EVALUATION OF POST EXTRACTION HEMOSTASIS IN CARDIAC PATIENTS WITH GELATAMP DENTAL DRESSING WITHOUT STOPPING ASPIRIN AND CLOPIDOGREL THERAPY

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partial fulfillment of the requirements

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BRANCH – III

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THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

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2014 – 2017

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I hereby declare that this dissertation titled **"EVALUATION OF POST EXTRACTION HEMOSTASIS IN CARDIAC PATIENTS WITH GELATAMP DENTAL DRESSING WITHOUT STOPPING ASPIRIN AND CLOPIDOGREL THERAPY"** is a bonafide and genuine research work carried out by me under the guidance of **Dr.K.PRABHUSANKAR, M.D.S., Professor, Head of the Department,** Department of Oral and Maxillofacial Surgery, Best Dental Science College, Madurai – 625104.

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DECLARATION

TITLE OF DISSERTATION	EVALUATION OF POST EXTRACTION HEMOSTASIS IN CARDIAC PATIENTS WITH GELATAMP DENTAL DRESSING WITHOUT STOPPING ASPIRIN AND CLOPIDOGREL THERAPY
PLACE OF STUDY	BEST DENTAL SCIENCE COLLEGE, MADURAI – 625104.
DURATION OF THE COURSE	3 YEARS
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TRIPARTITE AGREEMENT

This agreement herein after the "Agreement" is entered into on this day 30th Dec 2016, between the Best Dental Science College represented by its **Principal** having address at Best Dental Science College, Madurai – 625104, (hereafter referred to as, 'the College')

And

MR. Dr .K. PRABHUSANKAR aged 43 years working as **Professor** in Department of Oral and Maxillofacial Surgery at the College, having residence address at 23, Telephone Road, Aruppukottai – 626101 (herein after referred to as the 'Principal Investigator')

And

Mr. Dr. G. MURALIDHARAN aged 27 years currently studying as **Post Graduate student** in Department of Oral and Maxillofacial Surgery, Best Dental Science College, Madurai- 625104 (here in after referred to as the 'PG/Research student and co-investigator')

Whereas the PG/Research student as part of his curriculum undertakes to research on **"EVALUATION OF POST EXTRACTION HEMOSTASIS IN CARDIAC PATIENTS WITH GELATAMP DENTAL DRESSING WITHOUT STOPPING ASPIRIN AND CLOPIDOGREL THERAPY"** for which purpose PG Principal Investigator shall act as Principal Investigator and the college shall provide the requisite infrastructure based on availability and also provide facility to the PG/Research student as to the extent possible as a Co-investigator.

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Date: 30/12/16

Signature of the Candidate

Place: MADURAI

DR. G. MURALIDHARAN.

S.NO	ABBREVIATION	MEANING
1	ADP	Adenosine diphosphate
2	Ag	Silver
3	APTT	Activated Partial Prothrombin Time
4	ASA	Acetylsalicylic acid
5	BT	Bleeding time
6	COX	Cyclo-oxygenase
7	CT	Clotting time
8	CVD	Cardiovascular disease
9	DNA	Deoxyribonucleic acid
10	GI	Gastrointestinal
11	GP	Glycoprotein
12	ISI	International sensitivity index
13	LMWH	Low Molecular Weight Heparin

14	MI	Myocardial infarction
15	MRSA	Methicillin resistant Staphylococcus aureus
16	NSAIDS	Non-Steroidal Anti-Inflammatory Drugs
17	OMFS	Oral and Maxillofacial Surgery
18	OPG	Orthopantomogram
19	Post-op	Post-operative
20	Pre-op	Pre-operative
21	PT	Prothrombin
22	RCT	Randomized Controlled Trail
23	VAS	Visual Analogue Scale

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Introduction

INTRODUCTION

Blood is a fluid connective tissue of the body. Blood carries oxygen to all the parts of our body through blood vessels from lungs. Blood composed of red blood cells, white blood cells, platelets and plasma proteins. Platelets and clotting factors that are present in circulating blood plays a vital role in arrest or stoppage of bleeding. This process is called as hemostasis. Hemostasis is an important physiologic mechanism of the body to prevent excessive blood loss when the blood vessel is severed or injured. [1]

Hemostasis occurs by initial vasoconstriction and formation of clot. Formation of clot involves two main process; Platelet aggregation and coagulation (formation of fibrin strands). Coagulation or clotting is defined as the process in which blood loses its fluidity and becomes a jelly-like mass few minutes after it is shed out. Coagulation of blood occurs through a series of reactions due to the activation of a substances necessary for clotting mechanism is called clotting factors.

Thirteen clotting factors are identified: listed in table-1

TABLE-1

Factor I	Fibrinogen
Factor II	Prothrombin
Factor III	Thromboplastin (Tissue factor)
Factor IV	Calcium
Factor V	Labile factor (Proaccelerin or accelerator globulin)

Factor VI	Presence has not been proved
Factor VII	Stable factor
Factor VIII	Antihemophilic factor (Antihemophilic globulin)
Factor IX	Christmas factor
Factor X	Stuart-Prower factor
Factor XI	Plasma thromboplastin antecedent
Factor XII	Hageman factor (Contact factor)
Factor XIII	Fibrin-stabilizing factor (Fibrinase)

Coagulation is complex cascade process of enzymatic events that forms the fibrin stands. Formation of prothombin activator that converts prothrombin into thrombin occurs in either though intrinsic or extrinsic pathway. The intrinsic pathway is initiated within the bloodstream by platelet thromboplastin. Heparin influences this pathway by inhibiting factors XIIa, XIa, and IXa, its anticoagulant activity is monitored by activated partial thromboplastin time (aPTT). The extrinsic pathway functions outside the bloodstream, initiated by tissue thromboplastin. This pathway is influenced by warfarin because it inhibits hepatic synthesis of factor VII, the most essential factor in the extrinsic pathway. Therefore the anticoagulant activity of warfarin is usually monitored using the prothrombin time (PT). (figure-1). [1, 2]

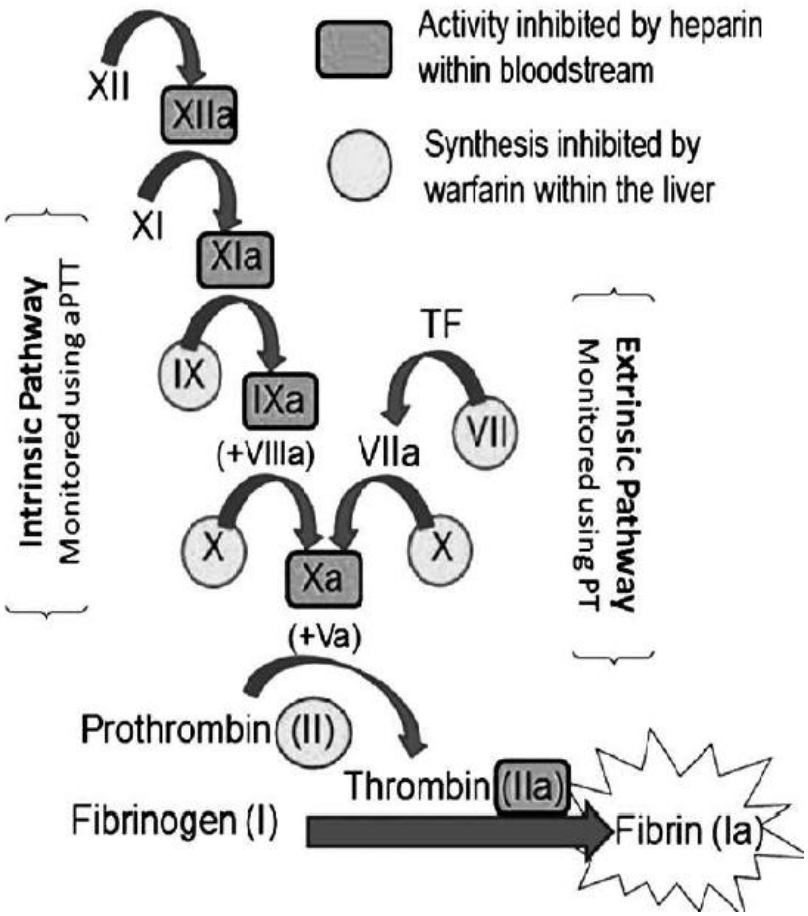


FIGURE- 1: THE COAGULATION PATHWAY

At the site of arterial injury, platelets initiates hemostatic plug and thus contributes for the formation of arterial thrombosis that leads to increased incidence of ischemic stroke and myocardial infarction. Venous thrombi commence as fibrin strands, appear red in colour because of entrapped red blood cells, and can get embolize at distant sites, usually in pulmonary arteries causing pulmonary embolism. To prevent as well as to treat cardiovascular and cerebrovascular thromboembolic conditions, antithrombotic therapy is indicated. Antithrombotics includes inhibition of platelet aggregations (Antiplatelet), inhibition of fibrin strands formation (Anticoagulant), and dissolution of fibrin clot (fibrinolytic) .[2, 3] (figure-2)

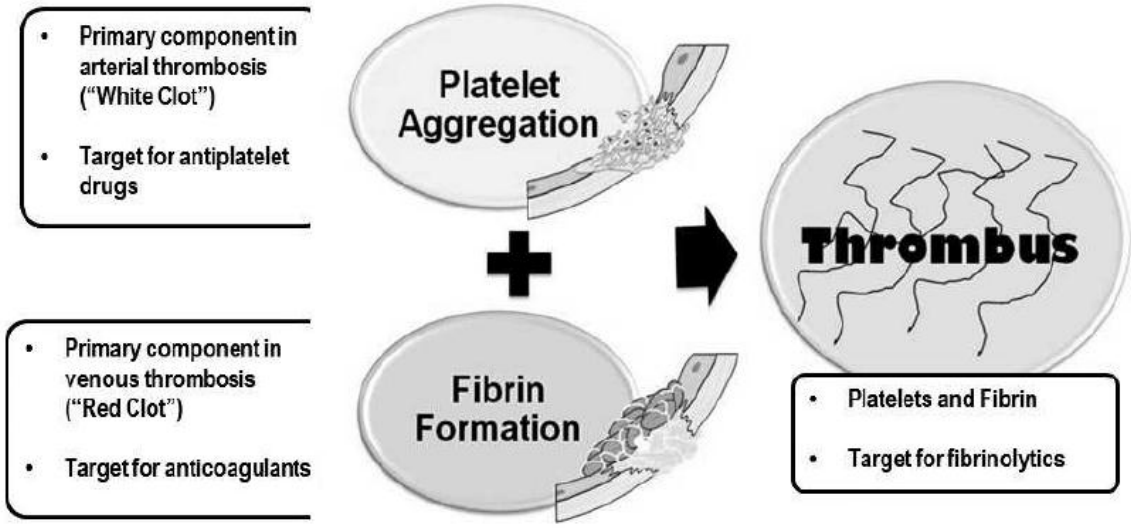


FIGURE- 2; Thrombus consists of 2 principal components: an aggregate of platelets and a fibrin mesh. Platelet activity consists of adherence to vessel walls (adhesion) and to one another (aggregation). The fibrin mesh is synthesized during a complex cascade of enzymatic reactions leading to the formation fibrin strands (coagulation).

The common indications if antithrombotic therapy are arterial thrombosis, ischemic heart disease, myocardial infarction, both stable and unstable angina, coronary artery bypass and placement of a stent, non-hemorrhagic stroke, transient ischemic attacks (ischemic stroke), peripheral arterial disease, atrial fibrillation, etc. [2, 4]

Hippocrates, 2000 years back recommended chewing willow leaves that contains salicylic acid during child birth for analgesia. In 1899, the chemist Felix Hoffman of the Bayer Company was the first to isolate pure acetylsalicylic acid, later calling it "Aspirin" for commercial manufacture and

sale, as it became the widely used drug for its analgesic, antipyretic, anti-inflammatory, and anti-thrombotic effects.

Later newer antiplatelet medication emerged such as clopidogrel, ticlopidine, cilostazol, dypyridamole, ticagrelor, prasugrel, abciximab, tirofiban and ebtifibatide. These newer drug has higher antithrombotic effect as well as bleeding risk more than aspirin. When oral surgical procedures is planned for these patients both the surgeons and the physicians should weigh the potential bleeding risks in continuing the medications versus the thromboembolic risks in interrupting them before procedure. [5]

Traditional method of treating these patients is by stopping the antiplatelet medication 7 to 10 days or at least for 3 days prior to the oral surgical procedure.[3] Aspirin begins irreversibly inhibiting thromboxane A2-induced platelet aggregation within 1 hour of ingestion, and clopidogrel selectively inhibits adenosine diphosphate (ADP)-induced platelet aggregation within 2 hours, this lasts for 7–10 days of the mean platelet life [2, 4].

If antiplatelet drug is discontinued hypercoagulable state or rebound phenomenon occurs by abnormal increase in production thromboxane A2, increased activity of ADP receptor that involve in platelet aggregation, decreased fibrinolysis and decreased antithrombin level.[3, 6,7, 8]

Antiplatelet drug increases the risk of post-operative bleeding especially in patients who were under dual antiplatelet therapy where the risk is higher because of their synergistic effect. Physicians and Oral & maxillofacial surgeons advice patients to stop taking antithrombotics before extraction of tooth due to fear of excess intra and post-operative bleeding. However, this can increase the incidence of fatal thromboarterial events within

10 days of stopping the drugs. Thus the oral surgeons have to maintain the balance between the risk of increased post-operative bleeding and the risk of thromboembolic events. The increase in the risk of thromboembolic events outweighs the risk of post-operative bleeding as it can be managed with local hemostatic measures. [9]

Various studies suggest to extraction procedures continuing the antiplatelet therapy under optimal therapeutic INR level in which local hemostatic measures to control the prolonged bleeding. [3]

The ideal oral surgery hemostatic agent should be safe, packaged, sterile, single-use, well tolerated, bacteriostatic, preformed for operator convenience, remain where applied and should get dissolve in first post-operative week.[10]

Extractions of teeth, is unlike surgery in most other parts of the body, have less incidence of encountering major blood vessels. The extracted sockets can be easily accessible to undergo local hemostatic methods such as pressure application (biting on gauze) and using hemostatic materials like cellulose, gelatin foams, gelatamp, hemcon dressing, microfibrillar collagen, sutures, hemostatic solutions, tannic acid, tranexamic acid, and fibrin glue etc [11, 12]

Gelfoam is an absorbable gelatin sponge, available as a sterile sponge like dressing. This sponge holds many times its weight in blood and provides a stable scaffold for clot formation. Thus the mode of action of the Gelfoam is believed to be related to formation of a mechanical matrix that facilitates clotting. It has very little tissue reaction and gets absorbed within 4 to 6 weeks.[13]

Though silver has not been proven as safe and effective element, it has been used in alternative medicine in colloidal form. Silver has been used in 18^{th} century for the wound management in form of $AgNO_3$(silver nitrate) for treating ulcer. In 19^{th} century antibacterial activity of silver ion is first discovered, in 1920s colloidal silver was accepted by the US Food and Drug Administration (FDA) for wound management. In 1960s Silver again used for management of burn patient in form of 0.5% $AgNO_3$. In 1968 silver was combined with sulphonamide antibiotic to produce silver sulfadiazine cream which acts a broad spectrum silver based antibiotic cream that were widely used for management of burns. Silver based wound dressing also used in infected wound with antibiotic-resistant bacteria. [14, 15]

Silver-impregnated dressings have been shown to reduce iatrogenic infection rates and improve wound healing. Silver ion decreases inflammation due its antibacterial effect which consequently decreases pain perception and promotes wound healing. [16]

Gelatamp(colloidal silver ion impregnated in gelfoam) is effective against wide range of microrganisms, which are found in the oral cavity. It has been found to be very effective against bacteria, which are resistant to antibiotics. The finely dispersed colloidal silver provides a large active surface for the continuous release of silver ions. As silver does not dissolve easily it is not washed out of the gelatin sponge but is continually released as the sponge is resorbed. This gives Gelatamp a depot antimicrobial effect throughout the resorption process. It remains in the alveolus and completely resorbed within 4 to 6 weeks.[11]

The purpose of this study is to evaluate and compare the post-operative clinical outcome, such as post-operative bleeding, pain, and wound healing on patients taking aspirin and clopidogrel between Gelatamp group and non Gelatamp group in the extracted sockets.

