterial DNA synthesis.

Inhibition of COX also decreases prostaglandins in the epithelium of the stomach, making it more sensitive to corrosion by gastric acid. This is also the main side effect of diclofenac. Diclofenac has a low to moderate preference to block the COX2-isoenzyme (approximately 10-fold) and is said to have therefore a somewhat lower incidence of gastrointestinal complaints than noted with indomethacinand aspirin.

The action of one single dose is much longer (6 to 8 hours) than the very short half-life that the drug indicates. This could be partly because it persists for over 11 hours in synovial fluids.

Diclofenac may also be a unique member of the NSAIDs. There is some evidence that diclofenac inhibits the lipoxygenasepathways, thus reducing formation of the leukotrienes (also pro-inflammatory autacoids). There is also speculation that diclofenac may inhibit phospholipase A_2 as part of its mechanism of action. These additional actions may explain the high potency of diclofenac – it is the most potent NSAID on a broad basis.

There are marked differences among NSAIDs in their selective inhibition of the two subtypes of cyclo-oxygenase, COX-1 and COX-2.Much pharmaceutical drug design has attempted to focus on selective COX-2 inhibition as a way to minimize the gastrointestinal side effects of NSAIDs like aspirin. In practice, use of some COX-2 inhibitors with their adverse effects has led to massive numbers of patient family lawsuits alleging wrongful death by heart attack, yet other significantly COX-selective NSAIDs such as diclofenac have been well-tolerated by most of the population.

Diclofenac is a proven, commonly prescribed nonsteroidal anti-inflammatory drug (NSAID) that has analgesic, anti-inflammatory, and antipyretic properties, and has been shown to be effective in treating a variety of acute and chronic pain and inflammatory conditions. As with all NSAIDs, diclofenac exerts its action via inhibition of prostaglandin synthesis by inhibiting cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) with relative equipotency. However, extensive research shows the pharmacologic activity of diclofenac goes beyond COX inhibition, and includes multimodal and, in some instances, novel mechanisms of action (MOA).

Research suggests diclofenac can inhibit the thromboxane-prostanoid receptor, affect arachidonic acid release and uptake, inhibit lipoxygenase enzymes, and activate the nitric oxide-cGMP antinociceptive pathway. Other novel MOAs may include the inhibition of substrate P, inhibition of peroxisome proliferator activated receptor gamma (PPARgamma), blockage of acid-sensing ion channels, alteration of interleukin-6 production, and inhibition of N-methyl-D-aspartate (NMDA) receptor hyperalgesia. The diversity in diclofenac's MOA

may suggest the potential for a relatively more favorable profile compared with other NSAIDs.[72]

CONTRAINDICATIONS

- Hypersensitivity against diclofenac
- History of allergic reactions (bronchospasm, shock, rhinitis, urticaria) following the use of Aspirin or another NSAID
- Third-trimester pregnancy
- Active stomach and/or duodenal ulceration or gastrointestinal bleeding
- Inflammative intestinal disorders such as Crohn's disease or ulcerative colitis
- Severe insufficiency of the heart (NYHA III/IV)
- Recently, a warning has been issued by FDA not to use to treat patients recovering from heart surgery
- Severe liver insufficiency (Child-Pugh Class C)
- Severe renal insufficiency (creatinine clearance <30 ml/min)
- Caution in patients with preexisting hepatic porphyria, as diclofenac may trigger attacks
- Caution in patients with severe, active bleeding such as cerebral hemorrhage
- NSAIDs in general should be avoided during dengue fever.

PIROXICAM

Piroxicam, 8*E*)-8-[hydroxy-(pyridin-2-ylamino)methylidene]-9-methyl-10,10-dioxo-10λ^6-thia-9-azabicyclo[4.4.0] deca-1,3,5-trien-7-ones a non-steroidal anti-inflammatory drug of the oxicam class used to relieve the symptoms of rheumatoid and osteoarthritis, postoperative pain; and act as an analgesic, especially where there is an inflammatory component.

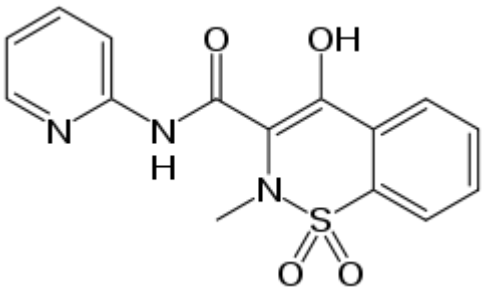


Figure 2. Chemical structure of piroxicam

Piroxicam belongs to the group of nonsteroidal anti-inflammatory drugs. It exerts strong anti-inflammatory, analgesic, and antipyretic action. The mechanism of action is explained with the powerful and long lasting, but reversible, inhibition of the prostaglandin synthesis. There are also other effects like the inhibition of platelet aggregation and the influence on the white blood cells. Piroxicam accumulates selectively in the inflamed tissues and penetrates in the synovial fluid.[73]

Piroxicam, a potent inhibitor of prostaglandins, is effective and well-tolerated in the treatment of primary dysmenorrhea. A single 40 mg dose has been shown to rapidly reduce the uterine hypercontractility of primary dysmenorrhea. In clinical trials vs placebo, piroxicam in a dose of 40 mg once

daily for two days followed by 20 mg once daily thereafter demonstrated superior efficacy. In more than 1,400 piroxicam-treated menstrual cycles and more than 200 placebo-controlled cycles, a similar incidence of side effects-7% and 8.4% respectively-was observed.[74]

The effect of piroxicam on the healing of surgical wounds was tested in a double-blind, placebo-controlled trial of 100 patients who were undergoing surgery for problems related to trauma, arthrosis, or single-site primary tumors. The patients were randomly assigned to receive either an intramuscular injection of 40 mg of piroxicam or placebo 3 to 4 hours after surgery (day 0) and on the first postoperative day. On the second postoperative day, the patients received an injection of 20 mg of piroxicam or placebo. The antibiotic cefamandole (2 gm twice daily) was concurrently administered to all patients for the first 2 days. The group was followed up for a total of 14 days. Statistically significant differences in improvement between treatments favoring piroxicam were found for wound swelling, oozing, necrosis, redness, edema, and hematoma by day 1 or 2; in general, these differences remained evident up to day 5 ($P < 0.001$). For most of the parameters measured, more than 90% of the patients receiving piroxicam were symptom free by day 3 or 4; an equivalent proportion of patients receiving placebo were frequently not symptom free until day 8 or 9. Furthermore, overall efficacy was rated as either excellent or good for all piroxicam-treated patients compared with only 16% of patients receiving placebo. These study results indicate that piroxicam improves wound healing when used within the first 48 hours after orthopedic surgery.[3]

A study to compare the effects of three piroxicam regimens and aspirin on fecal blood loss (FBL) was conducted among 39 healthy men. Fourteen of the subjects also underwent prestudy and poststudy gastroscopy. There was an increase in FBL after aspirin, 972 mg 4 times a day, whereas piroxicam, 20 mg once a day, 5 mg four times a day, and 10 mg four times a day induced no observable increase in fecal blood loss. There was gastroscopic evidence of irritation in the aspirin group, but not in any of the piroxicam groups.[75]

CONTRAINDICATIONS[73]

- Hypersensitivity to piroxicam or other drugs from the group of oxicams;
- Gastrointestinal hemorrhages or peptic ulcer;
- Severe hepatic diseases;
- Renal dysfunction;
- Pregnancy and breast feeding;
- Children younger than 15 years.

METHODOLOGY

The present study was conducted in the Department of Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of January 2010 to December 2010.

Study design

A one year randomized controlled trial.

Place

The present study was conducted in the Department of Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum attached to Jawaharlal Nehru Medical College, Belgaum.

Study period

One year from January 2010 to December 2010.

Source of data

All the patients undergoing appendicectomies for uncomplicated appendicitis and uncomplicated inguinal hernia repairs.

Sample size

A total of 60 patients divided into two groups of 30 each.

Sampling method

Based on the thumb rule a total of 60 patients divided into two groups of 30 each were studied.

Randomization

Based on the computer generated randomization patients were allocated into two groups that is;

- Group A (n=30) – Patients received Inj. Piroxicam.
- Group B (n=30) – Patients received Inj. Diclofenac.

Selection criteria

Inclusion

- The patients undergoing appendicectomy for uncomplicated appendicitis and repair of uncomplicated inguinal hernia.
- Aged between 20 to 45 years.

Exclusion

- Patients with;
    - History of significant hepatic, renal, hematologic or active heart disease.
    - Concurrent peptic ulceration or acute gastritis.
    - Known hypersensitivity to NSAIDs.
    - Diabetes Mellitus.

- Pregnancy or lactation.
- Peritonitis.
- Patients with history of drug abuse.
- Patients developing post operative wound infections.

Procedure

Ethical clearance for the study was obtained from Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belgaum. Based on the selection criteria, patients undergoing appendicectomies for uncomplicated appendicitis and uncomplicated inguinal hernia repairs in the Department of Surgery, KLES Dr. Prabhakar Kore Hospitals and Medical Research Centre, Belgaum during the study period were evaluated for eligibility. The eligible patients were briefed about the nature of the study and a written informed consent (Annexure I) was obtained from the selected patients. Thorough history was taken and clinical examination was done for all patients and findings were recorded on predesigned and pretested proforma (Annexure II).

Investigations such as complete blood count, liver function tests, blood urea and serum creatinine, random blood sugar (RBS), fasting blood sugar, post prandial blood sugar (if RBS was high), echocardiogram, test for human immunodeficiency virus and HbsAg were done. Specific investigations such as, ultrasound abdomen in case of appendicitis was done.