Aim and Objectives

AIM AND OBJECTIVES

AIM

The aim of the study is to evaluate the use of Gelatamp dental dressing as a haemostatic agent in cardiac patients continuing aspirin and clopidogrel following dental extraction.

OBJECTIVE

Dental extraction in cardiac patients taking aspirin and clopidogrel can be difficult as these patients present a significant risk for post-operative haemorrhagic complications. This study is performed to evaluate the use of Gelatamp (colloidal silver ion impregnated in gelfoam) dental dressing following dental extraction in cardiac patients taking aspirin and clopidogrel without stopping the therapy.

Review of Literature

REVIEW OF LITERATURE

Lemkin (1974) described about prolonged post-operative bleeding after oral surgery due to aspirin therapy and he controlled the same with platelet transfusion. He recommended to stop the aspirin 7 days prior to the procedure to avoid such post-operative complications. [17]

McGaul (1978) explained about the intra and post-operative increased bleeding time due to aspirin therapy in normal patients. This study concluded to stop aspirin 7 to 10 days prior to the procedure and also suggested not to take the aspirin immediately after the procedure.[18]

Souto et al (1996) did a comparative study between two groups. They did extractions in group A patients without interrupting the anticoagulant therapy but they used antifibrinolytic agents such as tranexamic acid for hemostasis. In group B patients they administered calcium heparin prior to the procedure. They concluded that post-operative bleeding can be controlled effectively in group A patients in a safe and less troublesome method.[19]

Richard Stern et al (1997) explained that normal INR coagulation profile would be 1. Patients under anticoagulant therapy would be 2.5 to 3.0. Dental invasive procedures can be done safely in INR range of about 1.5 to 2.5. They also suggested that INR level is a reliable method for monitoring and evaluating the patients under anticoagulant therapy. [20]

Blinder et al. (1999) compared post-operative hemostasis after extraction in three groups of patients who were under continued anticoagulant therapy. Group 1 using gelatin sponge and suture, group 2 using tranexamic mouth wash along with gelatin sponge and suture, group 3 using fibrin glue with gelatin sponge and suture. They got equivalent results in all the three groups and thus suggested that dental extraction could

be performed safely without interruption in patients' oral anticoagulant drug regimen along with gelatin sponge and suture for post-operative hemostasis. [21]

Sonken et al (1999) claimed that aspirin can be withheld for about 48 hours before the procedure (instead of 7 to 10 days) to reduce the post-operative bleeding complication and thus prolonged action of platelet reactivity can also be decreased. [22]

Ardekian et al. (2000) did a prospective randomized controlled clinical comparative study in low dose aspirin (100 mg) taking patients between test group (stopped aspirin prior to the procedure) and control group (continuing the low dose aspirin). They concluded that dental extractions can be performed safely without severe post-operative bleeding in patients on continued low dose aspirin therapy. [23]

Campbell et al (2000) compared the blood loss after minor oral surgery in patients with continued anticoagulant therapy with control group in whom the anticoagulant regimen is stopped 72 to 96 hours prior to the procedure. They also included additional control group in which the non anticoagulated patients were included to enroll the base line bleeding values. They found no significant post-operative blood loss between these groups and suggested that alternation of drug regimen is not needed provided that INR should be under therapeutic range. [24]

Collet et al (2000) retrospectively analyzed 475 consecutive myocardial infarction patients, 11 of whom had interrupted aspirin therapy within 15 days prior to hospital admission. One of these patients discontinued aspirin 8 days before dental surgery and suffered a myocardial infarction 2 days later. [25]

Patrick J Vezeau (2000) explained normal post extraction socket healing is initiated by clot formation and organization. Any disruption to this sequelae will result in post-operative healing impairment. He suggested medications such as antifibrinolytics (EACA and TXA), topical antibiotics especially clindamycin and

tetracycline and steroids for better clot stabilization and improved wound healing in extracted sockets. [26]

Hirsh et al (2001) explained that the goal of anticoagulant therapy is to prevent clot formation and Warfarin is the most common drug used in this therapy. Warfarin is an antagonist of vitamin K, which is necessary for synthesis of clotting factors II, VII, IX and X, as well as the naturally occurring endogenous anticoagulant proteins C and S. They suggested the therapeutic range of INR as 2.0 to 3.0. [27]

Daniel et al (2002) explained aspirin to stop 7 days prior to the procedure as it is a irreversible inhibitor of cyclooxygenase enzyme and not to stop NSAIDS which is a reversible inhibitor of cyclooxygenase enzyme. They also suggested to stop ADP receptor blocker and phosphodiesterase inhibitor for 7 days and 24 hours respectively prior to the procedure to avoid post-operative haemorrhagic complications. [28]

Little (2002) reviewed and explained that arterial thrombosis were mainly due to platelet aggregation so antiplatelet therapy has a prime role in treating arterial thrombosis. Venous thrombosis was mainly due to hypercoagulable state thus these conditions were treated by anticoagulants. They also explained that if the patient is under heparin it should be discontinued 1 to 2 hours and if it is LMWH 2 to 4 hours prior to the procedure in a hospital set up. They recommend non interruption of oral antithrombotic drug regimen for minor oral surgical procedure with local hemostatics such as gelfoam, thrombin, oxycel, surgical for post-operative hemostasis. If major oral surgery is planned and excessive bleeding is anticipated, antiplatelet therapy should be discontinued 7 days prior to surgery with appropriate medical consultation. [29]

Scully (2002) suggested to stop the antiplatelet therapy if the patient is taking more than 100 mg of aspirin daily or if he/she has associated bleeding disorders. He also explained that if the patient is having bleeding time more than 20 minutes then the

patient has to be monitored by the general physician and the antiplatelet therapy has to be stopped prior to the procedure. [30]

Smout et al (2003) did a survey by questionnaire method to 137 vascular surgeons in UK, 90 completed questionnare were returned among that 90 % of the vascular surgeons suggested to continue antiplatelet therapy peri operatively for carotid and peripheral vascular surgery. They also suggested that most of the vascular surgeons switch over for alternative therapy such as heparin if the patient has GI intolerable reasons for aspirin. [31]

M. Tendera et al (2003) explained that dual drug regimen (aspirin and ticlopidine/ clopidogrel) were proven to be more effective in prevention of cardiovascular events than single drug (aspirin) alone. [7]

Collet et al (2004) explained that oral anticoagulant cessation was found to be a prime predictor of death and major ischemic events. This finding supports the hypothesis of a rebound phenomenon after oral anticoagulant interruption, leading to acute coronary thrombosis that has been triggered in more anxious patients due to surgical stress. This superimposed thrombotic tendency increases thrombin level. [32]

McFadden et al (2004) investigated that the potential risk of stent occlusion should be considered when discontinuation of antiplatelet therapy is contemplated in patients with drug-eluting stents. [33]

O. Ross Bierne (2005) explained that LMWH should be started subcutaneously after with drawl of warfarin and discontinued 24 hours prior to the minor oral surgery and started 12 to 24 hours after the procedure till warfarin is shifted. O. Ross Bierne recommends narcotic analgesics for post-operative pain care as other analgesics impair anticoagulant mechanism. O. Ross Bierne suggested oral surgical procedures can be done safely with INR 2 to 4 without interrupting the warfarin in low risk individuals. [34]

Burger et al (2005) reviewed that low dose aspirin can be stopped if increased bleeding risk is assumed or expected more than the cardiovascular risk events especially in intracranial surgeries. They also suggested that the oral surgical procedures can be done with or without discontinuing aspirin but he recommends to use local hemostatic measures to control bleeding. [35]

Ferrari et al (2005) studied 1236 patients with acute coronary syndrome, 51 of whom were hospitalized within 1 month of aspirin withdrawal. They reported 1 in13 cases was due to aspirin withdrawal for dental treatment. They hypothesize that withdrawal of aspirin increases the platelet reactivity thus increases the incidence of coronary thrombosis . [8]

Madan et al (2005) investigated the effects of continuing aspirin therapy (75-100 mg per day) in 51 subjects receiving oral surgical procedures. Only one case (third molar surgery) had increased intraoperative bleeding that was controlled by local measures. There was no postoperative bleeding in any of the 51 cases. [36]

Herman et al (2006) explained that Silver is promoted within alternative medicine in the form of colloidal silver, though it has never been proven safe and effective. The silver ion (Ag+) is bioactive and in sufficient concentration readily kills bacteria in vitro. Silver also kills bacteria in external wounds in living tissue and therefore physicians use wound dressings containing silver sulfadiazine (Ag-SD) or silver nano-materials to treat external infections. [37]

Afriaman et al (2007) did a literature review and selected 64 publications from the world workshop in oral medicine IV and framed recommendations that minimally invasive procedures can be done without stopping antithrombotics if INR level is less than 3.5 . Their review concluded that the risk of thromboembolism outweigh the post-operative bleeding in patient continuing anticoagulant and anti-platelet therapy. [38]

Al- Mubarak et al (2007), investigated 214 patients who were under warfarin for a period of greater than 1 year and divided these patients into 4 groups: no suturing and discontinued (group 1) or continued warfarin (group 2), and suturing and discontinued (group 3) or continued warfarin (group 4). They suggested that dental extraction can be done safely in patient continuing oral anticoagulant with INR less than or equal to 3.0. [39]

Brennan et al (2007) updated and reviewed that dental extractions can be performed with minimal bleeding risk in patients on continuous low-dose aspirin. In "extenuating" circumstances, when antiplatelet therapy should be interrupted, then the interruption should be for no more than 3 days to minimize the risk of thrombosis. [40]

Ion Chopra (2007) explained that Wound dressings containing silver has constantly evolving in current topical medications due to the recent increase of antibiotic-resistant bacteria thus silver becomes he effective alternative agent for management of wound healing. Ion Chopra also suggested topical silver dressing should release high level of silver ions to prevent silver resistant and to get rapid bactericidal effect. [14]

Pototski et al (2007) reviewed the risk of bleeding under continued aspirin use to increase by 1.5-fold, but that this can be controlled with local hemostatic measures with no life-threatening bleeding. Dual antiplatelet therapy was found to increase major bleeding events by 1% as compared to aspirin monotherapy, but no life-threatening complications were reported and no transfusions were required and can be managed by local hemostatic measures. Hence they suggested that there is no need to expose patient to the risk of thromboembolism, cerebrovascular accidents, or myocardial or renal infarction by discontinuing antiplatelet therapy before minor oral surgical procedures, which could endanger the patient's life. [41]

Ward et al (2007) did a survey by questionnaire method to 188 registered OMFS at the Michigan society of OMFS in 2005 regarding aspirin cessation prior to the dentoalveolar procedure in which they got response from 127 surgeons. With this survey results they suggested not to discontinue or alter the oral anticoagulant therapy for low risk patients and for moderate and high risk patients they suggest hospitalization and heparinization prior to the procedure. [42]

Yepes et al (2007) explained that hypercoagulable state is uncommon in dental scenario. Complications can be minimized by obtaining adequate patient history and opinion from physician/ haematologist. They also suggested local hemostatic agents such as gelfoam and thrombin after the procedure. [43]

Cai et al (2008) explained that Gelatamp is effective against wide range of microorganisms, which are found in the oral cavity. It has been found to be very effective against bacteria, which are resistant to antibiotics. The finely dispersed colloidal silver provides a large active surface for the continuous release of silver ions. As silver does not dissolve easily it is not washed out of the gelatin sponge but is continually released as the sponge is resorbed. This gives Gelatamp a depot antimicrobial effect throughout the resorption process. Gelatamp has the great advantages of both hemostatic and bactericidal effect. It remains in the alveolus and completely resorbed within 4 weeks. [44]

David Keith Cundiff (2008) reviewed to investigate the incidence of venous thromboembolism after the discontinuation of oral anticoagulants and found out that 2 % of patients are under increased risk of venous thromboembolism within first 2 months of anticoagulant therapy cessation. [45]

Krishnan et al (2008) investigated whether to stop antiplatelet therapy before extraction in aspirin taking patients. They selected 82 patients and divided them into three group.Group1(n=25) stopped aspirin before extraction, group 2(n=32) continued aspirin, and

gropu 3 patients had no aspirin at all. They found no significant difference in both bleeding time and clotting time between these groups. Thus they suggest that patient under aspirin therapy can undergo routine dental extractions continuing the drug regimen would not cause increased risk of excessive or prolonged bleeding. [46]

Malmquist et al 2008 investigated about the hemcon dental dressing, a chitosan based product to evaluate the haemostasis and healing in surgical wound sites. They did a randomized controlled study on 74 patients in that 9 patients were under anticoagulant therapy. They found better haemostatic and healing properties while comparing with control group. Thus they suggest not to stop the anticoagulant therapy prior to the procedure provided that the wound site has to be managed with local haemostatic agents such as hemcon dental dressing. [10]

Morimoto et al (2008) investigated post-operative haemorrhage in 270 patients. 134 received warfarin alone, 49 receiving warfarin and antiplatelet and 87 antiplatelet alone. They did 513 extractions in 306 occasions under therapeutic INR range . They encountered prolonged post-operative haemorrhagic episodes about 11 occasions. 7 in warfarin patient alone, 2 in patients with warfarin and antiplatelet and 2 in antiplatelet alone which was managed by local haemostatic measures. Thus they suggested that patients under antithrombotic therapy with INR less than 3 can undergo invasive dental procedures in which the post-operative bleeding complications were managed by local haemostatic agents such as oxidized cellulose, gelatin sponge fibrin glue. [47]

Patridge et al (2008) examined blood loss comparing two groups. Patients under aspirin therapy doesn't show significant increased blood loss with control group. Thus they recommend that dental extractions can be carried out safely without discontinuation of antiplatelet therapy.[48]

Bajkin et al (2009) compared post-operative bleeding after minor oral surgery in two groups. Group A with continuing oral anticoagulant and group B with LMWH as a bridging therapy. No significant increased bleeding episodes occurred in both a group. Thus from their study they concluded that minor oral surgical procedures can be done safely with local hemostatic measures with INR less than 4 in patients under antithrombotic therapy. The use of bridging mechanism of low molecular weight herparin can be reserved for major surgical procedure. [49]

Cardona-Tortajada F et al (2009) explained that no significant bleeding had occurred regardless of various types of antiplatelet drugs but they suggested not to extract more than 3 teeth and that too adjacent teeth has to be extracted not the opposite side or quadrant. [50]

Nooh et al (2009) examined bleeding episode with study group on continuous aspirin therapy and control non aspirin group patients which were again subdivided with sub group A and sub group B for simple and trans alveolar extractions respectively. They find no significant difference in post-operative haemorrhage between these groups and thus suggested that subjects who received 81 mg ASA daily could undergo dental extraction without bleeding risks. [51]