Patients were allocated to two groups according to randomization procedure that is group A which received injection piroxicam and group B which received injection diclofenac. All the patients received injection ciprofloxacin

500 mg twice daily for one day and Inj ornidazole 500 mg twice daily for one day, followed by tablet ciprofloxacin-ornidazole twice daily for four days.

The first dose of Piroxicam (40 mg) or Diclofenac (75 mg) was administered on the day of the operation according to their groups respectively three to four hours after surgery which was defined as the day zero.

The patients received a single daily intramuscular injection of two ml Piroxicam (40 mg) or intramuscular injection of three ml Diclofenac (75 mg) on day one followed by single injection of piroxicam (20 mg) one ml intramuscularly or Diclofenac (75 mg) three ml intramuscularly on day two.

Wound was inspected on third, fifth, seventh and fourteenth post-operative day. Based on the gross appearance the surgical wound was assessed. The characteristics of the wound were assessed and evaluated based on the following parameters.[3]

Characteristics of wound	None (0)	Mild (1)	Moderate (2)	Severe (3)
Degree of swelling				
Oozing				
Necrosis of wound edges				
Redness				
Edema				
Hematoma				

Based on these characteristics the wound healing was graded as;[3]

I. Good wound healing (0-5)
II. Average wound healing (6-12)
III. Poor wound healing (13-18)

End point of study was whether the wound heals with or without infection before fourteenth day of surgery.

Statistical Analysis:

Data obtained was tabulated and expressed as rates, ratios and percentages. Comparison was done by applying chi-square and Fisher's exact test. A probability value ('p' value) of less 0.05 was considered as statistically significant.

RESULTS

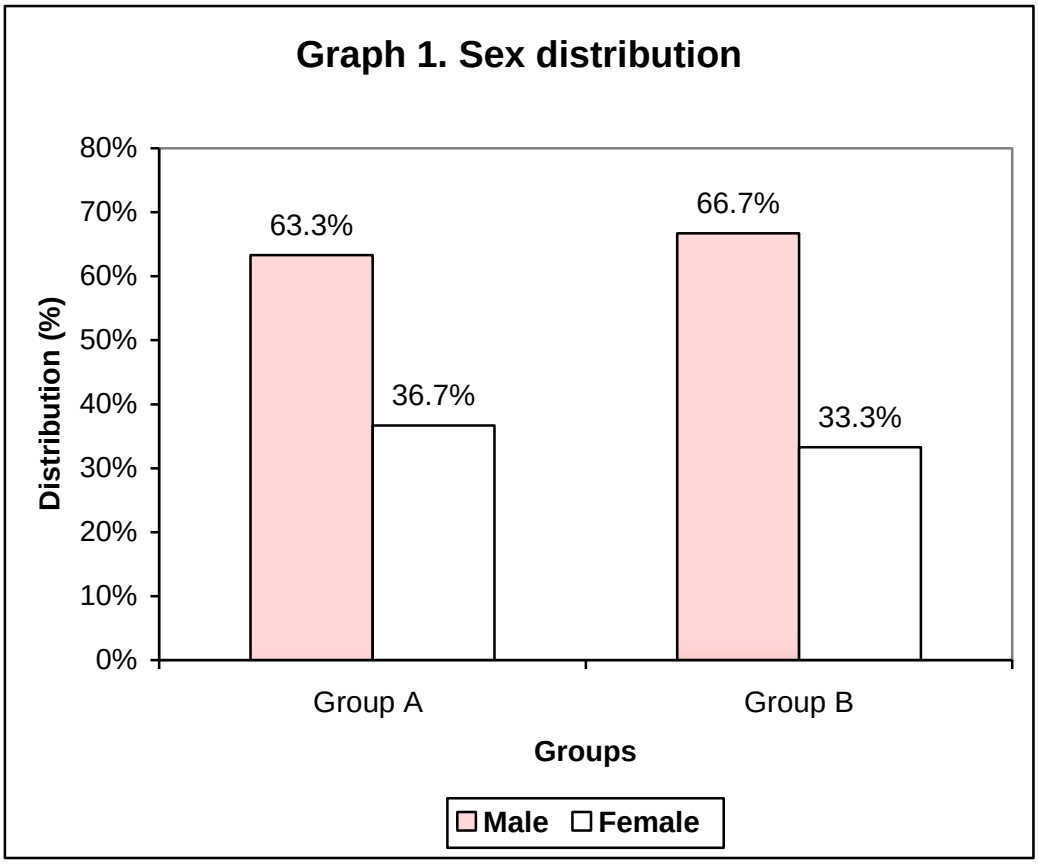
Based on the computer generated randomization patients were allocated into two groups that is;

- Group A (n=30) – Patients received Inj. Piroxicam.
- Group B (n=30) – Patients received Inj. Diclofenac.

Table 1. Sex distribution

Sex	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
Male	19	63.3	20	66.7
Female	11	36.7	10	33.3
Total	**30**	**100**	**30**	**100**

x^2=0.073 DF=1 p=0.787

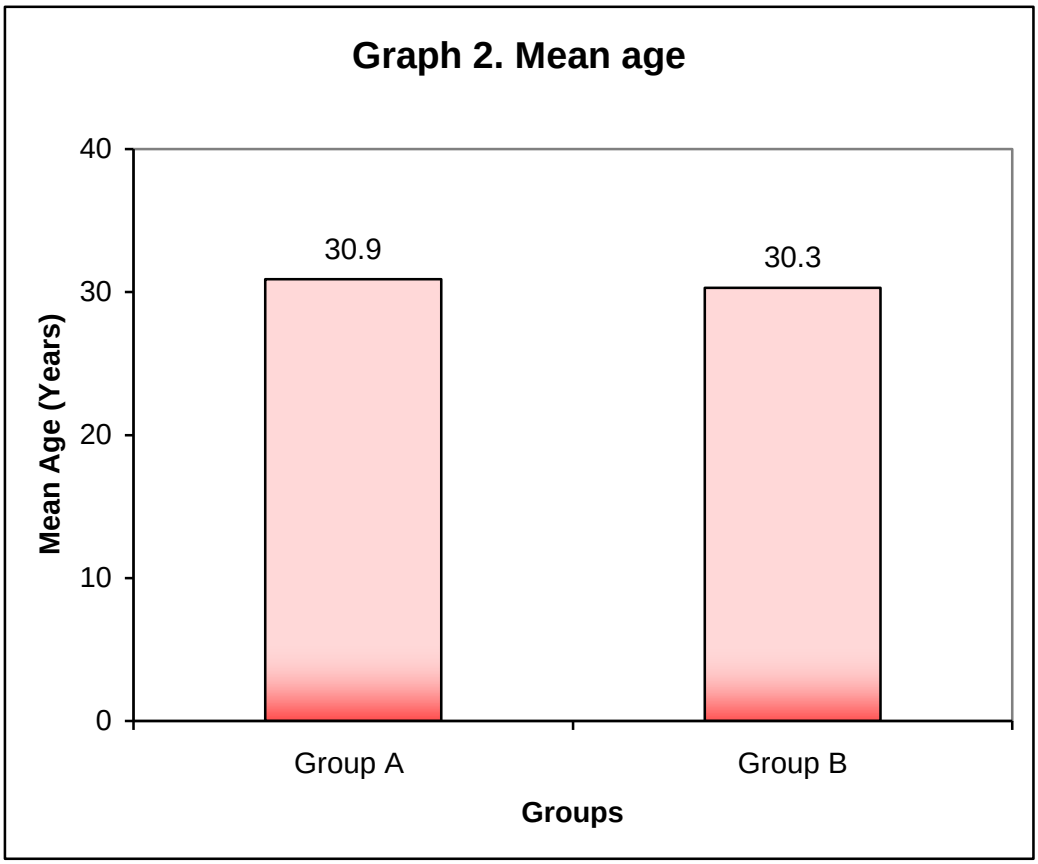


In group A there were 63.3% males and 36.7% were females with male to female ratio of 1.725:1. In group B there were 66.7% males and 33.3% females with male to female ratio of 2:1.

Table 2. Mean Age

	Mean age	
	Mean	**SD**
Group A	30.9	7.86
Group B	30.3	7.97

x^2=0.310 DF=58 p=0.758

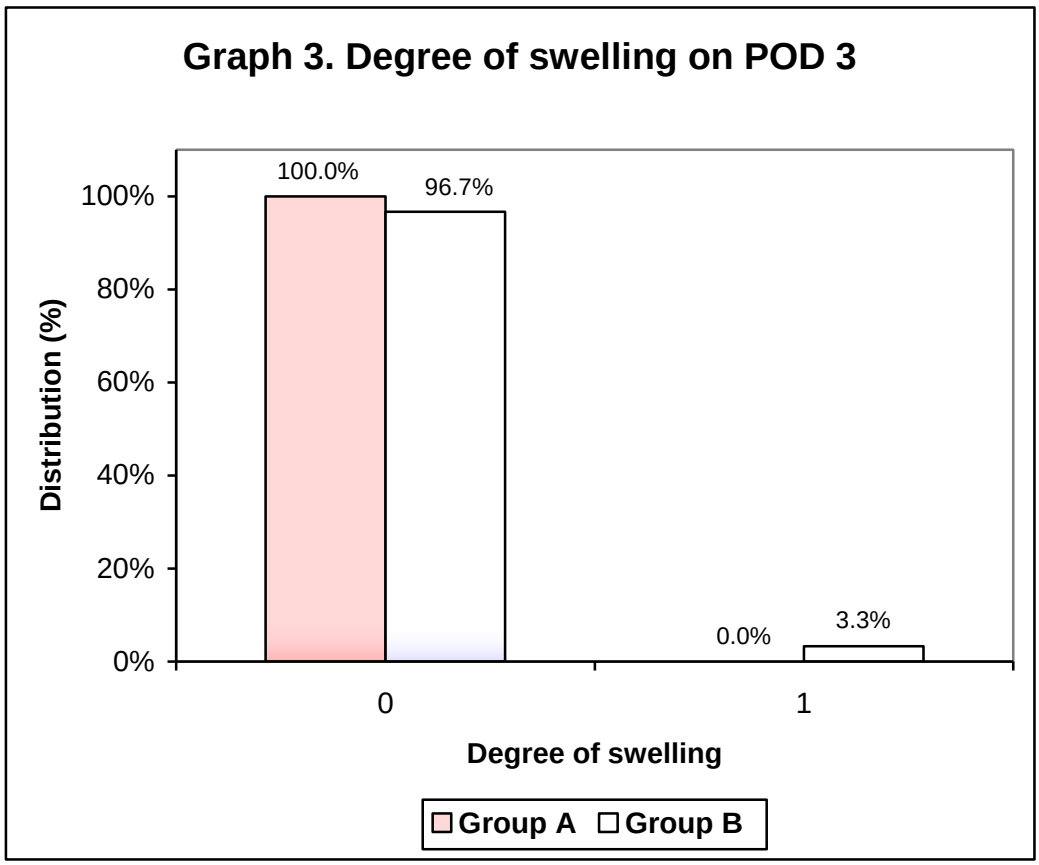


The mean age in group A was 30.9±7.86 years and in group B it was 30.3 ± 7.97 years suggesting both groups had similar age.

Table 3. Degree of swelling on POD 3

Degree of swelling	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
0	30	100.0	29	96.7
1	0	00	1	3.3
Total	**30**	**100**	**30**	**100**

p=1.000 (Fisher's exact test)

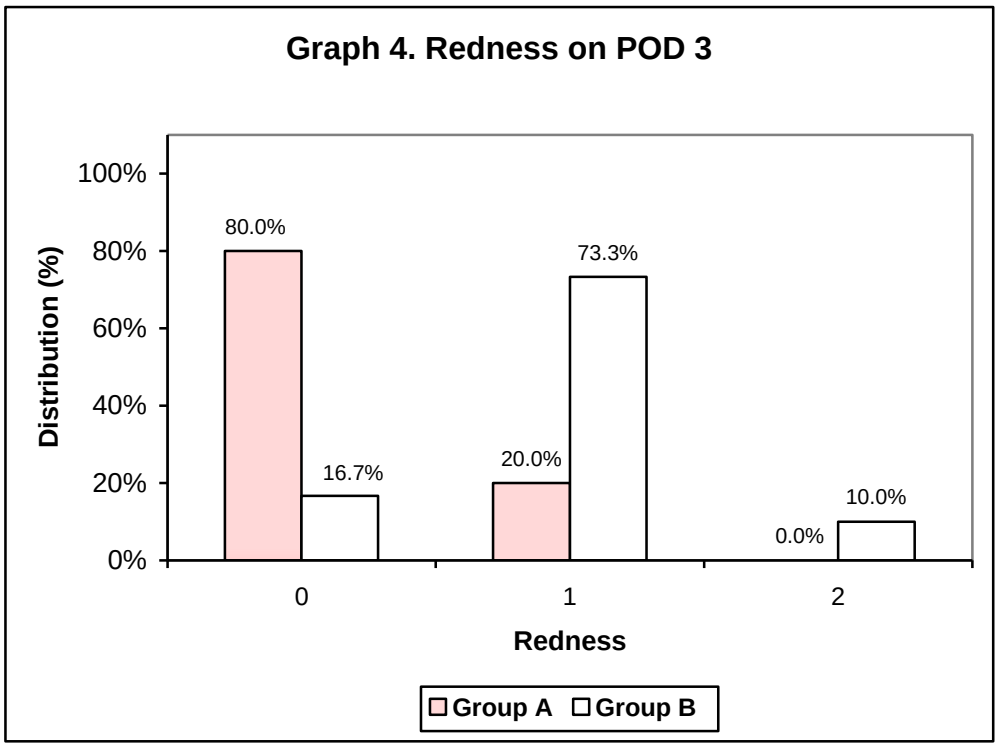


In group A swelling was not seen on POD 3 in all the patients whereas in group B 3.3% had swelling. However, this difference was not statistically significant.

Table 4. Redness on POD 3

Redness	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
0	24	80.0	5	16.7
1	6	20.0	22	73.3
2	0	00	3	10.0
Total	**30**	**100**	**30**	**100**

x^2=24.591 p=0.000

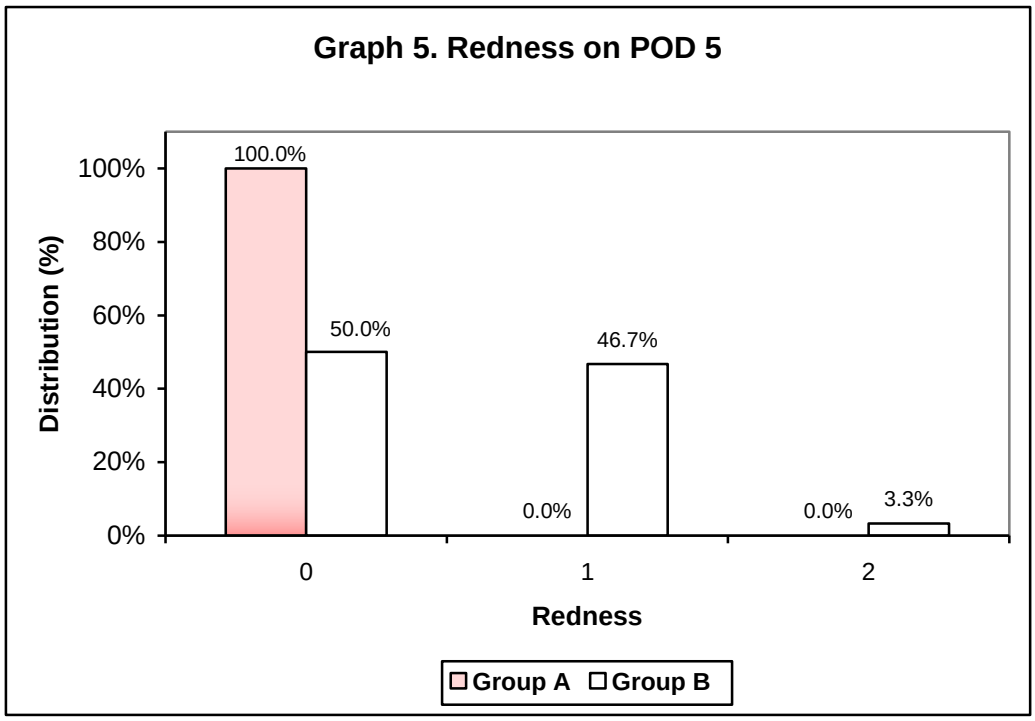


In this study, 80.0% of Group A and 16.7% of Group B patients were free from redness on POD 3. In the remaining, 73.3% and 10.0% of patients in group B had redness score of 1 and 2 respectively compared to 20% of patients in group A who had a score of 1. This difference was statistically significant.

Table 5. Redness on POD 5

Redness	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
0	30	100.0	15	50.0
1	0	00	14	46.7
2	0	00	1	3.3
Total	**30**	**100**	**30**	**100**

p=0.000 (Fisher's exact test)

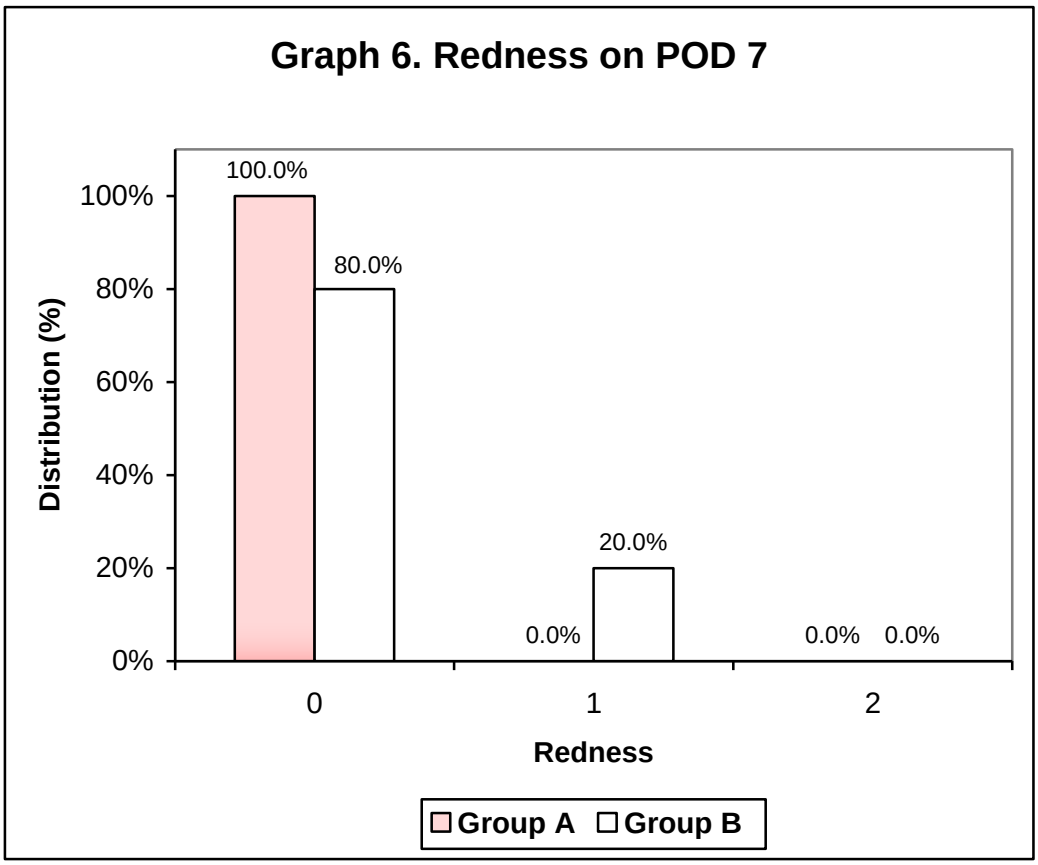


In this study all the patients in Group A were free from redness on POD 5 and compared to 50% in Group B. In the remaining 46.7% and 3.3% of patients in group B had redness score of 1 and 2 respectively. This difference was statistically significant.