Lordkipanidze et al (2009) reviewed that cessation of antiplatelet therapy is associated with a progressive recovery of platelet function and with a potential risk of rebound of thromboembolic vascular events due to excessive thromboxane-A2 activity and decreased fibrinolytic activity within time period of 8 to 25 days. They also suggested that this phenomenon is due to increased new platelet production after cessation of antiplatelet drugs. [52]

Alridge et al 2010 explained not to stop oral anticoagulant medication for non invasive dental procedures, provided that the INR should be below 4. For invasive oral surgical procedures patients should be heparinized and INR should be 1.5 to 2. If the

patient is in single antiplatelet therapy continuation of the same is suggested as the bleeding risk will be low when compared with the double antiplatelet therapy. [53]

Lillis et al (2011) performed a prospective study to compare the incidence of bleeding complications among patients taking aspirin monotherapy, clopidogrel monotherapy, and dual therapy with both aspirin and clopidogrel and patients not taking aspirin at all. The results showed that greater number of patients on dual antiplatelet therapy showed prolonged immediate bleeding when compared to control healthy patient group, and the difference was statistically not significant. Although there is greater incidence of prolonged immediate bleeding in dual antiplatelet therapy group, haemostasis is achieved easily by local haemostatic measures. Therefore, they concluded that the patient should not be liable to risk of thromboembolism by stopping either antiplatelet monotherapy or dual therapy. [54]

Medeiros et al (2011) did a double blind comparative prospective study in 63 coronary artery disease patients with and without acetylsalicylic acid suspension. They found no significant difference in hemorrhagic events and suggested not to stop acetylsalicylic acid drug regimen before procedure. [55]

Morimoto et al (2011) investigated post-operative bleeding in 382 patients who were under anticoagulant and antiplatelet therapy. Thus their study reported post-operative bleeding of 1.4% for single or dual antiplatelet therapy, 4.1% for warfarin, and 8.2% for combined warfarin and antiplatelet therapy after teeth extractions under therapeutic range of INR less than 3. They also found that all these bleeding episodes occurred within six days from the date of the procedure. [56]

Vaklavick et al (2011) analyzed and explained that suspending aspirin therapy resulted in a 3-fold increase in the incidence of cerebral infarction and major cardiovascular events compared with continuation of the therapy. They also explained

that there will be 1.5 fold increase in post-operative bleeding in patients under aspirin therapy which is less fatal when compared to highly fatal cardiovascular and cerebral events. [57]

Alexander Grobe et al (2012) performed oral osteotomy in 405 patients safely in patients under 64 mono antiplatelet (clopidogrel 75 mg/ day) and in 60 dual antiplatelet therapy (clopidogrel 75 mg/ day and aspirin 100mg/day). The remaining 281 procedures were done in non-antithrombotic patients. They found no excessive bleeding events thus recommended minor oral surgery without interrupting the drug regimen. [58]

Bajkin et al (2012) conducted a prospective study to evaluate the post-extraction bleeding in patients on aspirin monotherapy, oral anticoagulant therapy, and dual therapy with aspirin and oral anticoagulant (71 patients in each group). None of the patients on aspirin monotherapy had post-operative bleeding. [59]

Kamoh et al (2012) explained preoperative assessment should include thorough history, clinical examination and appropriate investigations to identify risk of bleeding. They suggested early morning appointment for these patients. Intra operatively if increased bleeding occurred, it should be managed with figure of eight suture, pressure pack for 3 to 5 mins, gelfoam, surgical, etc. post operatively they suggest 4.8% tranaxemic acid mouth wash for 7 days and follow up. [14]

Park et al (2012) investigated dental extractions in 100 patients who were under gone coronary stenting procedure with double and triple antiplatelet therapy. They did exactions on 2223 non antithrombotic patients from health promotion center. 1 case from control group reported with excessive bleeding event and 2 cases reported in study group. Thus they concluded that dental extraction can be done safely in coronary stenting patients with multiple antiplatelet therapies. [60]

Becker et al (2013) explained the formation of clot involves two main process; Platelet aggregation and Formation of fibrin strands (coagulation). Platelet aggregation occurs through cohesion of activated platelets through fibrinogen strands while coagulation is complex cascade process of enzymatic events that forms the fibrin stands. Antithrombotics includes that inhibit platelet aggregations (Antiplatelet), inhibit fibrin strands formation (Anticoagulant), dissolves fibrin clot (fibrinolytic). [2]

Girotra et al (2013) did prospective comparative study to investigate the post-operative hemorrhage after minor oral surgical procedures in 1121 patients which were divided into study group (n=546) - patients under antithrombotic agents and control group (n=575) - normal patients without any such medications. They reported no significant difference in post-operative bleeding events between these two groups except in patients under dual antiplatelet therapy which was managed with local hemostatic measures such as gelfoam dental dressing and tranexamic mouth wash. Thus from their study they suggested that for minor oral surgical procedures it is not mandatory to stop antithrombotic drug regimen and if the patient is in dual antiplatelet therapy local hemostatic can be used for hemostasis. [4]

Napenas et al (2013) reviewed the bleeding complications in dental patients on antiplatelet agents. They focused on 15 studies, which showed the postoperative bleeding complications in patients on single or dual antiplatelet therapy is insignificant. The authors concluded there is no need to stop single or dual antiplatelet therapy for invasive dental procedures provided local haemostatic agents should be used to control the post-operative haemorrhage. [61]

Van Diermen et al (2013) searched the literature and expert recommendations from 2007 to 2012 and concluded that antithrombotic medications including dual antiplatelet therapy should not be interrupted for simple dental procedures, including extractions and minor invasive procedures. [62]

Verma et al (2013) compared post extraction bleeding events between aspirin taking group with non-aspirin patients with 30 patients on each group and concluded that there is no need to stop the antiplatelet dose of aspirin prior to simple tooth extraction as there was 0% incidence of post-operative bleeding in study group patients.[63]

Abbound et al (2014) investigated reduction in pain with silver dressing by comparing 55 patients in study group who had silver nylon dressing with 54 patients in control group who had normal gauze dressing. Study group reported less pain perception, faster re epithelialization and decreased surgical site infection. Thus they found that increased antibacterial effect and decrease in the frequency of changing silver wound dressing decreases the pain in the wound. [16]

Broekema et al (2014) did comparative prospective study 206 individuals, 103 each between two groups of patients who were under antithrombotics and who were not under such medications. Among the 103 patients 71 were under thrombocyte aggregate inhibitor and 32 were under vitamin k antagonist. 9 % and 6 % post-operative bleeding episodes reported in antithrombotics and vitamin k antagonist groups respectively after minor oral surgery which was managed by 5% tranexamic mouthwash 7 days post operatively. 2 % of hemorrhagic episodes had occurred in control group which not a significant difference. Thus they suggested that dentoalveolar surgery is safe in patients being treated with anticoagulants under INR range of 1.8 to 3.5. [64]

Eichhorn et al (2014) compared the bleeding tendency in cutaneous head and neck surgeries in between study group continuing aspirin and vitamin k antagonist and control non antithrombotic patients. Totally 468 procedures, 259 in study group and 209 in control group were done. In their study they reported mild post-operative bleeding in 10/ 259 study group and 6/209 control group which seems to be not significant. Thus

they concluded that cutaneous head and neck surgeries can be performed safely in patients under antiplatelet and anticoagulant therapy. [65]

J. Lee et al (2014) compared 212 non aspirin patients with 248 aspirin taking patients to evaluate the platelet recovery time period after cessation of aspirin by arachidonic acid platelet aggregation test for every 24 hours till 5th day. From their study they found out that platelet recovery takes place around 96 hours (4th day) after cessation of aspirin. Thus they suggest to stop aspirin 96 hours prior to the complex dental procedures. [66]

Marx et al (2014) explained and reviewed that silver can occurs in three oxidation states among that Ag[+1] state is used as an antibiotic in medicine as it is only stable oxidation state. Silver sulfadiazine and silver nitrate are used mainly in burns care since 1968. Colloidal silver ion is used as a topical agent in wound dressing. They also explained the antibacterial mechanism of silver is through lysis of bacteria by cell membrane damage, intracellular DNA disruption and by formation of free radicals which is detrimental to bacteria. They reviewed argyria as a common harmless side effect. They suggested using high concentration of silver in wound dressing to have bactericidal effect. [67]

Wahl MJ (2014) did a literature review and reported only 0.2 % post-operative excessive bleeding episodes after the minor oral surgical procedures in patients under antithrombotic therapy. Wahl MJ also explained that nonfatal bleeding risk which can be managed with local hemostatic agents is less life-threatening the fatal cardiovascular events. Thus the author supports not to stop interruption of drug regimen [11]

Bajkin et al (2015) investigated the post-operative bleeding in highly anticoagulant therapy who needs extensive surgical therapy. 125 patients were studied by dividing them into three groups. Group A includes 54 patients who were highly anticoagulated with INR less than 3.5(simple extractions were planned), In group B 60

patients were included with INR range 2 to 3.5 (minimally extensive procedures such transalveolar method, biopsies were planned), In group C 11 patients were included with INR greator than 3.5. 85 healthy patients under gone same procedure as in group Aand B as a control group. Group C reported highest post operative hemorrhage of about 18.2 % which was a managed with local hemostatis measures. Thus from their study the auther concluded that patients taking single or dual antiplatelet drugs may have teeth extracted safely without interruption of treatment using only local hemostatic measures to control post-operative bleeding under INR range of about 3.5 to 4.2. [68]

Duceppe et al (2015) reviewed and updated perioperative aspirin does not support prevention of myocardial infarction in patients undergoing non cardiac surgery and they found increased risk of bleeding for about 8 days if aspirin is continued before surgery. They explained increase in troponin level results in during non-cardiac surgeries that causes mortality with in first 30 days after the procedure. They also explained that release of catacholamines due to stress and tissue injury in perioperative period alter the fibrinolysis mechanism thus paves way for acute coronary thrombosis. [6]

Hanken et al (2015) did a retrospective study by revisiting the medical records to evaluate the post-operative bleeding events on more extensive minor oral surgeries such as those procedures need osteotomy like impactions and transalveolar method in patients continuing aspirin therapy. 297 procedures were included in study group and 179 procedures were included in control group patients with no such medications. They reported post-operative bleeding events of about 5 % and 2 % in study and control group respectively which were managed with fibrin glue, methyloxcellulose, and acrylic splint. Thus from their study they suggested anticoagulant patients undergoing dental osteotomies has no significant increased post-operative bleeding risk events. [69]

Olmos-Carrasco et al (2015) in their prospective study on 181 patients who underwent dental osteotomy procedures reported 8.3 % of excessive post-operative bleeding in patients continuing dual antiplatelet therapy which was managed by tranexamic mouth wash 6^{th} hourly for 10 days. They suggest not to interrupt drug regimen for dental osteotomy procedures in patients continuing dual antiplatelet therapy. [70]

Zhao et al (2015) did meta-analysis to determine whether to stop aspirin prior to the procedure. They selected 3 RCTs and 7 controlled trails that met their inclusion criteria. Totally 1752 patients were analyzed in 529 were on aspirin therapy and 1229 patients were not in aspirin therapy. From their meta-analysis they observed higher post-operative bleeding rates in aspirin continuing patients and they also find no significant difference in bleeding time. [71]

Maani et al (2015) did a comparative study to evaluate the effectiveness of Gelatamp to avoid post-operative dry socket and hemostasis after extraction in patients continuing anticoagulant therapy. They compared study group (n=25) who were under anticoagulant therapy with control group (n=25) who stopped medication prior to the procedure. Gelatamp was packed in study group and compared with the control group. Their study concludes that no significant bleeding episodes occurred between two groups and Gelatamp as an effective local hemostatic material. [12]

Schreuder et al (2015) did a literature review on indications, mechanism of action of antiplatelet therapy and management considerations. They finally concluded that the risk of increased cardiovascular events during cessation of antiplatelet therapy outweighs the risk of increased bleeding during and after extraction, so they suggest not to interrupt the antiplatelet therapy for exodontia. They also recommend local hemostatic measures such as pressure gauze, tranexamic acid, gelfoam for hemostasis.[72]

A.D. Opera et al (2016) concluded that perioperative management of anticoagulation therapy should be based on patient related and surgery related. This will helps in decision making in interrupting the anticoagulation and changes in anesthetic care according to the surgical procedure and patient's systemic status. [73]

Lu et al (2016) investigated the post-operative bleeding events by comparing two groups. Study group patients continuing antiplatelet drug regimen while control without antiplatelet therapy. Their study reported post-operative bleeding rate of 1.8 % in study sub group with single antiplatelet and 4.2% in dual antiplatelet therapy. While in control group it was 0.7 % which is not significant comparing with study group. Thus they concluded not to interrupt both single and double antiplatelet therapy prior to extraction. They also explained that cessation of these drugs will increase the fatal risk of thromboembolism as post-operative bleeding can be managed with local hemostatic measures. [3]

Yuliang Dong et al (2016) investigated gelatin sponge with colloid silver in infected cranial bones in 10-week-old female Sprague-Dawley rats with gelatin alone and obtained better bone healing results especially against methicillin resistant Staphylococcus aureus (MRSA). They also explained that the porous structure of gelatin sponge allowed it to hold blood as much as 55-75 times than its weight and provide a stable scaffold for clot formation, prevents tissue collapse and maintains the space for bone healing and colloidal silver ion has antimicrobial action against methicillin resistant Staphylococcus aureus (MRSA). [74]

Materials and Methods

MATERIALS AND METHODS

This is a randomized controlled clinical trial approved by the institutional review board and ethical committee. Informed consent was obtained from all patients before their inclusion in the study. This study was conducted on 88 patients with an age range of 32 to 62 years, who were referred to the Oral and Maxillofacial Surgery Department, Best Dental Science College, Madurai.

All patients were cardiac patients and under aspirin or/and clopidegrol therapy with no known or controlled diabetic or/and hypertension, who preferred extraction as a treatment option.

Gelatamp (Gelatamp gelatine sponge with colloidal silver Coltène/Whaledent Ltd. President Suite Kendal House Victoria Way Burgess Hill West Sussex, RH15 9NF/U.K.) is made of foam gelatine and finely dispersed (colloidal) silver. Silver forms silver ions in moist conditions. The porous foam structure absorbs its own weight in blood several times over, promotes thrombocyte aggregation due to the large surface and fills the wound cavity. Gelatamp remains in the alveolus and is completely resorbed within 4 weeks. (Figure – 4 & 6)

INCLUSION CRITERIA

Patients' age ranged between (32 - 62) years old of both sexes,

Patients with known diabetic and hypertension under controlled condition.

Patients under aspirin and/ or clopidogrel therapy with INR ≤ 3.5 .

EXCLUSION CRITERIA

Patients who had INR value greater than 3.5,

Patients with history of bleeding disorders or with severe systemic diseases,

Patients under warfarin and heparin therapy,

Immuno-compromised patients.

The patients were randomly divided into two groups: group A is a Gelatamp group, where the extraction sockets were packed with Gelatamp and sutured with 3.0 black silk. The allocation of patients into either group was random nonblind as there was no way to mask the Gelatamp group from the control group. Group B is a non-Gelatamp group, where the extraction sockets were sutured with only 3.0 black silk.

A full medical history was taken and an IOPA/ an orthopantogram and clinical examination were performed. Antibiotic prophylaxis was given to all patients one hour pre-operatively, in the form of 875mg Amoxicillin and 125 mg Clavulanic acid.

GROUP A

Local anesthesia, 2% lidocaine and 1:80,000 epinephrine was given to the patients using standard injection techniques. Dental extractions were then performed as atraumatic as possible, using extraction forceps and elevators when needed. Immediately following extraction the extracted socket is sutured along with Gelatamp pack at the height of alveolar bone. Whenever needed the gelatamp is trimmed using scissors to fit inside the socket.

GROUP B

Same procedures were done as in group A but in this group the extracted sockets were sutured only with 3.0 black silk without placing any haemostatic material into the socket.

Antibiotics were continued three days post-extraction in the form of 875 mg amoxicillin and 125 mg clavulanic acid once a day. Analgesics were prescribed every 8 h for 3 days in the form of paracetamol 500 mg. Patients were given a leaflet outlining the usual post-extraction instructions and a 24-h on-call emergency telephone number to contact if any serious bleeding occurred during non-office hours.

Post-extraction sites were monitored to assess the grade of post-operative bleeding immediately after extraction, 5 minutes, 30 minutes, 2hours after extraction and 1^{st} & 7^{th} post-operative day using bleeding index. Pain scores were evaluated using the Visual Analogue Scale (VAS) where 0 means no pain and 10 being the worst pain the patient had ever experienced. Socket healing is assessed

by presence or absence of broken down blood clot, dry socket and inflammation & infection in 7th day. Sutures were removed one week following extraction.

THE POST OPERATIVE EVALUATION WAS DONE CLINICALLY AS FOLLOWS

POSTOPERATIVE BLEEDING

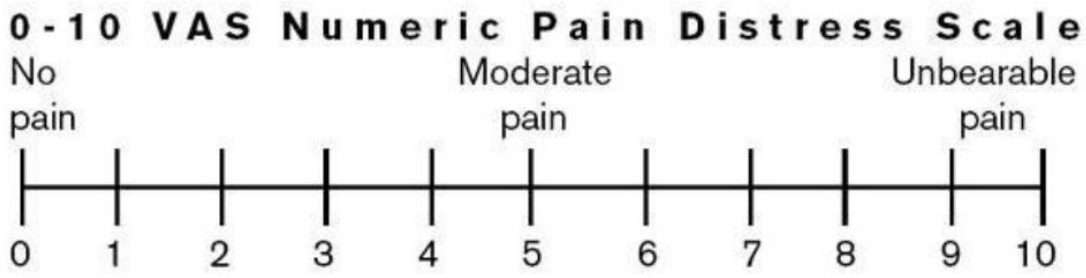
Hemostasis was evaluated after extraction by clinical observation using following bleeding index.

Bleeding was assessed postoperatively by bleeding index [12]:

Grade 0: Very low (almost no bleeding).
Grade 1: Low (slight oozing of blood from the socket which usually stops by its self or after pressure is applied).
Grade 2: Normal. (Clinically significant).
Grade 3: High. (Bleeding occurs after clot has significantly formed).
Grade 4: Very high (excessive bleeding that could not be controlled by local hemostatic agents or stitches).

POST-OPERATIVE PAIN

Pain was evaluated though VAS [10] (visual analogue scale) at first, third and seventh days postoperatively, taking pain scores from 0 to 10. Patients were asked about the pain severity according to VAS as follow:



POSTOPERATIVE HEALING:

Adequate socket healing was evaluated clinically at the seventh postoperative day by following clinical observation:

- Presence or absence of broken down blood clot.
- Presence or absence of sign and symptom of dry socket.
- Presence or absence of inflammation and infection

STATISTICAL ANALYSIS

The information collected regarding all the selected cases was recorded in a Master Chart. Data analysis will be done with the help of computer using **SPSS statistical package- Version 22.**

Using this software range, frequencies, percentages, means, standard deviations, chi square , 't' value and 'p' values were calculated. 't' test was used to test the significance of difference between quantitative variables and Yate's and Fisher's chi square tests for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

Photographs

PHOTOGRAPHS

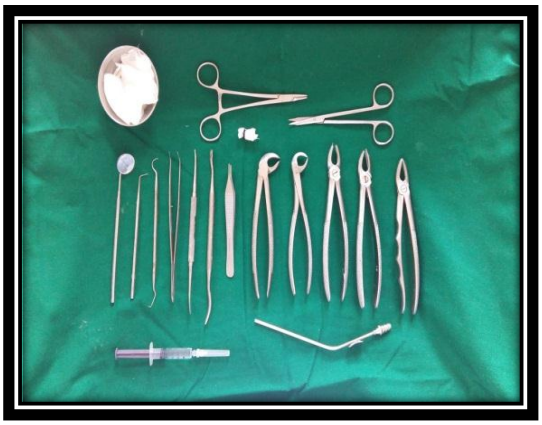


Figure- 3: Armamentarium

Figure- 4: Gelatamp

Figure- 5: Local anaesthesia

Figure- 6: Gelatamp Sponge

Comparison of post operative bleeding index between study group and control group

Study group

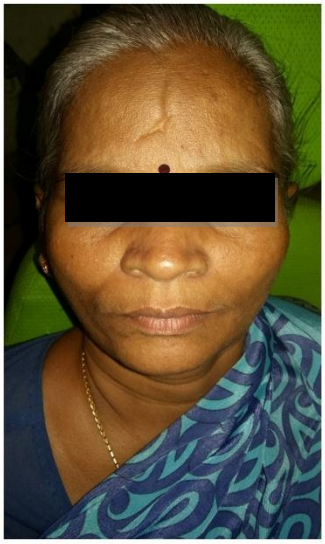


Fig:7.1 Extra oral - Frontal

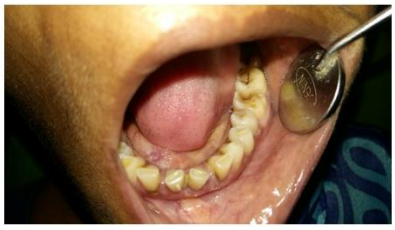


Fig:7.2 Intraoral pre op

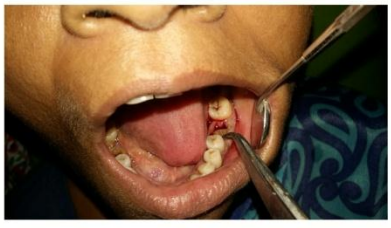


Fig:7.3 Geltamp placement

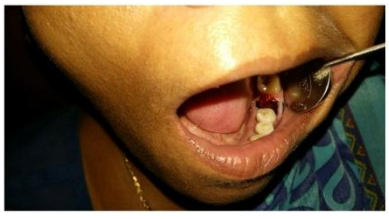


Fig:7.4 Immediately after extraction

Control group

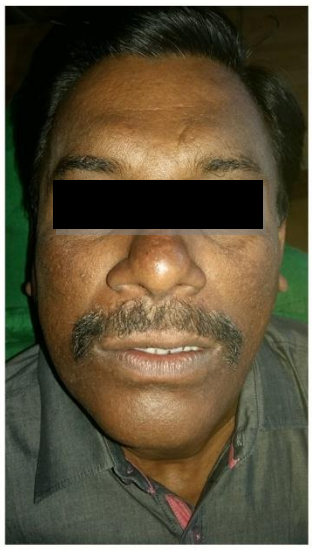


Fig:8.1 Extra oral - Frontal

Fig:8.2 Extraction

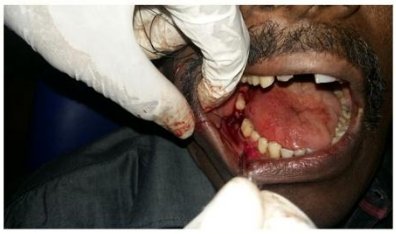


Fig:8.3 Suturing

Fig:8.4 Immediately after extraction

Comparison of post operative bleeding index between study group and control group

Study group

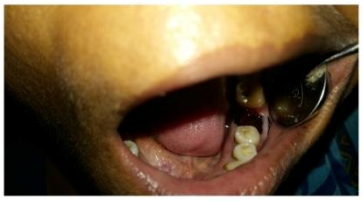
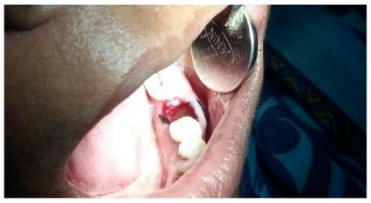


Fig:7.5 Five minutes after extraction



ʒ:7.6 Thirty minutes after extraction

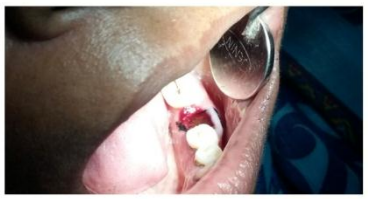


Fig:7.7 Two hours after extraction

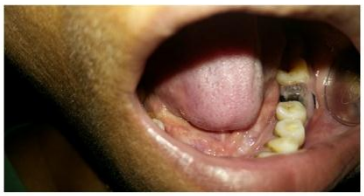


Fig:7.8 First post op day

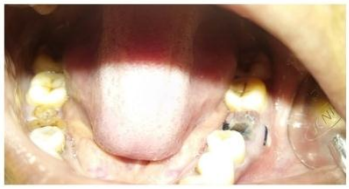


Fig:7.9 Seventh post op day

Control group

Fig:8.5 Five minutes after extraction

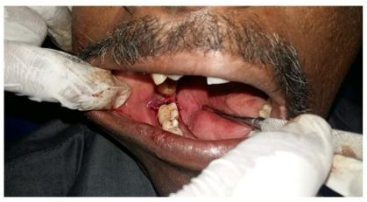


Fig:8.6 Thirty minutes after extraction

Fig:8.7 Two hours after extraction

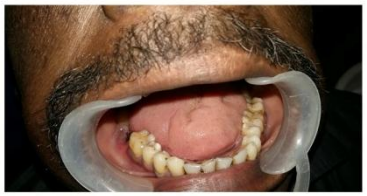


Fig:8.8 First post op day

Fig:8.9 Seventh post op day

Results and Statistics

RESULTS

In this study, 88 patients (age range of all the 88 patients varied from 32 – 62 years old) were divided equally into 2 groups:

Group 1 (study group) consisting of 44 patients which includes 24 males and 20 females. Group 2 (control group) consisting of 44 patients which includes 24 males and 20 females. Table -1 and Table -2 shows that both the study and control groups included 38 molars (maxillary molars- 23 and mandibular molars- 15) and 6 premolars (maxillary premolars – 3 and mandibular premolars – 3) in the present study.

Graph -1 shows 30 patients were on single (aspirin/clopidogrel) and 14 patients were on dual (aspirin and clopidogrel) antiplatelet therapy in both study group and control group respectively.

POST OPERATIVE BLEEDING:

Table 3 shows:

- Immediately after tooth extraction, the bleeding grade was recorded after the placement of gelatamp in study group and after suturing the socket in the control group. The p value of this variable is $p<0.562$ which is found to be statistically not significant.
- After 5 minutes, 30 minutes, 2 hours, first and seventh day postoperative the p value were $p<0.793$, $p<0.682$, no p value, $p<0.296$, no p value respectively. It was found that there were no significant differences between the two groups.

The incidence of postoperative bleeding was higher in the control group (grade 2, 36/44, 81.8 %) than in the study group (grade 2 15/44, 34.1 %) immediately after extraction. The post-operative bleeding after 5 minutes is also found to be higher in control group (grade 1- 31/44, 70.4 %) compared to study group (grade 1 – 12/44, 27.2%) but difference was statistically not significant. In 30 minutes after extraction the bleeding was very less in study group (grade 1- 1/44, 2.3 %) when compared to control group.

POST-OPERATIVE PAIN:

Table 4 shows the comparison between the two groups regarding visual analogue scale at different periods of follow up. From this table, it was found that the p value of first and third post-operative day were $p<0.079$, $p<0.194$ respectively, which was statistically not significant. The p value of the 7^{th} post-operative day was $p<0.011$ which was found to be statistically significant.

The post-operative pain scores were less in study group when compared to control group.

In 1^{st} post-operative day study group has mild to moderate pain (score 2 = 21/44 and score 3 = 23/44) when compared to control group which had moderate to severe pain (score 4 = 2/44. Score 5 = 22/44, score 6 = 15/44, score 7 = 4/44, score 8 = 1/44).

In 3^{rd} post-operative day study group experiences a range of no pain to mild pain (score 0 = 1/44, score 1=21/44, score 2 = 9/44) when compared to

control group which had moderate pain (score 4 = 10/44, score 5 = 28/44, score 6 = 5/44, score 7 = 1/44)

In 7th post-operative day study group has almost no pain (score 0 = 42/44, score 1 = 2/44) when compared to control group which had mild to moderate pain (score 3 = 8/44, score 4 = 28/44, score 5 = 7/44, score 6 = 1/44)

POSTOPERATIVE HEALING:

Postoperative Healing on seventh postoperative Day: Adequate socket healing was detected in all patients of both groups without any sign or symptoms of dry socket, broken down blood clot, and inflammation & infection.

Table-1 shows number teeth extracted in the study group

Tooth	Maxillary	Mandible	Total
Molar	23	15	38
Premolar	3	3	6
Total number of patients in study group			44

Table-2 shows number of teeth extracted in the control group

Tooth	Maxillary	Mandible	Total
Molar	23	15	38
Premolar	3	3	6
Total number of patients in control group			44

Table-3: Comparison of postoperative bleeding index between study and control groups

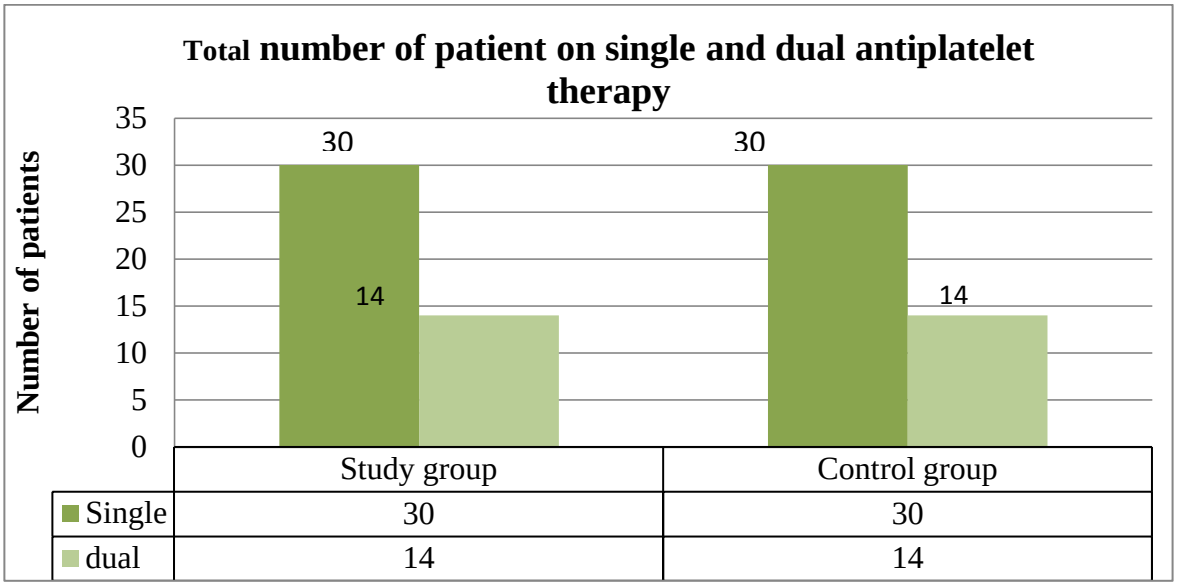
	Immediate		5 mins		30 mins		2 hrs		Day 1		Day 7	
STUDY GROUP	No	%	No	%	No	%	No	%	No	%	No	%
Grade 0	0	0	32	72.7	43	97.7	44	100	42	95.5	44	100
Grade 1	29	65.9	12	27.2	1	2.3	0	0	2	4.5	0	0
Grade 2	15	34.1	0	0	0	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0	0	0	0	0
CONTROL GROUP												
Grade 0	0	0	8	18.1	30	68.1	44	100	37	84.1	42	95.5
Grade 1	8	18.1	31	70.4	14	31.8	0	0	7	15.9	2	4.5
Grade 2	36	81.8	5	11.4	0	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0	0	0	0	0
p VALUE	0.562		0.793		0.682		-		0.296		-	