Table 6. Redness on POD 7

Redness	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
0	30	100.0	24	80.0
1	0	00	6	20.0
2	0	00	0	00
Total	**30**	**100**	**30**	**100**

p=0.024 (Fisher's exact test)

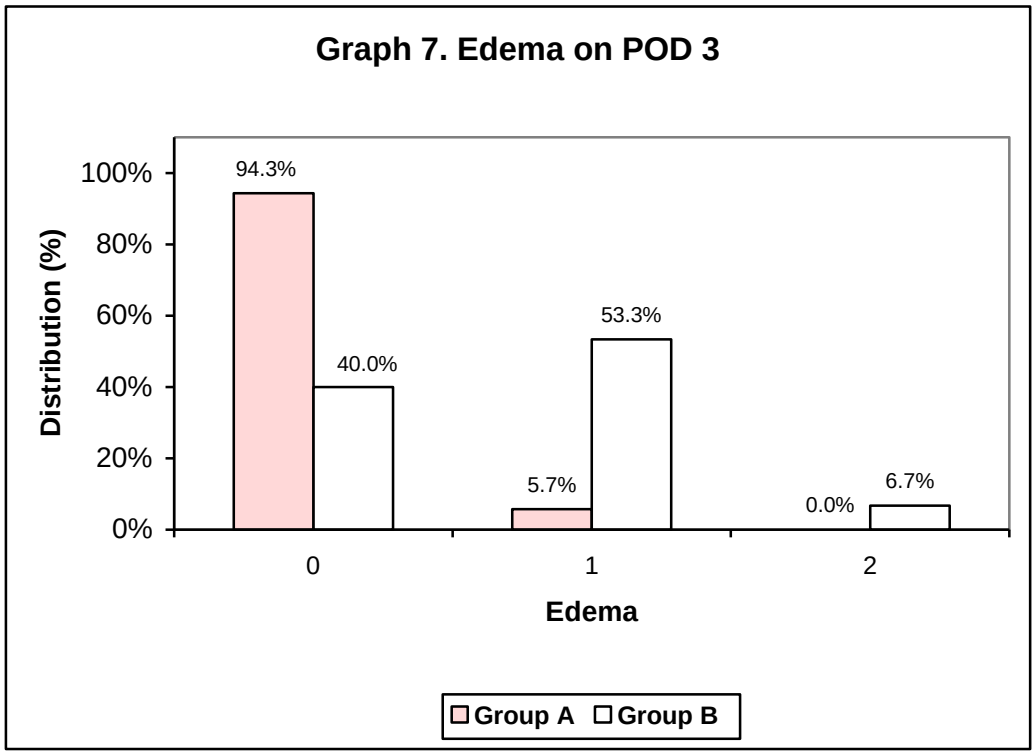


In this study 20% of patients in group B had redness score of 1 on POD 7. This difference was statistically significant.

Table 7. Edema on POD 3

Edema	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
0	28	94.3	12	40.0
1	2	5.7	16	53.3
2	0	00	2	6.7
Total	**30**	**100**	**30**	**100**

x^2=19.289 p=0.000

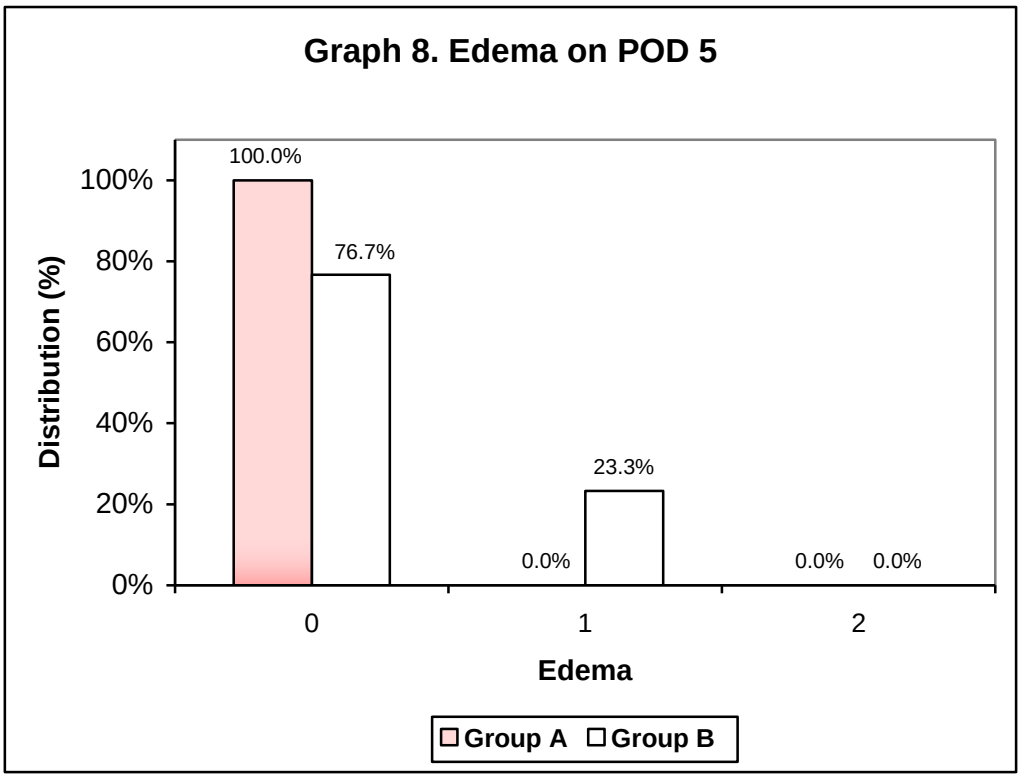


In this study 94.3% of patients in group A and 40.0% in group B were free from edema on POD 3. Edema score of 1 and 2 in 53.3% and 6.7% of patients in group B was noted respectively compared to 5.7% of patients in group A who had a score of 1. This difference was statistically significant.

Table 8. Edema on POD 5

Edema	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
0	30	100	23	76.7
1	0	00	7	23.3
2	0	00	0	00
Total	**30**	**100**	**30**	**100**

p=0.011 (Fisher's exact test)

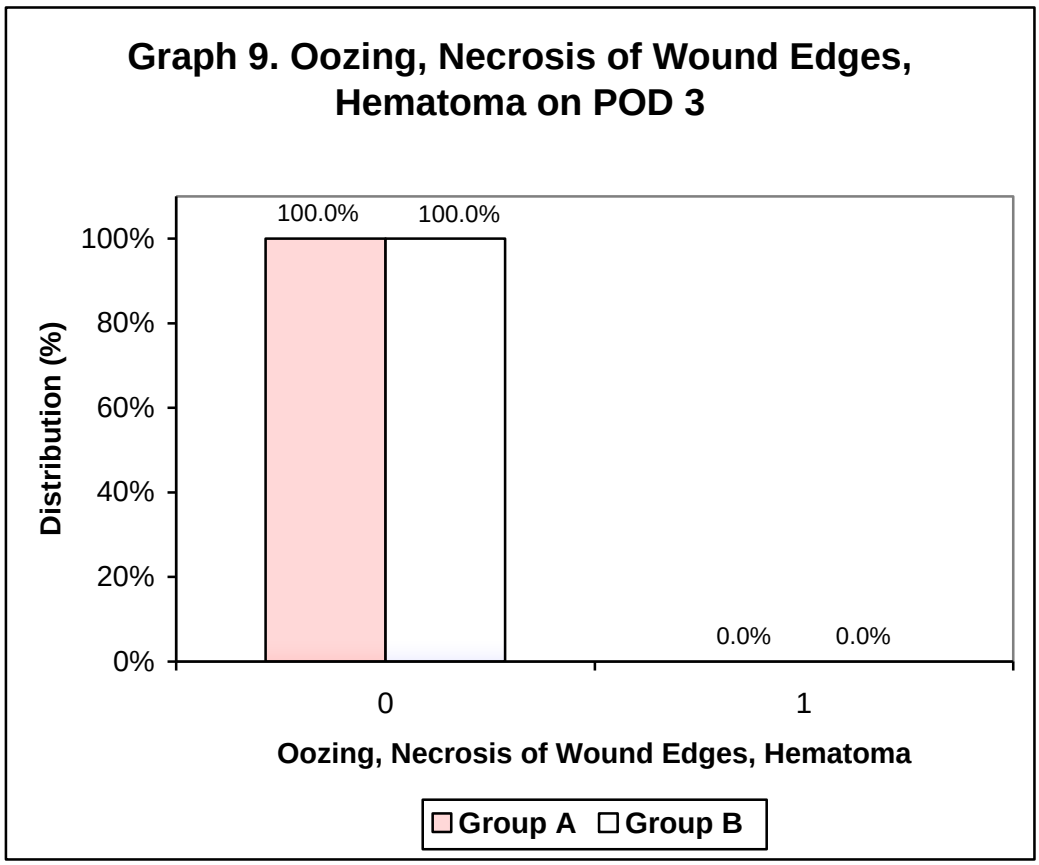


In this study all patients in Group A were free from edema on POD 5 when compared to 76.7% of patient in group B. Edema score of 1 was seen in 23.3% of patients in group B. This difference was statistically significant. On POD 7 patients in both the groups had no edema.