Table 4: Comparison of post-operative pain between study and control group

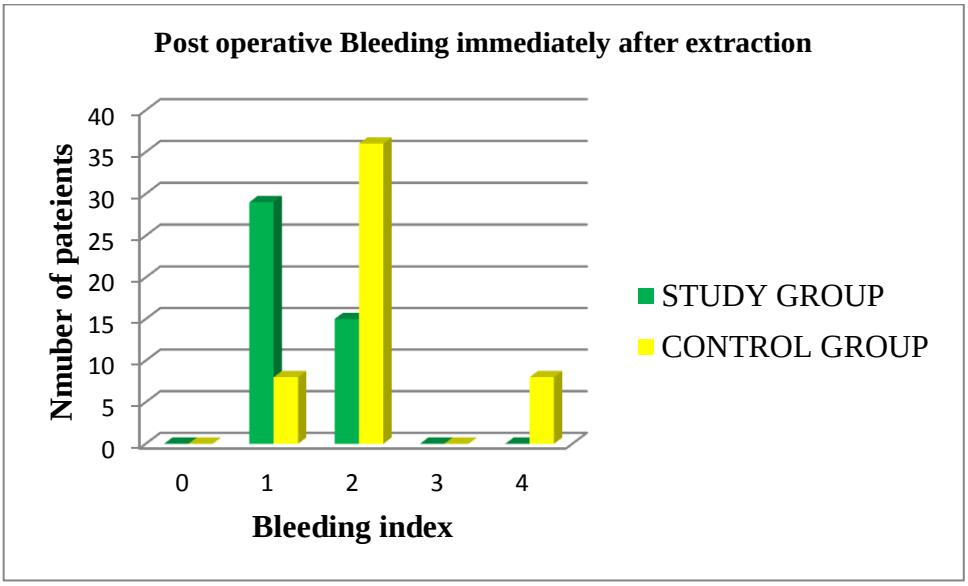
	1st	3rd	7th
STUDY GROUP			
Score 0	0	14	42
Score 1	0	21	2
Score 2	21	9	0
Score 3	23	0	0
Score 4	0	0	0
Score 5	0	0	0
Score 6	0	0	0
Score 7	0	0	0
Score 8	0	0	0
Score 9	0	0	0
Score 10	0	0	0
CONTROL GROUP			
Score 0	0	0	0
Score 1	0	0	0
Score 2	0	0	0
Score 3	0	0	8
Score 4	2	10	28
Score 5	22	28	7
Score 6	15	5	1
Score 7	4	1	0
Score 8	1	0	0
Score 9	0	0	0
Score 10	0	0	0
p value	0.079	0.194	0.011

GRAPH-1

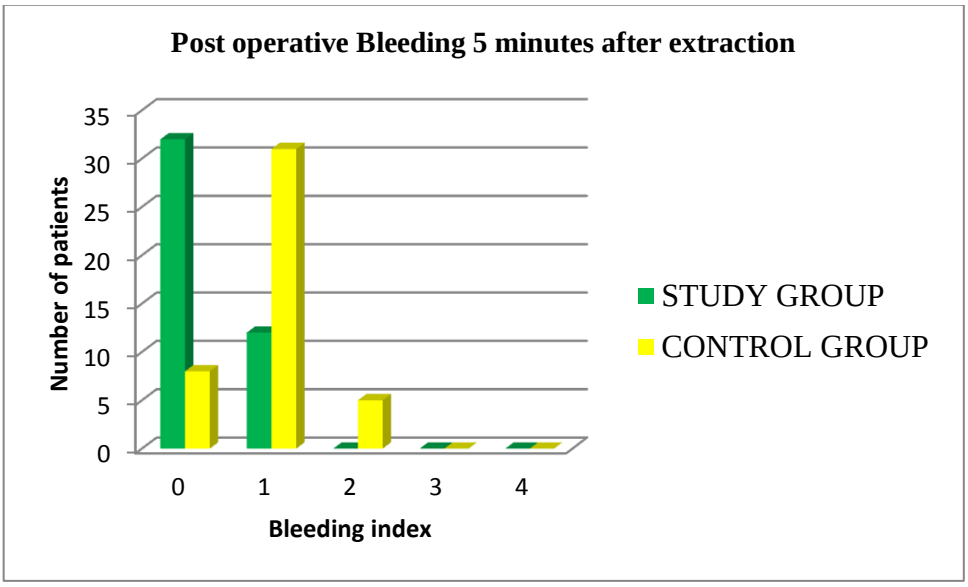
Number of patients on single and dual antiplatelet therapy in study and control groups



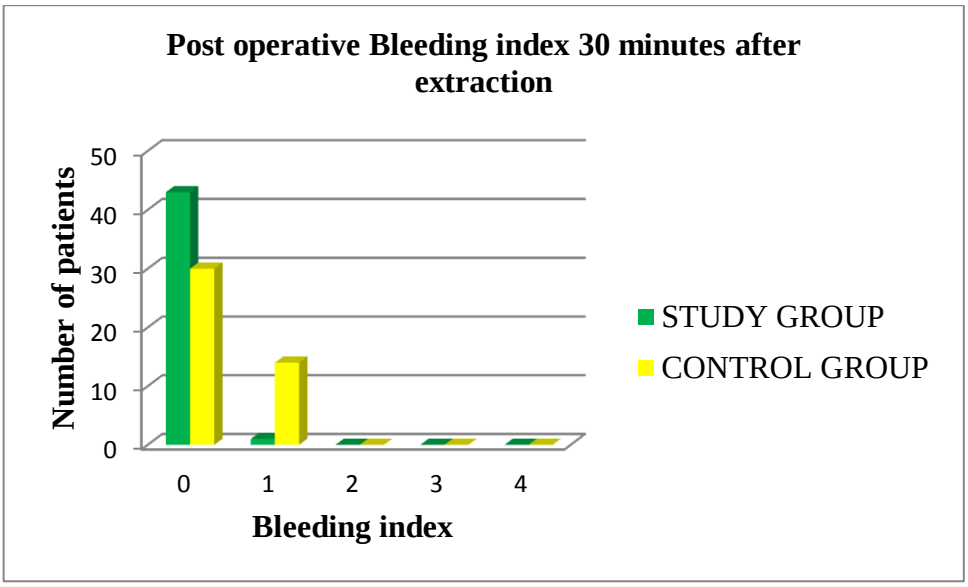
GRAPH-2: Comparison of post-operative bleeding index immediately after extraction between study and control groups



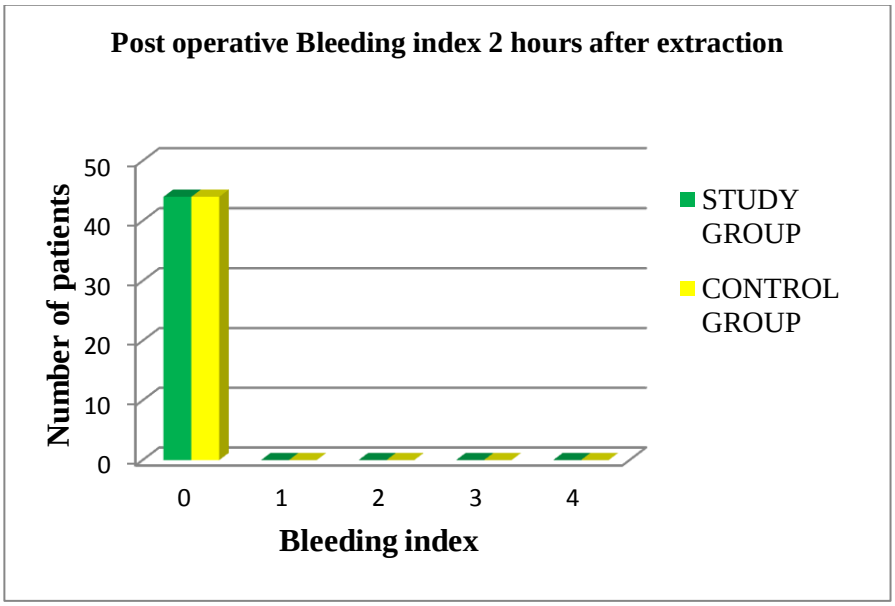
GRAPH-3: Comparison of post-operative bleeding index 5 minutes after extraction between study and control groups



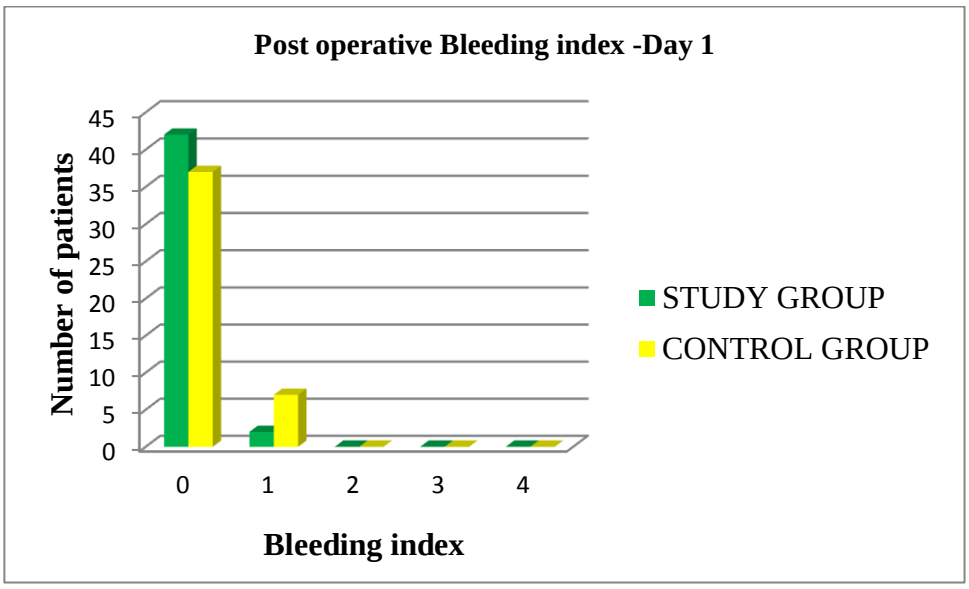
GRAPH-4: Comparison of post-operative bleeding index 30 minutes after extraction between study and control groups



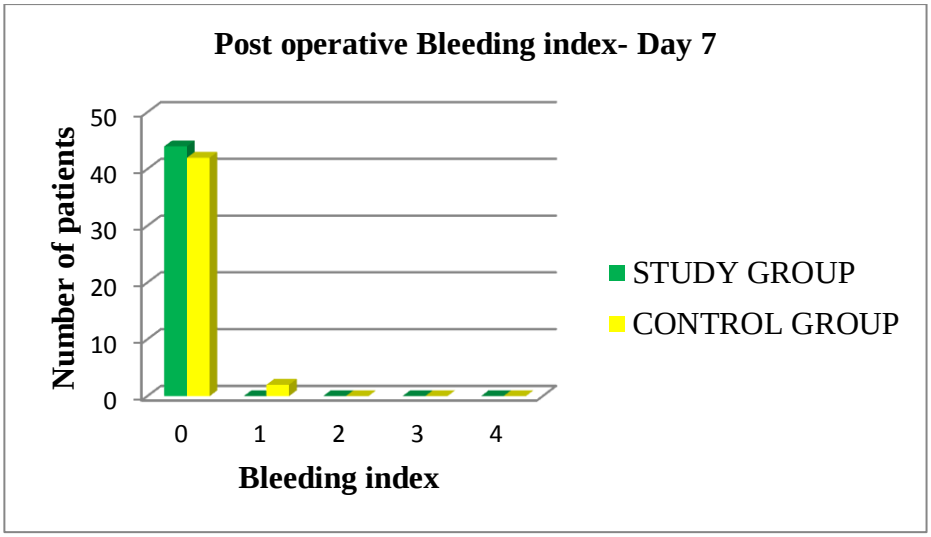
GRAPH-5: Comparison of post-operative bleeding index 2 hours after extraction between study and control groups



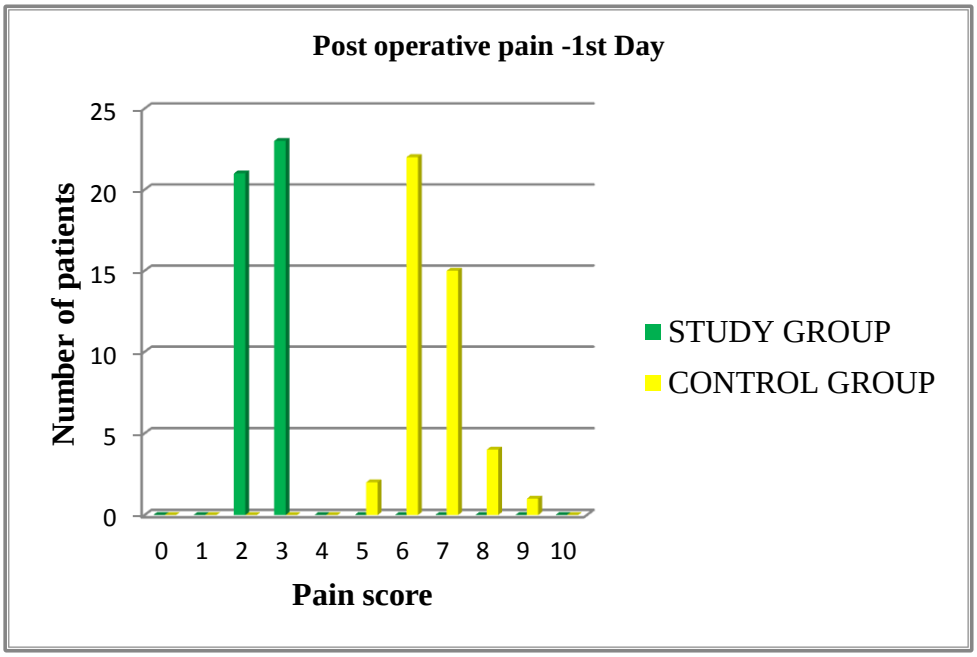
GRAPH-6: Comparison of post-operative bleeding index on day 1 after extraction between study and control groups