Table 9. Oozing, Necrosis of Wound Edges, Hematoma on POD 3

Oozing, Necrosis of Wound Edges, Hematoma	Group A (n=30)		Group B (n=30)	
	Number	Percentage	Number	Percentage
0	30	100	30	100
1	00	00	00	00
Total	**30**	**100**	**30**	**100**

p=1 (Fisher's exact test)

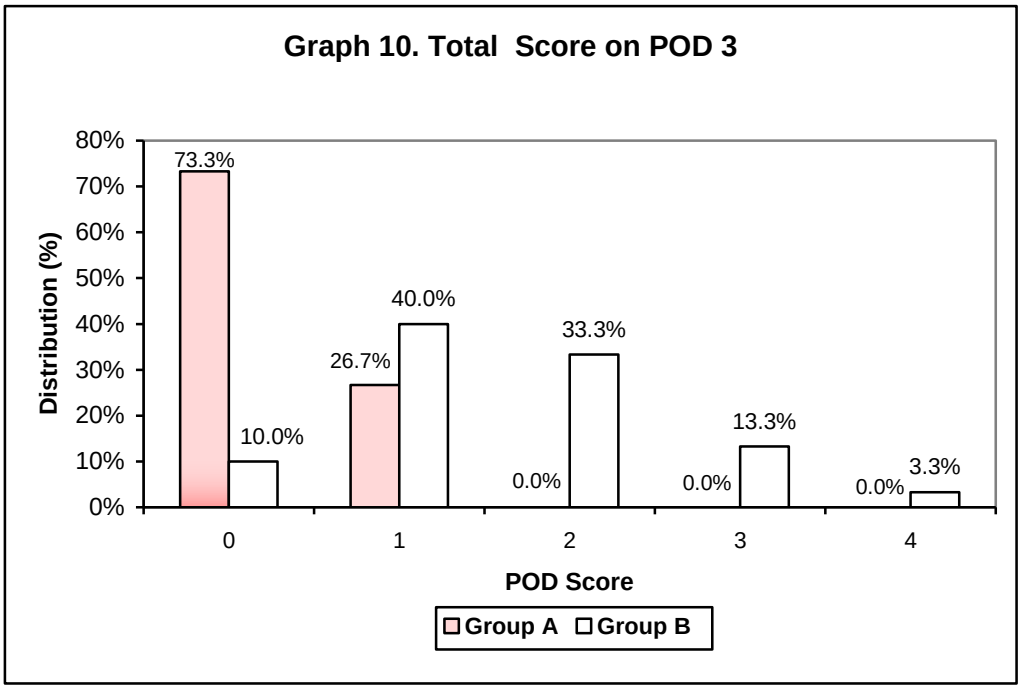


In this study no oozing, necrosis of wound edges and hematoma formation was noted in patients with group A and B.

Table 10. Total score on POD 3

Total score	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
0	22	73.3	3	10.0
1	8	26.7	12	40.0
2	0	00	10	33.3
3	0	00	4	13.3
4	0	00	1	3.3
Total	**30**	**100**	**30**	**100**

x^2=24.754 DF=1 p=0.000

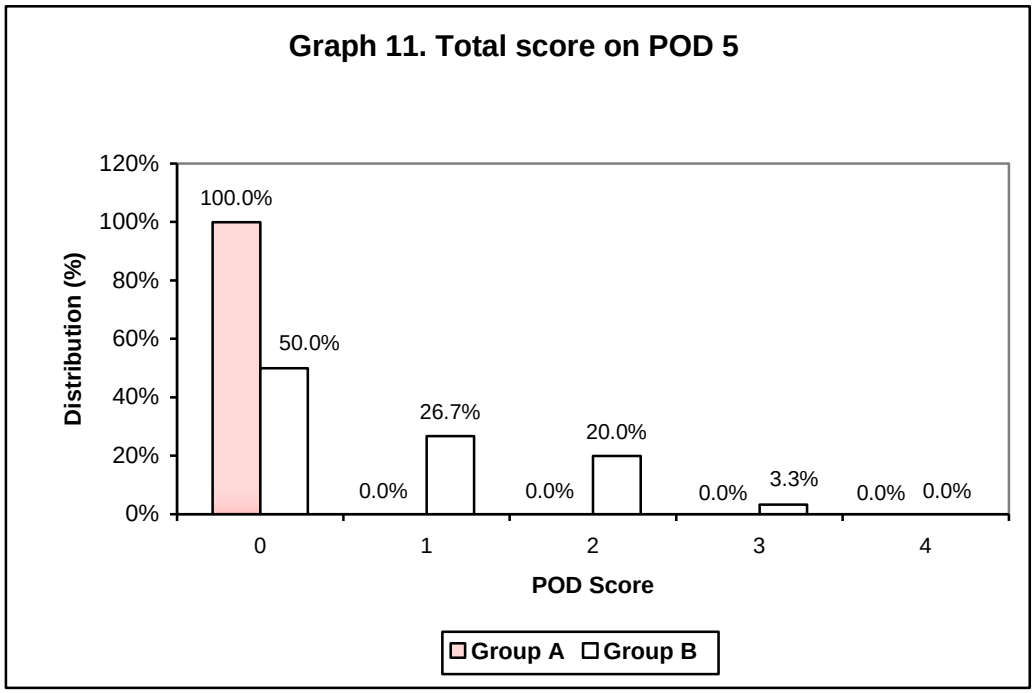


In the present study majority (73.3%) patients in group A were free from all the symptoms whereas in group B majority of the patients (40%) had a total score as 1 on POD 3. This difference was statistically significant.

Table 11. Total score on POD 5

Total Score	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
0	30	100.0	15	50.0
1	0	00	8	26.7
2	0	00	6	20.0
3	0	00	1	3.3
4	0	00	0	00
Total	**30**	**100**	**30**	**100**

p=0.000 (Fisher's exact test)

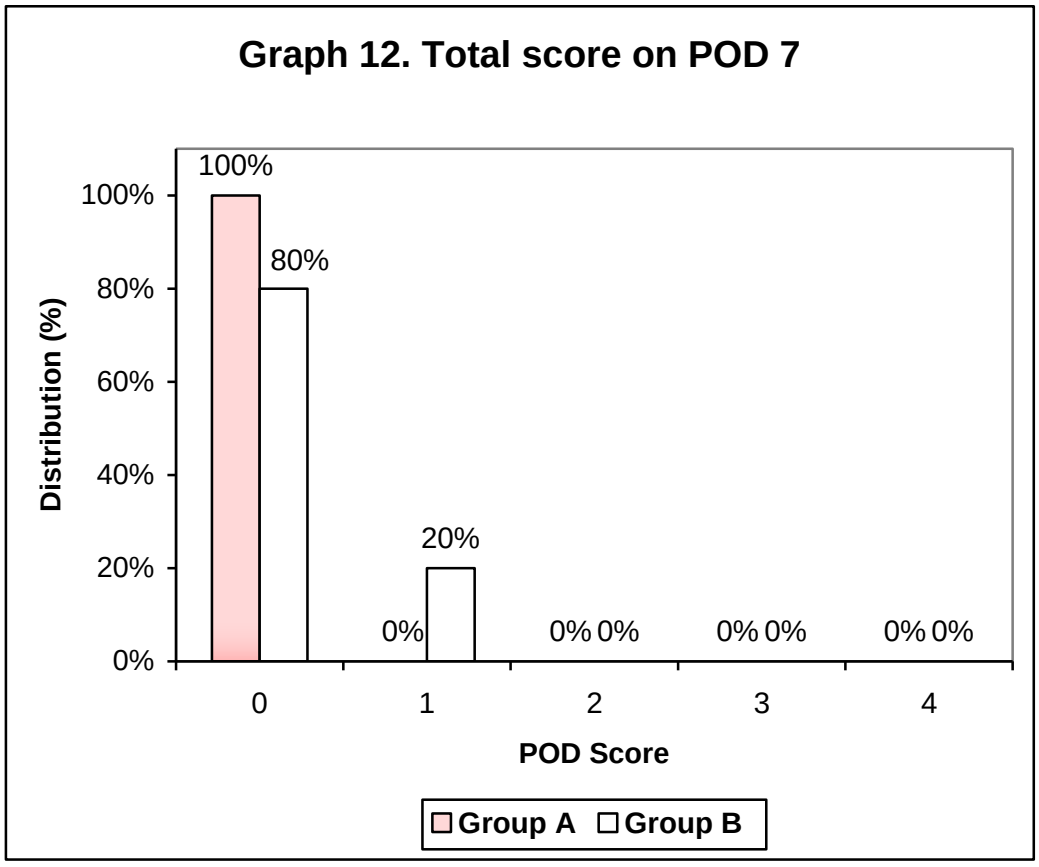


In the present study all the patients (100%) in group A were free from all the symptoms whereas in group B 50% of patients had a total score between 1 to 3 on POD 5. This difference was statistically significant.

Table 12. Total score on POD 7

Total Score	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
0	30	100.0	24	80.0
1	0	00	6	20.0
2	0	00	0	00
3	0	00	0	00
4	0	00	0	00
Total	**30**	**100**	**30**	**100**

p=0.024 (Fisher's exact test)

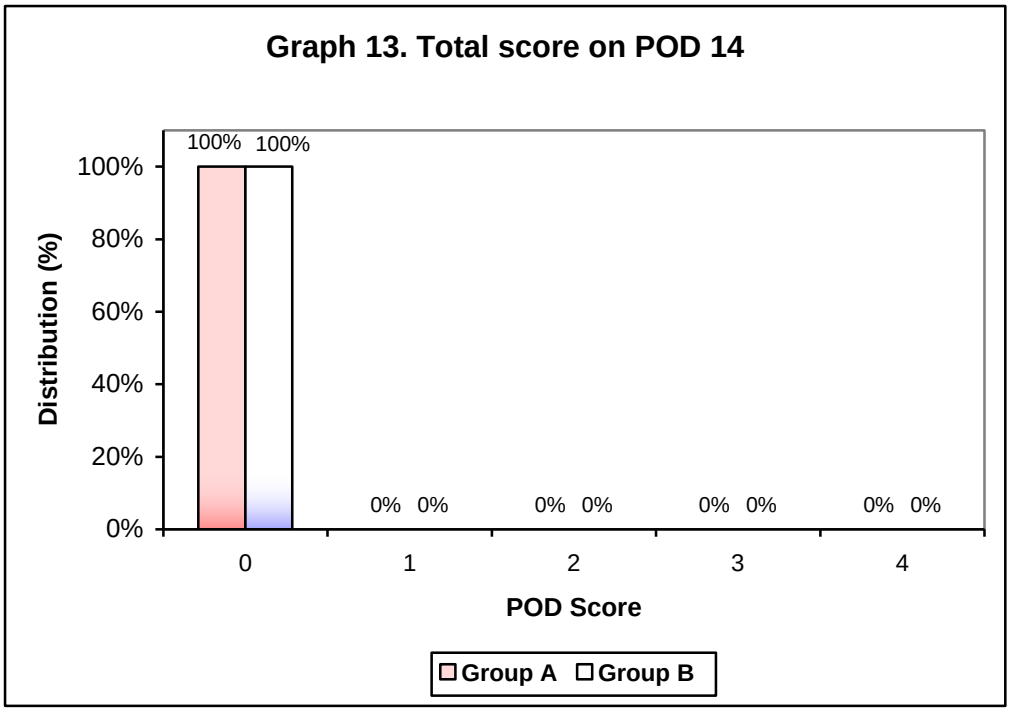


Symptoms persisted in 20% of patients belonging to Group B on POD 7.

Table 13. Total score on POD 14

Total Score	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
0	30	100.0	30	100.0
1	0	00	0	00
2	0	00	0	00
3	0	00	0	00
4	0	00	0	00
Total	**30**	**100**	**30**	**100**

p=1 (Fisher's exact test)

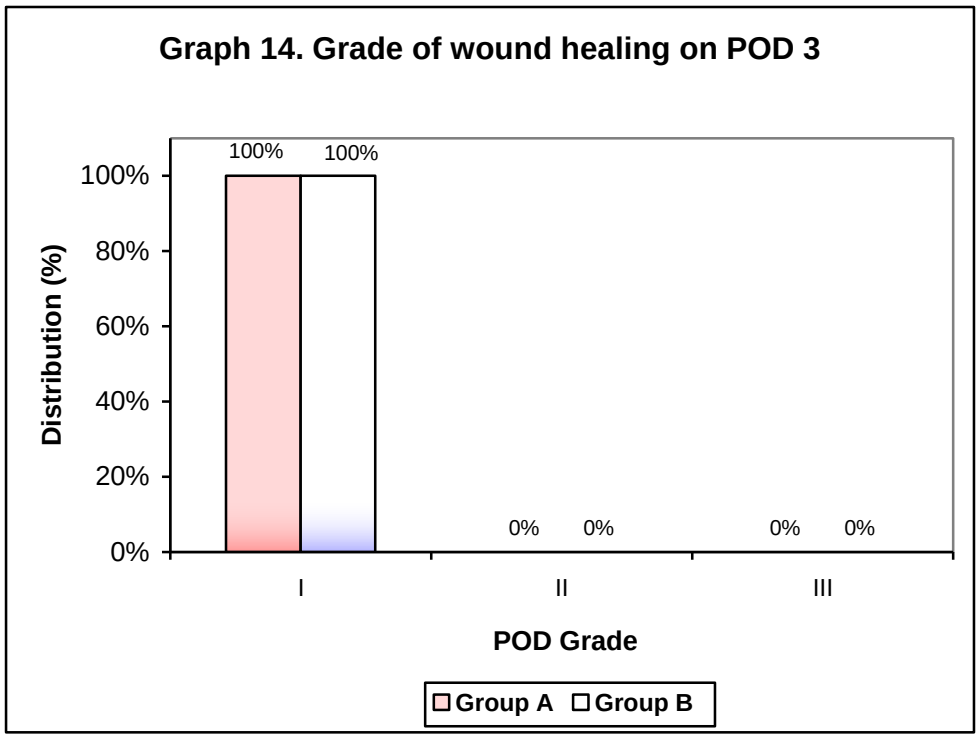


In this study no oozing, redness, edema, necrosis of wound edges, swelling and hematoma formation was noted in patients both the groups on POD 14.

Table 14. Grade of wound healing on POD 3

Grade	Group A (n=30)		Group B (n=30)	
	Number	**Percentage**	**Number**	**Percentage**
I	30	100.0	30	100.0
II	0	00	0	00
III	0	00	0	00
Total	**30**	**100**	**30**	**100**

p=1 (Fisher's exact test)



In this study both the groups that is Group A and B were graded under grade I from the POD 3 onwards.

DISCUSSION

The process of wound healing constitutes an array of interrelated and concomitant events. Understanding these processes and various factors affecting these processes continue to expand.

Tremendous advancements have been made in understanding the process of wound healing. The cell types and the order in which they appear in the wound have been established; many growth factors and their functions have been demonstrated.[16] Despite the advances in understanding the science of wound healing, many more steps have yet to be discovered and illustrated. The frontier of this field includes the prevention of hypertrophic and keloid scar formation and, ultimately, any visual remnant of the wound.

Drugs such as NSAIDs, COX-2 inhibitors, corticosteroids, DMARDs and biologic response modifiers affect inflammation and local immune responses, which are necessary for proper wound healing in the perioperative setting, thereby potentially resulting in undesirable postoperative complications. Such complications include wound dehiscence, infection, and impaired collagen synthesis. The end result is delayed healing of soft tissue.[76]

For certain drugs, such as methotrexate, trials have been conducted in humans, whereas, with other drugs, either small-animal studies on wound healing are available.[76]

In some cases, discontinuation of therapy may be required up to four weeks before surgery because of the long half-lives of the drugs. In doing so,

patients may experience an exacerbation or worsening of disease. Individual patient should be evaluated for risk factors, disease severity, and the pharmacokinetics of available therapies weighing the risks and benefits of discontinuing therapy in the perioperative setting.[77]

Patients with rheumatoid arthritis may already be at increased risk of impaired wound healing because of a reduction in skin thickness that occurs independently of corticosteroid use. Patients with rheumatoid arthritis are also generally at greater risk of infection[77,78] and vasculitis.[79,80] The presence of diabetes mellitus may predispose patients to infection, typically from compromised microvascular blood flow and higher serum glucose levels, which may impair the ability of neutrophils to fight infection.[81-83]

Immuno-suppressed patients, such as those who are positive for the human immunodeficiency virus or are treated with chemotherapy, will undoubtedly experience increased rates of infection. Peripheral arterial disease may also contribute to poor wound healing because of a reduction in blood flow and tissue perfusion. Patients who are deficient in vitamin C[84] or are taking other drugs such as anticoagulants,[85] tetracycline,[86] or erythromycin[38] are predisposed to infection.

Piroxicam is an N-heterocyclic carboxamide of 1,2 benzothiazine 1,1 dioxide with analgesic and anti-inflammatory activity. It is a potent acidic anti-inflammatory agent structurally distinct from the current agents such as indometacin, phenylbutazone or naproxen. Pharmacokinetic studies indicate a longer plasma half-ife for piroxicam than for these agents. The high potency,

long half-life and absence of cardiovascular or cental nervous system effects have encouraged clinical trials of piroxicam.[87] Hence the present study was undertaken to compare and evaluate the effect of piroxicam versus diclofenac on wound healing in clean abdominal wounds.

There are various reasons to suspect that NSAIDs would impair wound healing, because inflammation is the process whereby cells are recruited to remove necrotic debris and to initiate healing.[88] In the case of NSAID piroxicam, however, there are animal studies[88,89] indicating that the opposite may be true.

In a previous study,[88] authors induced injuries of the musculotendinous junction in rats and discovered that treatment with piroxicam had a positive effect on healing and delayed the stress failure of the muscle tendon attachment. Eleven days after the wound was induced, the rats receiving piroxicam had stronger and stiffer muscles that the untreated controls, an effect that may be partly explained by an increase in collagen metabolism. Similarly, medial ligament of the knees of male Sprague-Dawley rats were injured and it was found that, administration of piroxicam during the first six days after injury resulted in a 42% increase in ligament strength by day 14 relative to placebo treated controls ($p<0.01$).

The results of animal studies[88,89] such as these suggest that an investigation of the effects of piroxicam on wound healing should be extended to humans. Hence, the present one year randomized controlled trial was conducted on all the patients undergoing appendicectomies for uncomplicated appendicitis and uncomplicated inguinal hernia repairs in the Department of Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the

period of January 2010 to December 2010. Based on the thumb rule a total of 60 patients divided into two groups of 30 each were studied. Based on the computer generated randomization patients were allocated to two groups that is group A (Inj. Piroxicam) and Group B (Inj. Diclofenac).

In the present study, males outnumbered females (63.3% males and 36.7% females in group A; 66.7% males and 33.3% females in group B) with male to female ratio between of 1.72 to 2:1. The mean age in group A was 30.9 ± 7.86 years and in group B it was 30.3 ± 7.97 years suggesting demographic characteristics of the study population were comparable in both groups. Similar study comparing piroxicam with placebo from Belgium reported 56% males and 44% females in placebo group and 46% males and 54% females in piroxicam group.