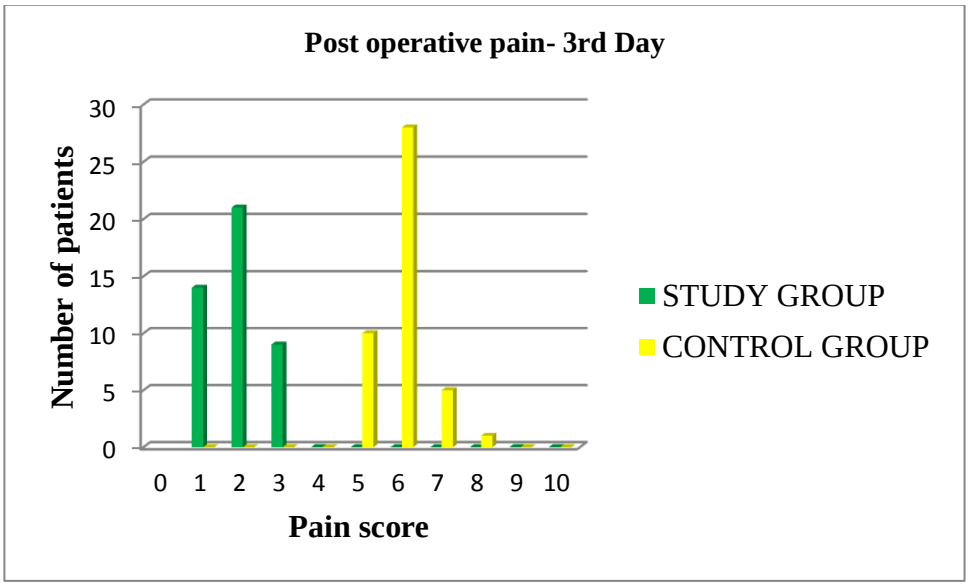
GRAPH-7: Comparison of post-operative bleeding index on day 7 after extraction between study and control groups



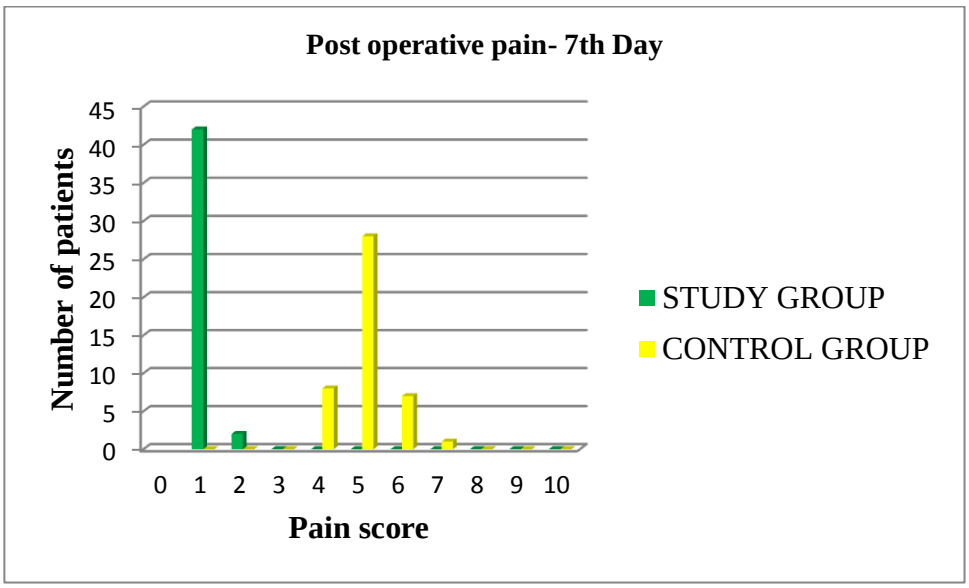
GRAPH- 8: Comparison of post-operative pain on 1st day after extraction between study and control groups



GRAPH-9: Comparison of post-operative pain on 3rd day after extraction between study and control groups



GRAPH- 10: Comparison of post-operative pain on 7th day after extraction between study and control groups



Discussion

DISCUSSION

Medical advances have increases the life expectancy and prevalence of chronic illness among the human population. Conditions that become more prevalent with increase in age are MI (myocardial infarction), arterial thrombosis, ischemic heart disease, both stable and unstable angina, coronary artery bypass and placement of a stent, transient ischemic attacks (ischemic stroke), peripheral arterial disease, atrial fibrillation etc. Medical management for these conditions include administration of antiplatelet agents such as aspirin, clopidogrel, ticlopidine, cilostazol, dypyridamole, ticagrelor, prasugrel, abciximab, tirofiban, ebtifibatide and anticoagulants such as warfarin, heparin, LMWH etc. [74]

Platelets involves in formation of prothrombin activator through intrinsic pathway which is responsible for onset of blood clotting. Thrombosthenin a contractile protein, present in platelets, plays an important role in clot retraction. Resting platelets have specific receptors for ligands such as epinephrine, thrombin, serotonin, collagen, adenosine diphosphate (ADP), and thromboxane A2 (TXA2) which involves in platelet activation. When activated, intracellular calcium levels gets elevated and the platelet expresses glycoprotein (GP) IIb/IIIa receptors that bind to strands of fibrinogen. This results in platelet aggregation. (Figure- 9)

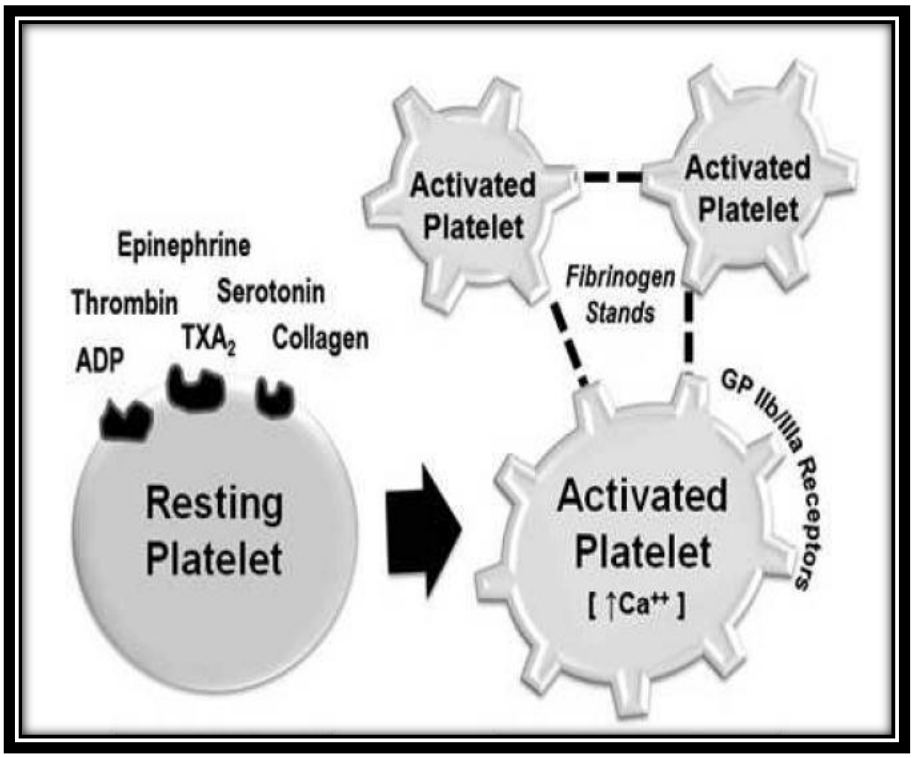


FIGURE -9: Platelet aggregation and actions of antiplatelet drugs

Antiplatelet drugs inhibit aggregation by targeting specific receptor sites and also by inhibiting the synthesis of substances that involves in platelet aggregation. The newer antiplatelet drugs were more potent in their mechanism of action. (Table-6)

TABLE-6

ANTIPLATELET DRUG	**MECHANISM OF ACTION**
Aspirin	Inhibits TXA_2 Synthesis
Clopidogrel Prasugrel Ticagrelor	Inhibit ADP Receptor Activation
Dipyridamole	Lowers ca^{++} by

Cilostazol	elevating cAMP
Abciximab Tirofiban Eptifibatide	Block GP IIb/IIIa Receptor

Aspirin, acetylsalicylic acid (ASA) is a non-steroidal anti-inflammatory drug that exhibits analgesic, antipyretic, anti-inflammatory, and antiplatelet properties. It is the most commonly used drug in the prevention and treatment of thromboembolic diseases and also as used as a powerful secondary prevention agent in reducing the risk of myocardial infarction and ischemic stroke by up to 25% in patients diagnosed with cardiovascular disease . [7]

Its mechanism of action involves an irreversible inhibition of the activity of cyclooxygenase-1 (COX-1) and modification of the enzymatic activity of COX-2. COX is an enzyme responsible for the conversion of arachidonic acid to prostaglandins, prostacyclin, and thromboxane A2. Thromboxane-A2, a strong platelet agonist, is a specific eicosanoid lipid found in platelets important in promoting platelet aggregation over-damaged endothelium in blood vessels.[3] Complete reversal of antiplatelet activity occur approximately 2 weeks after cessation of therapy.[40,61]

Clopidogrel is an antiplatelet drug with a mechanism of action causing irreversible inhibition of an ADP (adenosine diphosphate) receptor, which is important in promoting platelet aggregation and cross-linking of platelets by fibrin. It is a prodrug and gets activated in the liver by cytochrome P450 enzymes. Action starts within 2 hours of ingestion, and antiplatelet effect lasts for lifetime of the platelets. [41]

Platelet activation occurs with binding of adenosine diphosphate (ADP) to the ADP (P2Y12) receptor. Thienopyridines (clopidogrel, ticlopidine, and prasugrel) selectively and irreversibly inhibit the platelet ADP receptor. Glycoprotein (GP) IIb-IIIa (which is an integrin receptor for fibrinogen and von Willebrand factor) inhibitors block platelet aggregation, whereas aspirin inhibits cyclo-oxygenase (COX) that blocks the formation of thromboxane A2 (TXA2).(figure-10)

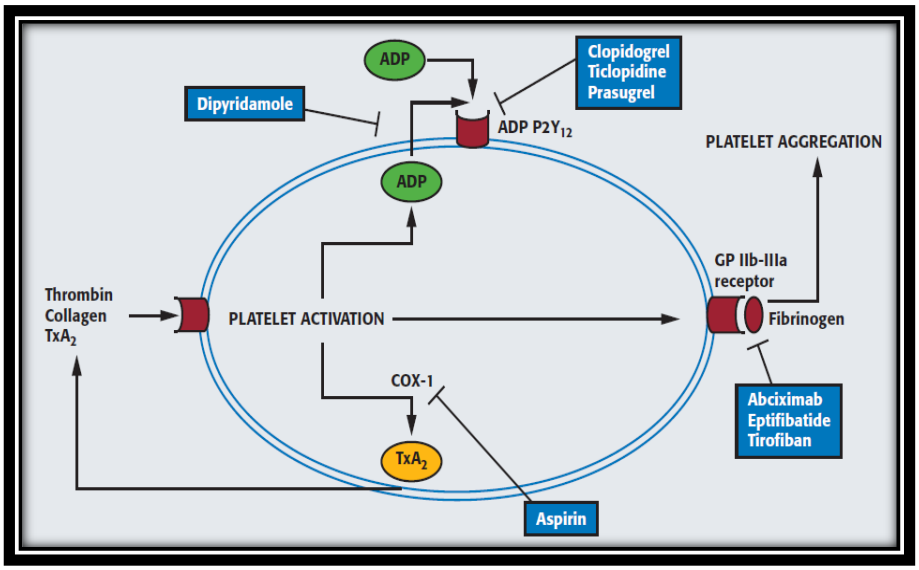


FIGURE – 10: Mechanism of action of antiplatelet drugs

Antiplatelet drugs can increase the gastrointestinal bleeding, haemorrhagic stroke, and risk of post-operative bleeding. In patients with dual antiplatelet drugs, the risk is higher due to their synergistic effect. [67]

Exodontia is the simplest and commonest procedure done in oral and maxillofacial surgery. Some authors advices the patients to stop taking aspirin before tooth extraction for fear of excess bleeding. Lemkin et al. in 1974 explained bleeding after extraction continuing aspirin therapy which required

platelet transfusion for correction so they suggested to stop the aspirin therapy prior to extraction.[17] McGaul[18] and Daniel [28]. stated that continuing aspirin causes post-operative bleeding so they also advised discontinuation for 7-10 days before extraction i.e., lifespan of a platelet. Sonksen [22] (1999) suggested to stop 48 hours prior to the extraction procedure which contrary to McGual[18] and Daniel [28]. Scully[30] suggested cessation of aspirin prior to extraction if the patient is taking more than 100 mg of aspirin per day.

Vaklavick explained that there was a 3 fold increase in life threating cerebral and cardiac thromboembolic events after the cessation of aspirin.[55] **Schreuder** reviewed the risk of thromboembolic events outweighs the risk of bleeding episodes after the antithrombotic medication withdrawal. [71]

Scientific evidences showed that stopping antiplatelet therapy is associated with a progressive recovery of platelet function and with a potential risk of rebound of thromboembolic vascular events due to excessive thromboxane-A2 activity and decreased fibrinolytic activity within 8 to 25 days.[52] .According to J. Lee from their study, platelets regains it action within 96 hours in which the platelet recovery time period is even more earlier when compared to the previous studies. [66]

Wahl and Howell were one of the authors to conclude that the risk of haemorrhage after extraction may be greatly outweighed by the risk of thromboembolism after withdrawal of anti-thrombotic therapy. [75]

Ferrari and Collet explained that the withdrawal of aspirin increases the platelet reactivity thus increases the incidence of coronary thrombosis. The mean delay in stroke and MI after aspirin cessation is approximately 10 days

(range 4–17 days), which is relative to the time interval of the platelet rebound effect .[8]

Practitioners used PT, PTT, BT, and CT as investigations for evaluating the coagulation profile. But in 1983 WHO recommended INR (International normalized ratio) to assess the accurate value of anticoagulation levels. The INR is calculated from the ratio of patient's PT and control PT, raised to the power of (ISI) international sensitivity index (PT=Patient PT/ Control PT) [ISI]. Normal range and therapeutic range for anticoagulation were given as 0.8 to 1.2 and 2.0 to 4.0 respectively. [41]

O. Ross Bierne suggested extraction procedures can be done safely with INR 2 to 4 without interrupting the antithrombotic therapy in low risk individuals. [34] Afriaman, Al- Mubarak, Morimoto recommended to do extraction with INR less than 3.0 without stopping antithrombotic therapy.[38, 39, 47]

Alridge et al 2010 explained not to stop oral anticoagulant medication for extraction, provided that the INR should be below 4.[53] Broekema et al (2014) suggested that extraction of tooth was safe in patients being treated with anticoagulants under INR range of 1.8 to 3.5.[64]

Bajkin et al (2015) from their study concluded that extraction can be done safely without interruption of treatment in patients taking single or dual antiplatelet drugs under INR range of about 3.5 to 4.2. [67]

The American College of Chest Physicians recommends continuing the antiplatelet drugs perioperatively in patients who require surgical procedures within 6 weeks of placement of a metal stent or 6 months of

placement of a drug-eluting stent. Acute myocardial infarction has followed in such patients after withdrawal of antiplatelet therapy. [76,77]

Verma and Hanken concluded that there is no need to stop the antiplatelet dose of aspirin prior to tooth extraction as there was no significant incidence of post-operative bleeding present in their patients.[63,68]

Nooh in his study concluded that subjects who received 81 mg aspirin daily could undergo dental extraction without bleeding risks.51 van Diermen, Girotra, Napenas suggest not to interrupt dual antiplatelet therapy for extraction procedures.[4,61,62]

The American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Physicians, American College of Surgeons, American Dental Association, National Health Service, and numerous authors recommend maintaining the antiplatelet therapy in oral surgical procedures and applying the necessary local haemostatic measures to control the haemorrhage.