In the present study among patients in group A, swelling was not seen on post operative day (POD) 3 whereas in group B 3.3% had swelling. However, this difference was not statistically significant (p=1.000).

In the present study, 80.0% of patients in group A and 16.7% of Group B patients were free from redness on POD 3. In the remaining, 73.3% and 10.0% of patients in group B had redness score of 1 and 2 respectively compared to 20% of patients in group A who had a score of 1. This difference was statistically significant (p<0.0001). On POD 5 all the patients in Group A were free from redness compared to 50% in Group B. In the remaining 46.7% and 3.3% of patients in group B had redness score of 1 and 2 respectively (p<0.0001). On POD 7, 20% of patients in group B had redness score of 1 (p=0.024).

In the present study on post operative day three edema score of 1 and 2 in 53.3% and 6.7% of patients in group B was noted respectively compared to 6.7% of patients in group A who had a score of 1. This difference was statistically significant ($p<0.0001$). On post operative day 5 all patients in Group A were free from edema when compared to 76.7% of patient in group B. Edema score of 1 was seen in 23.3% of patients in group B. This difference was statistically significant ($p=0.011$). On post operative day seven, patients in both the groups had no edema. Also, oozing, necrosis of wound edges and hematoma formation was not seen in both the groups. Overall better results were seen in patients with group A with significantly less redness and oedema.

In the present study majority among patients in group A on post operative day three 73.3% patients were free from all the symptoms and all the patients (100%) were free from all the symptoms on post operative day five suggesting significantly better results in group A ($p<0.05$). Whereas, in group B majority of the patients (40%) had a total score of 1 on post operative day three, 50% of patients had a total score between 1 to 3 on post operative day five and symptoms persisted in 20% of patients on post operative day seven.

In this study both the groups that is Group A and B were graded under grade I (Good wound healing) from the POD 3 onwards. Overall the individual score and total scores had no influence of the final grading (outcome) of the wound.

A similar study[3] from Belgium found, significant difference between the two groups for swelling, oozing, necrosis of wound edges, redness, edema and

hematoma during the first five days after surgery, with better results in the piroxicam group. Moreover, for nearly all the parameters of inflammation measured and more than 90% of the patients receiving piroxicam were free of the various symptoms by day four whereas the equivalent proportions of placebo patients were not in general symptoms free until days 8 to 12.

Surgical damage to body tissue starts an inflammatory process that involves recruitment of specific cells in the wound area and is compounded by necrotic tissue debris, capillary microthrombosis, edema, hematoma and bleeding. The effects of NSAIDs on objective signs of surgical wound healing have not been reported frequently in the literature.[3]

Future advances in wound healing will focus on affecting the agents that influence the processes involved in the repair of damaged tissue. Laser techniques, nonlaser techniques, and other modalities are being explored to enhance the proliferation of cells, the migration of cells, and the acceleration of the healing of wounds.[90,91]

Human cell–conditioned media developed in embryologiclike conditions has been shown to improve healing times in postlaser facial skin.[92] Fetal tissue can heal scarless due to the unique characteristics of fetal epithelial and mesenchymal cells and the functioning of the fetal immune system.[93] Hyperbaric oxygen has also been used to promote healing.[94] Stem cells, in particular adipose-derived stem cells, have been shown to ameliorate wound healing, and continued research in these areas appears promising.[95,96]

CONCLUSION

Overall, the present study showed better results on wound healing in patients who received Inj piroxicam with significantly less post operative redness and oedema. However, this did not have significant difference in the final outcome of the grading of the wound.

SUMMARY

The primary function of the skin is to serve as a protective barrier against the environment. The process of wound healing constitutes an array of interrelated and concomitant events. Understanding these processes and various factors affecting these processes continue to expand. The present study was undertaken to compare and evaluate the effect of piroxicam versus diclofenac on wound healing in clean abdominal wounds.

The present one year randomized controlled trial was conducted on all the patients undergoing appendicectomies for uncomplicated appendicitis and uncomplicated inguinal hernia repairs in the Department of Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of January 2010 to December 2010. Based on the thumb rule a total of 60 patients divided into two groups of 30 each were studied. Based on the computer generated randomization patients were allocated to two groups that is group A (Inj. Piroxicam) and Group B (Inj. Diclofenac).

In the present study, males outnumbered females with male to female ratio between of 1.72 to 2:1. The mean age in group A was 30.9 ± 7.86 years and in group B it was 30.3 ± 7.97 years. Among patients in group A, swelling was not seen on post operative day (POD) 3 whereas in group B 3.3% had swelling. 80.0% of patients in group A and 16.7% of Group B patients were free from redness on POD 3. On POD 5 all the patients in Group A were free from redness compared to 50% in Group B.

On post operative day three, edema score of 1 and 2 in 53.3% and 6.7% of patients in group B was noted respectively compared to 6.7% of patients in group A who had a score of 1. On post operative day 5 all patients in Group A were free from edema when compared to 76.7% of patient in group B. On post operative day seven, patients in both the groups had no edema. Also, oozing, necrosis of wound edges and hematoma formation was not seen in both the groups.

Among patients in group A on post operative day three 73.3% patients were free from all the symptoms and all the patients (100%) were free from all the symptoms on post operative day five suggesting significantly better results in group A ($p<0.05$). Whereas, in group B majority of the patients (40%) had a total score of 1 on post operative day three, 50% of patients had a total score between 1 to 3 on post operative day five and symptoms persisted in 20% of patients on post operative day seven.

In this study both the groups that is Group A and B were graded under grade I (Good wound healing) from the POD 3 onwards. Overall the individual score and total scores had no influence of the final grading (outcome) of the wound.

Overall, the present study showed better results on wound healing in patients who received Inj piroxicam with significantly less post operative redness and oedema. However, this did not have significant difference in the final outcome of the grading of the wound.

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ANNEXURE I – CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH

Mr. /Mrs. _____ are requested to enroll yourself in study titled **"A Comparative Study of the effect of Piroxicam versus Diclofenac on Wound Healing in clean abdominal wounds" A one year randomised control trial at the KLES Dr Prabhakar Kore Hospitals, Belgaum** conducted by **Dr. Chandrashekarreddy J. Madinur** Postgraduate student in M.S. (Gen. Surgery) under guidance of **Dr. A. S. Godhi** **MS FICS** at J.N.M.C, Belgaum.

INTRODUCTION AND PURPOSE

You have been requested to participate in research because you are fitting into the study group.

Your participation in research is voluntary. Your decision whether to or not to participate, will not affect your relationship with the J.N.M.C. If you decide not to participate, you are free to withdraw at any time.

Purpose of research is to compare the effect of Piroxicam and Diclofenac on Wound Healing.

PROCEDURE

In Abdominal surgeries during the post operative period the patient will be given either IM Piroxicam or Diclofenac according to the Randomization and the results will be compared.

RISKS & BENEFITS

There are no extra risks involved in this study. Complications, if at occur are those which are normally anticipated. This study will help to identify the effect of Piroxicam and Diclofenac on wound healing . The results obtained at the end of study will help other similar patients who get admitted in the hospital.

PRIVACY & CONFIDENTIALITY

The only people who will know that you are a research subject are members of the research team. No information about you or provided by you during research will be disclosed to others without your written permission except in emergency to protect your rights and welfare and if required by law.

AUTHORIZATION TO PUBLISH RESULTS

When the results of research are published or discussed, in conference, no information will be displaced that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed with your permission.

VOLUNTARY PARTICIPATION / WITHDRAWAL

I Mr./Ms._____ have been explained about the research study, the need of the study, the diagnostic intervention, their risks, benefits and alternatives available in my own vernacular language.

Taking part in this study is voluntary. I may choose not to take part in the study, or withdraw from the study anytime later. My decisions will not change

the present or future health care or any service I receive. The study doctor or sponsor may stop my participation in the study without any consent. While taking part in the study I will be told of any important new findings that may change my willingness to continue or take part. If I choose not to take part in the study I will receive the standard treatment for patients with my condition.

INSTITUTIONAL POLICY

If any foreseen complications or injury occurs during the period of study, treatment will be given to the participant within the limitations of KLE's Prabhakar Kore Hospital General Ward, Belgaum. No reimbursement, compensation or free medical care will be given. Participant will not be paid/offered any free gifts for participating in the research By Law.

CONTACT DETAILS

Participant can contact me anytime during the study period for clarification of doubts or any questions. Dr. Chandrashekarreddy J. Madinur (PG General Surgery). JNMC, Belgaum Phone No : +91-9916257689

CONSENT STATEMENT :

I, the undersigned, have been explained in my own vernacular language about the study and my participation in the study is voluntary. If I want, I can withdraw at any time. Also I have been given enough time to clear my doubts about the study and my rights as a study patient.

Participants name : _____ Signature : _____

Witness name : _____ Signature : _____

Researchers name: _____ Signature : _____

Place : _____ Date : _____

In case of any queries, you can contact the following:

Dr. V. D. Patil **MD, DCH**
Chairman, College Ethical Dissertation
And Research Committee,
J. N. Medical College,
KLE University, Belgaum – 10.

Dr. Ashok S. Godhi **MS, FICS**
Vice Principal &
Professor of Surgery,
J. N. Medical College,
KLE University, Belgaum – 10.

Dr. Chandrashekarreddy J. Madinur **(PG Gen. Surgery)**
Post graduate student,
Department of Surgery
J. N. Medical College,
KLE University, Belgaum – 10.

Signature of the study patient

ANNEXURE II – PROFORMA

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

NAME IP/OPD NO.