Several topical hemostatic agents are currently available for use in oral and maxillofacial surgery. The ideal hemostatic agent should be effective, safe to use within the body, and affordable. They can be divided into two categories: active and passive hemostatic agents. Passive hemostatic agents provide a framework where platelets can aggregate so that a stable clot can form. Active hemostatic agents have biologic activity and directly participate in the coagulation cascade to induce a clot. [13, 74]

Table- 7 shows the available hemostatic agents [4, 10, 13, 21, 43, 44, 47]

Hemostatic agents	**Structure and uses**
Cellulose (Surgicel, Ethicon)	Oxidized cellulose provides an absorbable physical matrix for clotting initiation.
Gelatin Foams (Gelfoam	Gelatin foams provide a clotting framework and effectively arrest small-vessel bleeding. It is manufactured as a film, sponge, or power.
HemCon Dental Dressing	This substance is made from chitosan, which is an N-acetyl glucosamine polysaccharide derived from the chitin in shrimp shells. It is in a sponge form and is hemostatic and also bacteriostatic
Microfibrillar Collagen	Microfibrillar collagen is a hemostatic agent that attracts platelets that adhere to its fibrils and undergo activation. This triggers aggregation of the platelets into thrombi in the interstices of the fibrous mass, initiating the formation of a

	physiologic platelet plug.
Hemostatic Solutions	Styptics are locally applied agents that stop bleeding by contracting tissue to seal injured blood vessels. Example- Aluminum solutions
Tannic Acid	Tannic acid is a commercial compound that is similar to the plant polyphenol tannin, which is a well-established hemostatic agent that effectively stops bleeding from mucous membranes via vasoconstriction
Tranexamic Acid 4.8% Oral Rinse	Tranexamic acid 4.8% oral rinse is an antifibrinolytic agent that stabilizes clots and facilitates clot formation by competitively inhibiting plasminogen, the enzyme responsible for activating plasmin
Fibrin Glue	Made up of fibrinogen and thrombin, fibrin glue makes a fibrin clot where applied to arrest bleeding
Gelatamp	95 % gelfoam and 5 % colloidal

	silver ion

Blinder compared post-operative hemostasis in patients under antithrombotic medications after extraction with gelatine sponge and suture in one group, along with tranexamic mouth wash with one group and fibrin glue with another group and found significant difference in hemostasis.[21]

Gelfoam is a porous, pliable, absorbable gelatin sponge that is prepared from purified pork skin gelatin. This product has properties that allow it to absorb about 40 times its weight in blood, and it can expand to 200% of its initial volume. When applied to a site, Gelfoam provides a mechanical matrix, which facilitates clotting. The spongy physical properties of the gelatin sponge hasten clot formation and provide structural support to the forming clot. Gelfoam has very little tissue reaction and liquefies in the oral cavity within a week, fully absorbing within 4 to 6 weeks. Although it is not necessary, thrombin can be applied to the Gelfoam before use to aid in hemostasis. [13]

Herman (2006), Cai (2005), Ion Chopra (2007), Marx et al (2014), Abbound (2014), Yuliang Dong et al (2016) described that silver dressings are used in the treatment of various wounds including ulcers, burns, and surgical sites. The pain-relieving effects of silver dressings is anecdotal , but it appears to occur in wide spectrum of clinical situations, including dental pain, skin graft donor sites, thermal burns, and anal fistulae. Silver ion decreases inflammation due its antibacterial effect which consequently decreases pain perception and promotes wound healing. [14, 15, 16, 37, 44]

Gelatamp was made up of 95 % gelatine sponge and 5 % colloidal silver ion .Gelatine sponge allow it to hold blood as much as 55-75 times than

its weight and provides a stable scaffold for clot formation prevents tissue collapse and maintains the space for bone healing. Various studies explained that colloidal silver ion was found to have increased antimicrobial effect and also describes there was a decrease in the frequency of changing silver wound dressing which decreases the pain in the wound and it also decrease the proinflammatory cytokines. Thus Gelatamp was considered to promote clot formation, provides favourable environment for extracted socket healing and decreases pain perception post operatively.[12, 44, 73]

DISCUSSION OF RESULTS

In this present study extraction was done in patients with INR $\leq$ 3.5 which is similar to Broekema.[64] The INR range in this present study was also agreed with Afriaman[38], Al- Mubarak[39], Morimoto[47] and O. Ross Bierne [34].

Sonksen[22] and Little[29] claimed that there are no significant post-operative bleedings after dental extractions as long as prolongation in bleeding time remains within acceptable limit (bleeding time up to 20 minutes) preoperatively. These studies were similar to this present study because no excessive bleeding was recorded in both the groups in 30 minutes. The present study results were also appear to concur with Krishnan[46] where they achieved haemostasis in 30 minutes after extraction continuing antiplatelet therapy.

In this present study the p value immediately, 5 minutes, 30 minutes, 1st day and 7th day after extraction were 0.562, 0.793, 0.682, no p value, 0.296, no p value, respectively. This results was not similar when compared with maani[12], as their study reported p value of 0.34, 0.37, 0.47, nil, 0.60, 1.0

and also maani[12] compared the study group with patients who stopped anticoagulant prior to the extraction which is contrary to this present study.

Immediately after extraction, the present study reported 65.9 % of grade 1 bleeding and 34.1 % of grade 2 bleeding which is not similar to maani[12] as they reported 8 % of grade 1 bleeding index and 92 % of grade 2 bleeding index of the same. Thus the present study has got better results immediately after extraction when compared to maani[12].

Five minutes after extraction, the present study reported 72.7 % of grade 0 and 27.2 % of grade 1 bleeding index. Maani[12] reported near equal results compared to the present study. They reported 76 % of grade 0 and 24 % of grade 1 bleeding index.

In thirty minutes, 2 hours, 1 day and 7 days after extraction, the present study reported 97.7 %, 100 %, 95.5 %, and 100 % of grade 0 bleeding index respectively. Which also similar to maani[12] where they reported 100 %, 100 %, 96 %, and 100 % of grade 0 bleeding index for the same. Thus these results were also similar compared to the present study.

Grade 2 bleeding index were reported in 34 % of cases in study group and 81% of cases in control immediately after extraction, in 2 hours after extraction grade 0 were reported in 100 % of cases in both study group and control group, in 1st post-operative day 4.5 % and 15.9 % of grade 1 bleeding index were reported in study and control groups respectively and 4.5 % of grade 1 bleeding index as reported in control group on 7th post-operative day which were managed by pressure gauze itself, but this didn't influence the patient morbidity and mortality. The risk of bleeding under continued aspirin use to increase by 1.5-fold, but that this can be controlled with Gelatamp to

obtain earlier haemostasis when compared to control group. No life-threatening complications were reported and no transfusions were required

Hence, there is no need to expose the patient to the risk of thromboembolism or cardiovascular events by discontinuing antiplatelet therapy before extraction.

Most studies fail to evaluate the intensity of pain and wound healing after extraction and none have yet compared the patient's post extraction pain between Gelatamp and non Gelatamp group. To evaluate the pain felt by patients, the current study used a VAS, which is the most widely used pain measurement instrument in many centres. The VAS is a simple, solid, sensitive, and reproducible tool for assessing pain in a given patient at different points in time.[10]

Study (gelatamp dental dressing) group is considered to offer advantages over the control- non Gelatamp group (only suture). Only one comparison has been made of (study group) gelatamp placement in patient continuing anticoagulant therapy versus (control group) normal suture after extraction in patient who stopped anticoagulant therapy 3 days prior to the procedure. Therefore, the present study also sought to explore patient pain/discomfort, using a subjective visual analogue scale (VAS) and wound healing to compare between study group and control group.

The results of this present study shows that the there is a significant decrease in the VAS score of study group when compared to control group with the difference being highest in the 7^{th} post-operative day in both clinically

and statistically. Also the results of this present study shows that the number of patients who felt no pain were also higher in the study group.

In the present study the p value for pain in 1st, 3rd, 7th post-operative day were p<0.079, p<0.194, p<0.011 respectively, which was found to be not similar when compared to maani[12] in which they reported p<0.74 for the 1st day, p<1.0 for the 3rd day and no p value for the 7th day.

The pain perception in the study group of the present were found to be mild to moderate in 1st , no pain to mild pain in 3rd and almost no pain in 7th post-operative days. These results were appeared to concur to the maani[12].

In the present study the adequate socket healing were found to be present without any incidence of broken down blood clot, dry socket and inflammation/infection which were also found to be similar to study done by maani and also with the literatures.[12,14,15,16,40,44]

The limitation of this present study is the smaller sample size. Patients on Warfarin, heparin and newer antiplatelet drugs are not included in this study. Randomized controlled trials with larger sample sizes are required to confirm the findings of this study.

Within the limitations of this study, it can be concluded that Gelatamp dental dressing is an effective alternative haemostatic agent with better pain control and wound healing potential after extraction in patients continuing aspirin and/ or clopidogrel therapy provided that the INR range should be ≤ 3.5.

Conclusions

CONCLUSION

- Antiplatelet therapy need not be altered or stopped before extraction within the therapeutic range of INR ≤ 3.5 .
- The post-extraction haemostasis can be effectively achieved by Gelatamp dental dressing.
- Adequate socket healing and decrease in post extraction pain can be achieved with Gelatamp dental dressing.
- The risk of haemorrhage after extraction may be greatly outweighed by the risk of thromboembolism after withdrawal of anti-thrombotic therapy

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Annexures

List of Annexures

S.NO	ANNEXURES
1.	Ethical approval by institutional review board – Best Dental Science College
2.	Information sheet and Informed consent (English and Tamil)
3.	Case sheet Proforma

BEST DENTAL SCIENCE COLLEGE

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ANNEXURE-I

Ref:UT:BDSC:IRB-EC/2014 Date:18.11.2014

From

Institutional Review Board-Ethical committee,
Best dental science college,
Madurai.

To

The Controller of Examinations,
The Tamil Nadu DR.MGR Medical University,
No. 69, Anna salai,
Guindy,
Chennai-600 032

Sir/Madam

The Dissertation topic titled "EVALUATION OF POST EXTRACTION HEMOSTASIS IN CARDIAC PATIENTS WITH GELATAMP DENTAL DRESSING WITHOUT STOPPING ASPIRIN AND CLOPIDOGREL THERAPY" submitted by Dr.MURALIDHARAN.G postgraduate student has been approved by Institutional Review Board of Best Dental Science College on 18.11.2014.

DR.K.S PREM KUMAR.M.D.S.,
VICE PRINCIPAL
MEMBER SECRETARY
INSTITUTIONAL REVIEW BOARD-ETHICAL COMMITTEE
BEST DENTAL SCIENCE COLLEGE
MADURAI

DR.PURUSHOTHAM MANVI.,M.D.S.,
PRINCIPAL
BEST DENTAL SCIENCE COLLEGE
MADURAI

INFORMATION SHEET FOR THOSE WHO PLAN TO PARTICIPATE IN THE RESEARCH PROJECT

(Form 1)

NAME OF THE RESEARCH PROJECT: EVALUATION OF POST EXTRACTION HEMOSTASIS IN CARDIAC PATIENTS WITH GELATAMP DENTAL DRESSING WITHOUT STOPPING ASPIRIN AND CLOPIDOGREL THERAPY.

We welcome you and thank you for having accepted our request to consider whether you/ your child/ your ward can participate in our study. This sheet contains the details of the study; the possible risks, discomforts and benefits for the participants. You can read and understand by yourself; if you wish, we are ready to read and explain the same to you. If you do not understand anything or if you want any more details we are ready to provide the details.

Information to the participants:

What is the purpose of the study?

- To evaluate the post extraction hemostasis in cardiac paients without stopping aspirin and cloidogrel therapy.
- To decrease the post extraction pain.
- To achieve adequate post extraction socket healing.

Who / where this study is being conducted?

This study is being conducted by Dr.G.Muralidharan Post Graduate Dental student belonging to department of Oral and Maxillofacial Surgery under the guidance of Prof.Dr. K. Prabhu Sankar., M.D.S. Head of the Department.

Why am I being considered as one of the participant?

Because of the presence of poor prognostic teeth.

Should I definitely have to take part in this study?

No. If you do not wish to participate you will not be included in this study. Also the dental treatments will continue without any prejudice.

If participating in this study, what are the responsibilities of the participant?

The participant may have to follow some simple rules. They are: keep cotton in the extracted tooth socket for half an hour. Do not spit for 24 hours. Do not prick the socket with sharp objects. Take soft foods for 3 days.

Are there any benefits for the participants/public?

Yes. Because the post extraction bleeding time can be decreased, post extraction pain can be decreased and adequate post extraction wound healing can be achieved .

Will there be any discomfort / risks to the participants?

- No risks. But some discomforts may be there
- Research discomfort: Minimal Allergy/ bleeding which can be treated with emergency drugs in the department.
- Procedural risk: bleeding, pain, headache, dizziness and nausea.

Will the participant be paid for the study?

No. The participant will not be paid.

While participating in this study, will the personal details of the participant be kept confidential?

Yes, confidentiality will be maintained.

Will the participant be informed of this study's results and findings?

Yes, if needed, the participant can get the details from us.

Can the participant withdraw from this study at any time during the study period?

Yes. The participant can withdraw at any time during the study period.

Name, details and signature of the PG

Dr.G. Muralidharan

Post Graduate Trainee.

Department of Oral and Maxillofacial Surgery,

Best Dental Science College.

INFORMED CONSENT

Form for Getting Informed Consent for those Participating in the Research Project

(Form 2)

NAME OF THE RESEARCH PROJECT: EVALUATION OF POST EXTRACTION HEMOSTASIS IN CARDIAC PATIENTS WITH GELATAMP DENTAL DRESSING WITHOUT STOPPING ASPIRIN AND CLOPIDOGREL THERAPY.

I, the participant/ parent/ guardian,

……..……

……have been informed about the details of the study in my own language.

I, the participant/ parent/ guardian, have understood the details about the study.

I, the participant/ parent/ guardian, know the possible risks and benefits for me/ my child/ my ward, by taking part in the study.

I, the participant/ parent/ guardian understand that I can withdraw from the study at any point of time and even then, I/ my child/ my ward will continue to get the medical treatment as usual.

I, the participant/ parent/ guardian understand that I/ my child/ my ward will not get any payment for taking part in this study.

I, the participant/ parent/ guardian will not object if the results of this study are getting published in any medical journals, provided my/ my child's/ my ward's personal identity is not reviewed.

I know what I am/ my child is / my ward is supposed to do by taking part in this study and I, the participant/ parent/ guardian assure that full co-operation will be given for this study.

Signature/Thumb impression of the participant / parent/ guardian

(Name/Address)

……

……

…….

Signature/Thumb impression of the witness

(Name/Address)

……

……

…….

Name & Signature of the investigator

…….

…….

ஆராய்ச்சியின் விளக்கம்

(படிவம் 1)

ஆராய்ச்சியின்பெயர்: ஆஸ்பிரின் மற்றும் கிலோபிடோ஺ரேல் மருந்துகளை உட்க்கொள்ளும் இதயநோயாளிகளுக்கு பல் எடுத்த பின்பு வரும் இரத்த கசிவை ஜெலாட்டம்ப் மூலம் நிருத்துதல்

வணக்கம். இந்த ஆராய்ச்சியில் பங்கேற்க உங்கள் சம்மதத்தை தெரிவிக்குமாறு நாங்கள் விடுத்த வேண்டுகோளை ஏற்று கொண்டமைக்கு நன்றி. இந்த ஆராய்ச்சி தொடர்பான தகவல்கள், இதில் பங்குபெறுவதினால் உங்களுக்கு ஏற்படக்கூடிய அசௌகரியங்கள், பாதிப்புகள் மற்றும் நன்மைகள் அனைத்தும் இப்படிவத்தில் கொடுக்கபட்டிருக்கின்றன. இதை நீங்களாகவே படித்து தெரிந்து கொள்ளளலாம். அல்லது நீங்கள் விருப்பப்பட்டால் நாங்கள் படித்துக் காட்டி புரியும்படி சொல்வதற்கு தயாராக இருக்கின்றோம். ஏதேனும் புரியவில்லை என்றாலும் அல்லது கூடுதல் தகவல்கள் தேவையென்றாலும், நாங்கள் உங்களுக்கு உதவதயாரக இருக்கின்றோம்.

1. **இந்த ஆராய்ச்சியின் நோக்கம் என்ன?**
   பல் எடுத்த பின்பு வரும் இரத்த கசிவை விரைவில் நிறுத்துவதற்கு, வலி குறைவதற்கு மற்றும் காயம் விரைந்து குணமடைவதற்கு

2. **இந்த ஆராய்ச்சி எங்கு மற்றும் யாரால் செய்யப்படுகிறது?**
   பெஸ்ட் பல் மருத்துவக்கல்லூரி மற்றும் மருத்துவமனையில்,
   பல் மற்றும் முக அறுவை சிகிச்சை பிரிவில், பட்டமேற்படிப்பு படிக்கும் டாக்டர் கு. முரளிதரன் என்பவர் பேராசிரியர் டாக்டர் பிரபு ஷங்கர் என்கின்ற பல் மருத்துவ மேலதிகாரியின் கண்காணிப்பில் இந்த ஆராய்ச்சியை செய்கின்றார்.

3. **இந்த ஆராய்ச்சியில் பங்கு பெறுவதற்கு என்னை தேர்ந்தெடுக்க காரணமென்ன?**

இந்த ஆராய்ச்சியில் பங்கு பெறுவதற்கான அனைத்து தகுதிகளும் உங்களுக்கு இருப்பதால், இதில் பங்கு பெற விருப்பத்தை கேட்கின்றோம்.

4. **இந்த ஆராய்ச்சியில் கட்டாயம் பங்கு பெற வேண்டுமா?**

இல்லை. இது உங்கள் விருப்பத்தை மட்டுமே பொறுத்தது. நீங்கள் விரும்பவில்லையெனில், உங்களை இந்த ஆராய்ச்சியில் ஈடுபடுத்தமாட்டார்கள். ஆராய்ச்சியில் பங்கு பெறாவிட்டாலும், உங்களுக்கு கிடைக்க வேண்டிய பல் மருத்துவ உதவி, எந்த பாரபட்சமும் இல்லாமல் தொடர்ந்து கிடைக்கும்.

5. **இந்த ஆராய்ச்சியில் நான்/ என் பிள்ளை பங்கேற்க வேண்டுமானால், எடுத்து கொள்ள வேண்டிய பொறுப்புகள் என்ன?**

சில எளிய பொறுப்புகளை எடுத்துக் கொள்ள வேண்டியிருக்கும். அவையானவை பல் எடுத்த பின்பு அரை மணி நேரம் கழித்து பஞ்சை எடுக்கவும், 24 மணி நேரம் எச்சில் துப்புதல் கூடாது பல் எடுத்த இடத்தை தூய்மையாக வைக்கவும். 3 நாட்களுக்கு கடினமான ஆகாரம் உட்கொள்ளுதல் கூடாது.

6. **இந்த ஆராய்ச்சியில் பங்கு பெறுவதினால் எனக்கு / சமுதாயத்திற்கு ஏதேனும் நன்மைகள் உண்டா?**

உண்டு. அவை இதயநோயாளிகளுக்கு பல் எடுத்த பின்பு வரும் இரத்த கசிவை விரைவில் நிறுத்த உதவும்.

7. **இந்த ஆராய்ச்சியில் பங்கு பெறுவதினால் எனக்கு அசௌகரியங்கள், பாதிப்புகள் ஏற்படுமா?**

பாதிப்புகள் ஏற்படவாய்ப்பில்லை. ஆனால் சில அசௌகரியங்கள் ஏற்பட வாய்ப்பிருக்கிறது..

அறுவை சிகிச்சையின் அசௌகரியங்கள்: பல் எடுத்த இடத்தில் ரத்த கசிவு, வலி, வீக்கம். (இவைகளை தடுப்பதர்கான மருத்துவ வசதி மருத்துவமனையில் வைக்கப்பட்டுள்ளது).

8. இந்த ஆராய்ச்சியில் பங்கு பெறுவதற்காக எனக்கு என்பிள்ளைக்கு ஏதேனும் சன்மானம் வழங்கப்படுமா?

இல்லை. சன்மானம் ஏதும் வழங்கப்படமாட்டாது.

9. இந்த ஆராய்ச்சியில் பங்கு பெறுவதையும், என்னை குறித்த விவரங்களையும் வேறு யாருக்கும் தெரியாமல் இரகசியமாக வைக்கப்படுமா?

ஆம். இரகசியமாக வைக்கப்படும்.

10. இந்த ஆராய்ச்சியின் முடிவுகள் பங்கு பெறுபவர்க்கு தெரிவிக்கப்படுமா?

விரும்பினால் எங்களிடமிருந்து பெற்றுக்கொள்ளலாம்.

11. இந்த ஆராய்ச்சிலிருந்து விருப்பத்திற்கேற்ப எந்நேரமும் நான் விலகிக்கொள்ள முடியுமா?

ஆம். எந்நேரமும் விலகிக்கொள்ளலாம்.

ஆராய்ச்சியளரின் தகவல் மற்றும் கையொப்பம்

கு. முரளிதரன்,

முதுகலை மாணவர்,

பல் மற்றும் முக அறுவை சிகிச்சை பிரிவு,

பெஸ்ட் பல் மருத்துவக்கல்லூரி மற்றும் மருத்துவமனை

தொலைபேசி எண்: **7200202525**

ஆராய்ச்சியில் பங்கு பெற ஒப்புதல் உறுதிமொழி அளிக்கும் படிவம்

(படிவம் 2)

ஆராய்ச்சியின் பெயர்: : ஆஸ்பிரின் மற்றும் கிலோபிடோ஼ரேல் மருந்துகளை உட்க்கொள்ளும் இதயநோயாளிகளுக்கு பல் எடுத்த பின்பு வரும் இரத்த கசிவை ஜெலாட்டம்ப் மூலம் நிருத்துதல்.

.....என்கிற எனக்கு இந்த ஆராய்ச்சியை பற்றிய முழு விவரங்களும் என் தாய்மொழியில் தரப்பட்டன. இதைப் பற்றி முழுமையாகத் தெரிந்து கொண்டேன்.

இதில் பங்கு பெறுவதினால் எனக்கு ஏற்படக்கூடிய அசௌகரியங்கள் மற்றும் நன்மைகள் பற்றியும் தெரிந்து கொண்டேன்.

இந்த ஆராய்ச்சியிலிருந்து என் சுய விருப்பபடி எந்த நேரமும் நான் விலகிக் கொள்ள முடியும் என்றும், அதனால் இம் மருத்துவமணையில் எனக்கு கிடைக்க வேண்டிய மருத்துவ உதவிகள் அனைத்தும் எந்த பாரபட்சமும் இல்லாமல் தொடர்ந்து கிடைக்கும் என்றும் தெரிந்து கொண்டேன்.

இதில் பங்குபெற எனக்கு எந்த வித சன்மானமும் தரப்படமாட்ட்டது என்றும் புரிந்து கொண்டேன்.

என்னைப் பற்றிய தனிப்பட்ட தகவல்களை வெளியிடாமல், இரகசியமாக வைத்திருந்தால், இந்த ஆராய்ச்சியின் முடிவுகளை பல் மருத்துவம் சார்ந்த பத்திரிக்கைகளில் பிரசுரமாவதற்கு எதிர்ப்பு தெரிவிக்க மாட்டேன்.

இந்த ஆராய்ச்சியில் பங்கு பெற நான் என்ன செய்ய வேண்டும் என்று தெரிந்து கொண்டேன். அதன்படி முழு ஒத்துழைப்பு கொடுக்க தயாராக உள்ளேன்.

பங்குபெறுபவரின்கையொப்பம்/ முகவரி:

. . . . . .
. . . . . .
. . . . . .

சாட்சியாளரின்கையொப்பம்/ முகவரி:

. . . . . .
. . . . . .
. . . . . .

ஆராய்ச்சியாளரின்கையொப்பம்:

கு. முரளிதரன்,

முதுகலை மாணவர்,

பல் மற்றும் முக அறுவை சிகிச்சை பிரிவு,

பெஸ்ட் பல் மருத்துவக்கல்லூரி மற்றும் மருத்துவமணை.

INFORMED CONSENT

Form for Getting Informed Consent for those Participating in the Research Project

(Form 2)

NAME OF THE RESEARCH PROJECT: EVALUATION OF POST EXTRACTION HEMOSTASIS IN CARDIAC PATIENTS WITH GELATAMP DENTAL DRESSING WITHOU STOPPING ASPIRIN AND CLOPIDOGREL THERAPY.

I, the participant/ parent/ guardian,

.....Jannaki.....52/F.....

.....have been informed about the details of the study in my own language.

I, the participant/ parent/ guardian, have understood the details about the study.

I, the participant/ parent/ guardian, know the possible risks and benefits for me/ my child/ my ward, by taking part in the study.

I, the participant/ parent/ guardian understand that I can withdraw from the study at any point of time and even then, I/ my child/ my ward will continue to get the medical treatment as usual.

I, the participant/ parent/ guardian understand that I/ my child/ my ward will not get any payment for taking part in this study.

I, the participant/ parent/ guardian will not object if the results of this study are getting published in any medical journals, provided my/ my child's/ my ward's personal identity is not reviewed.

I know what I am/ my child is / my ward is supposed to do by taking part in this study and I, the participant/ parent/ guardian assure that full co-operation will be given for this study.

9/11/16

Signature/Thumb impression of the participant / parent/ guardian

(Name/Address)

Melur, Madurai

Signature/Thumb impression of the witness (9/11/16)

(Name/Address)

Melur, Madurai

Name & Signature of the investigator

Dr. G. Muralidharan

ஆராய்ச்சியில் பங்கு பெற ஒப்புதல் உறுதிமொழி அளிக்கும் படிவம்
(படிவம் 2)

ஆராய்ச்சியின் பெயர்: : ஆஸ்பிரின் மற்றும் கிலோபிடோ்ரேல் மருந்துகளை உட்க்கொள்ளும் இதயநோயாளிகளுக்கு பல் எடுத்த பின்பு வரும் இரத்த கசிவை ஜெலாட்டம்ப் மூலம் நிருத்துதல்.

ஆனாகி 53/F என்கிற எனக்கு இந்த ஆராய்ச்சியை பற்றிய முழு விவரங்களும் என் தாய்மொழியில் தரப்பட்டன. இதைப் பற்றி முழுமையாகத் தெரிந்து கொண்டேன்.

இதில் பங்கு பெறுவதினால் எனக்கு ஏற்படக்கூடிய அசௌகரியங்கள் மற்றும் நன்மைகள் பற்றியும் தெரிந்து கொண்டேன்.

இந்த ஆராய்ச்சியிலிருந்து என் சுய விருப்பபடி எந்த நேரமும் நான் விலகிக் கொள்ள முடியும் என்றும், அதனால் இம் மருத்துவமணையில் எனக்கு கிடைக்க வேண்டிய மருத்துவ உதவிகள் அனைத்தும் எந்த பாரபட்சமும் இல்லாமல் தொடர்ந்து கிடைக்கும் என்றும் தெரிந்து கொண்டேன்.

இதில் பங்குபெற எனக்கு எந்த வித சன்மானமும் தரப்படமாட்ட்டது என்றும் புரிந்து கொண்டேன்.

என்னைப் பற்றிய தனிப்பட்ட தகவல்களை வெளியிடாமல், இரகசியமாக வைத்திருந்தால், இந்த ஆராய்ச்சியின் முடிவுகளை பல் மருத்துவம் சார்ந்த பத்திரிக்கைகளில் பிரசுரமாவதற்கு எதிர்ப்பு தெரிவிக்க மாட்டேன்.

இந்த ஆராய்ச்சியில் பங்கு பெற நான் என்ன செய்ய வேண்டும் என்று தெரிந்து கொண்டேன். அதன்படி முழு ஒத்துழைப்பு கொடுக்க தயாராக உள்ளேன்.

பங்குபெறுபவரின்கையொப்பம்/ முகவரி:

ஆனாகி 9.11.2016
மேஸ்ரி

சாட்சியாளரின்கையொப்பம்/ முகவரி:

9.11.2016

ஆராய்ச்சியாளரின்கையொப்பம்:

கு. முரளிதரன்,

முதுகலை மாணவர்,

பல் மற்றும் முக அறுவை சிகிச்சை பிரிவு,

பெஸ்ட் பல் மருத்துவக்கல்லூரி மற்றும் மருத்துவமணை.

ULTRA'S BEST DENTAL SCIENCE COLLEGE , MADURAI

DEPARTMENT OF ORAL & MAXILLOFACIAL SURGERY

THESIS CASE SHEET PROFORMA

Name of the operator: Dr. G. Muralidharan, PG Trainee DATE:

Name of the Guide: Dr. K. Prabhu Sankar.,M.D.S.,

Patient's No. : OP No. :

Patient's Name : Phone No. :

Age : Occupation :

Gender : Marital State :

Address : Date of Operation :

Chief complaint:

Past Medical History:

Nature of the disease:

Drug:

Dosage:

Duration:

Dental History:

Personal History:

Family History:

Clinical Examination:

1. General examination:

2. Local examination:

Extra oral examination:

Intra oral examination:

Provisional Diagnosis:

Radiographs and investigations:

Blood Investigations:

INR:

PT:

aPTT:

OTHERS:

Final diagnosis:

Treatment plan:

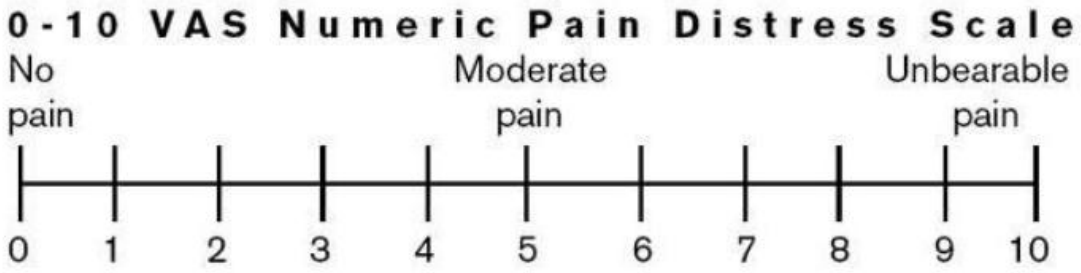
Treatment done:

ASSESSING PARAMETERS

1. Post-operative Bleeding index

Monitoring period	**Grading (Bleeding index)**
Immediately after extraction	
5 minutes after extraction	
30 minutes after extraction	
2 hours after extraction	
1st post-operative day	
7th post-operative day	

2. Pain assessment



1st post-operative day -

3rd post-operative day -

7th post-operative day -

3. WOUND HEALING

Healing parameters	**Presence/ absence**
Broken down blood clot	
Dry socket	
Inflammation & infection	