AGE DOA :

SEX DOD:

OCCUPATION

ADDRESS

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

<u>MEDICAL HISTORY</u> :

Diabetes	( )
Renal Failure	( )
Peptic Disorders	( )
Hepatic Failure	( )
Drug Abuse	( )
Pregnancy/Lactation	( )

<u>GENERAL EXAMINATION</u>: Vitals

Pulse Rate

B.P.

Temp

Respiratory Rate

SYSTEMIC EXAMINATION

INVESTIGATIONS

CBC

Blood Urea

Sr Creatinine

LFT

RBS

FBS

ECG

USG Abdomen

URINE:

Routine

Microscopy

WOUND OBSERVATION:

GRADING OF WOUND ON DAYs: 3, 5, 7, 14.

1 Good wound healing (0-5)

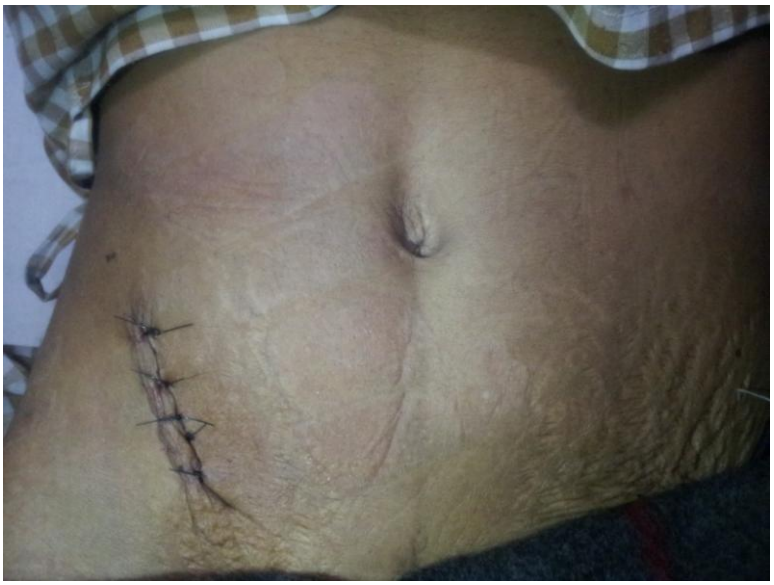
2 Average wound healing (6-12)

3 Poor wound healing (13-18)

Characteristics of wound	None (0)	Mild (1)	Moderate (2)	Severe (3)
Degree of swelling				
Oozing				
Necrosis of wound edges				
Redness				
Edema				
Hematoma				

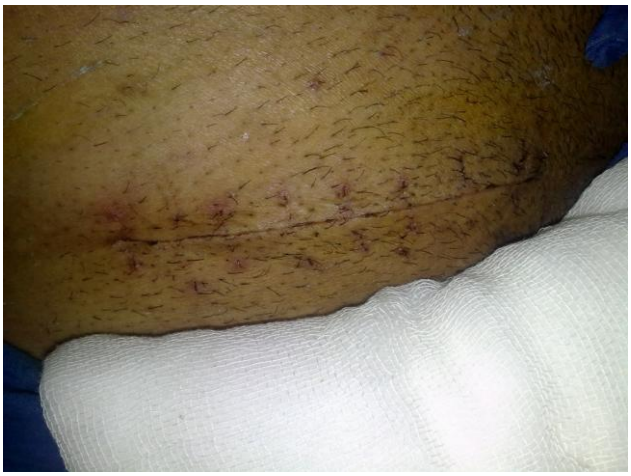
ANNEXURE III – PHOTOGRAPHS

Photograph 1. Injection Diclofenac and Injection Piroxicam

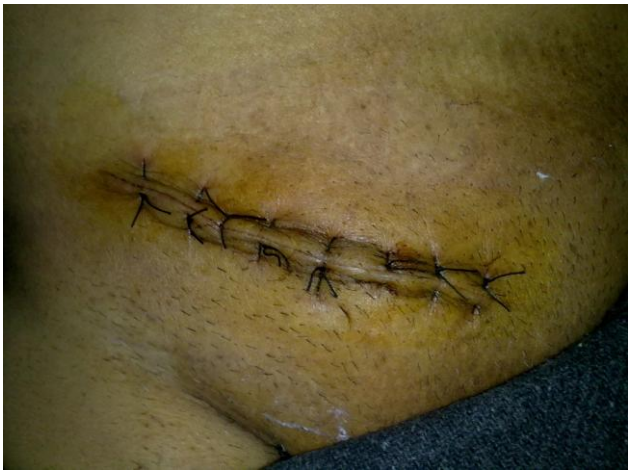


Photograph 2. Wound with minimal redness on post operative day 3 in group B (Diclofenac) in operated case of appendicectomy

Photograph 3. Wound with no redness on post operative day 3 in group A (Piroxicam) in operated case of appendicectomy



Photograph 4. Wound with redness persisting on post operative day 7 in group B (Diclofenac) in operated case of inguinal hernia



Photograph 5. Wound with no redness on post operative day 5 in group A (Piroxicam) in operated case of inguinal hernia

ANNEXURE IV MASTER CHART GROUP B (DICLOFENAC)

Serial Number	In Patient No.	Sex	Age (Years)	Date of admission	Diagnosis	Haemoglobin (gm%)	Total count (/mm^3)	Characteristics								Characteristics of wound																							
								Score				Grade				POD 3						POD 5						POD 7						POD 14					
								POD 3	POD 5	POD 7	POD 14	POD 3	POD 5	POD 7	POD 14	Swelling	Oozing	Necrosis	Redness	Edema	Hematoma	Swelling	Oozing	Necrosis	Redness	Edema	Hematoma	Swelling	Oozing	Necrosis	Redness	Edema	Hematoma	Swelling	Oozing	Necrosis	Redness	Edema	Hematoma
1	348923	M	21	5/1/2010	App	12.0	9,450	1	0	0	0	I	I	I	I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	348979	M	28	6/1/2010	App	12.0	10,250	1	0	0	0	I	I	I	I	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	349439	M	23	9/1/2010	App	14.4	16,300	2	0	0	0	I	I	I	I	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	350344	M	39	18/1/2010	Hrn	16.1	6,800	1	0	0	0	I	I	I	I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	350634	M	38	19/1/2010	Hrn	13.5	8,250	1	0	0	0	I	I	I	I	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	350790	M	24	20/1/2010	App	11.5	7,500	3	2	1	0	I	I	I	I	0	0	0	2	1	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0
7	352594	M	20	4/2/2010	App	12.5	9,800	1	0	0	0	I	I	I	I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	354685	M	21	20/2/2010	App	13.0	12,900	2	2	1	0	I	I	I	I	0	0	0	1	1	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0
9	355083	F	22	23/2/2010	App	11.0	8,900	0	0	0	0	I	I	I	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	359332	M	45	29/3/2010	Hrn	13.0	7,900	1	0	0	0	I	I	I	I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	359512	F	22	30/3/2010	App	13.2	9,600	0	0	0	0	I	I	I	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	360391	M	25	6/4/2010	App	14.0	8,900	1	0	0	0	I	I	I	I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	362337	M	40	21/4/2010	Hrn	12.7	6,600	2	1	0	0	I	I	I	I	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	362605	M	29	21/4/2010	Hrn	14.0	12,500	1	0	0	0	I	I	I	I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15	362717	F	45	22/4/2010	App	13.0	6,500	2	1	0	0	I	I	I	I	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16	364651	M	37	5/5/2010	Hrn	14.2	8,600	3	2	1	0	I	I	I	I	0	0	0	1	2	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0
17	365523	F	30	12/5/2010	App	12.5	9,900	2	2	1	0	I	I	I	I	0	0	0	1	1	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0
18	366957	M	28	22/5/2010	App	13.0	6,400	3	2	1	0	I	I	I	I	0	0	0	2	1	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0
19	367313	F	28	25/5/2010	App	13.0	7,800	1	0	0	0	I	I	I	I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	372978	M	42	2/7/2010	Hrn	13.0	10,900	2	1	0	0	I	I	I	I	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
21	373311	M	28	5/7/2010	App	13.0	9,700	2	1	0	0	I	I	I	I	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
22	373474	M	23	6/7/2010	App	14.0	5,400	1	0	0	0	I	I	I	I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
23	375905	F	28	21/7/2010	App	12.5	5,300	2	1	0	0	I	I	I	I	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	378264	M	19	5/8/2010	Hrn	14.9	9,800	3	2	0	0	I	I	I	I	1	0	0	1	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
25	384335	F	32	16/9/2010	App	10.2	5,000	2	1	0	0	I	I	I	I	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
26	384464	M	40	17/9/2010	Hrn	10.5	7,900	1	0	0	0	I	I	I	I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
27	390707	M	26	1/11/2010	App	12.0	10,600	1	1	0	0	I	I	I	I	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
28	391616	F	39	9/11/2010	App	13.0	14,500	4	3	1	0	I	I	I	I	0	0	0	2	2	0	0	0	0	2	1	0	0	0	0	1	0	0	0	0	0	0	0	0
29	392151	F	38	12/11/2010	App	12.2	7,200	1	0	0	0	I	I	I	I	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	394701	F	29	30/11/2010	App	12.0	6,850	2	1	0	0	I	I	I	I	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

ANNEXURE IV – KEY TO MASTER CHART

App	-	Appendicitis
Characteristics of wound		
0	-	None
1	-	Mild
2	-	Moderate
3	-	Severe
F	-	Female
Grading of wound healing		
Grade I	-	Good wound healing (0-5)
Grade II	-	Average wound healing (6-12)
Grade III	-	Poor wound healing (13-18)
gm	-	Gram
Hrn	-	Hernia
M	-	Male
mm	-	Millimeter
No	-	Number
POD	-	Post operative day