



ORIGINAL RESEARCH PAPER

Maxillofacial Surgery

EFFECT OF DUAL ANTI-PLATELET THERAPY ON TOOTH EXTRACTION- A PROSPECTIVE COMPARATIVE CLINICAL STUDY

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ABSTRACT

Objective: The purpose of this study was to assess the bleeding following tooth extractions in patients receiving continuous antiplatelet treatment. **Materials And Procedures:** Two groups of 64 individuals who needed to have teeth extracted while taking oral dual antiplatelet medications were randomly assigned. 32 patients in Group A had uninterrupted dual antiplatelet therapy, while 32 patients in Group B had stopped taking antiplatelet medication five days before the extraction after consulting a physician. Prior to extraction, the bleeding times of all patients were recorded. Under local anesthetic, teeth were simply extracted during the surgery. The extraction socket was filled with gel foam before being sutured with 3-0 silk. Gauze pressure packs were applied for one hour. Bleeding was compared between the two groups at 1, 8, 12, and 24 hours. The variables were compared using the chi-square test. $P < 0.05$ was considered to be significant. **Results:** Following extraction, neither group of patients experienced any substantial uncontrollable bleeding. **Conclusion:** Thus, without interrupting or changing their prescription, we advise routine extractions in patients taking long-term dual antiplatelet therapy. These patients do not have a higher risk of excessive or protracted postoperative bleeding when appropriate local hemostatic measures are taken.

INTRODUCTION

The series of mechanisms known as hemostasis prevents blood loss by causing fibrin to develop (clotting). Three phases make up this process: (i) the vascular phase, or the phase of neurogenic vasoconstriction, which reduces blood escape; (ii) the platelet phase, in which platelet aggregation takes place and concentrates many components needed for the third phase; and (iii) the plasma coagulation phase, which results in fibrin clotting. Platelets are responsible for forming the first hemostatic plug at the site of vascular injury. They also play a role in pathological processes and play a significant role in arterial thrombosis, which can result in myocardial infarction and ischemic stroke.²

These days, thromboembolic conditions including coronary artery disease and cerebrovascular disease are highly prevalent due to changing lifestyles and an extended life expectancy. More and more people are required to use antithrombotic medications as a result of an increase in the prevalence of cardiovascular diseases and heart disease. Antiplatelet medications are those that disrupt platelet activity. They are utilized in thromboembolic conditions. Aspirin and thienopyridines (e.g., clopidogrel) are two commonly prescribed oral antiplatelet medications.³

The production of thromboxane A₂ by the enzyme cyclooxygenase-1 (COX-1) is irreversibly inhibited by aspirin, which prevents physiological blood platelet aggregation and the formation of blood clots by obstructing extrinsic routes of coagulation and clotting over the platelet's lifespan, which is between 7 and 10 days.^{4, 5-7} Low doses of aspirin (75 mg/day) may take several days to fully block the cyclooxygenase-1 (COX-1) enzyme and have their full antiplatelet impact. The maximum antiplatelet impact of aspirin happens within 30 minutes at a dose of 160-325 mg/day. So, Aspirin is given in moderate doses (160-325 mg/day) when immediate anti-clotting action is required (such as in the treatment of acute heart attacks and unstable angina). Low doses (75-150 mg/day) are used for the long-term prevention of heart

attacks and strokes. Adenosine diphosphate receptors on platelets are altered by the prodrug clopidogrel, which prevents platelet aggregation. Clopidogrel's initial effect is dose-related, just like aspirin. After taking clopidogrel (75 mg/day) for a few days, the antiplatelet effect reaches its peak.

Due to concerns of significant postoperative bleeding in patients on antiplatelet therapy, it is a usual practice among dentists and medical professionals to halt dual anti-platelet therapy before any surgical procedure.⁸ However, stopping this drug suddenly might be fatal as it increases the risk of severe thromboembolism, myocardial infarction, and cerebrovascular accident. The status of disease may get worse if daily antiplatelet medications (aspirin/clopidogrel) are stopped or discontinued.⁹ Specifically, clopidogrel is considered to put patients at a high risk of bleeding whether for single or dual therapy¹⁰ since it takes 5-10 days for platelet activity to fully rebound after discontinuation.

The long-term Dual anti platelet therapy (DAPT) calls for the cardiologist to evaluate a patient's risk of bleeding and inquire about any anticipated surgical or dental treatments. The cardiologist typically is unable to tell the difference between urgent and elective procedures since they are unfamiliar with the details and methods employed in oral surgery.¹¹ A practical clinical concern is that most oral surgeons or dentists would like to defer doing essential treatments as a result of using Dual anti platelet therapy (DAPT) for an extended period of time. Hence, the rationale of the study is to evaluate the risk of bleeding complications in patients on dual antiplatelet therapy.

Materials And Methodology

This was a prospective, comparative clinical study conducted on 64 patients selected from those reporting to the Department of Oral and Maxillofacial Surgery, for the extraction of teeth and who were on dual anti platelet therapy. This study was approved by the Research Degree Committee,

of our institute (HSJ/21/186). Ethical approval for the study was granted by Institutional Ethics Committee (PUIEC210630-II-050) and (EC-D-2110-93). The patients were selected based on clinical and radiographic examination and bleeding time evaluation using Duke's method was done on the same day of extraction.

Inclusion Criteria

1. Patients who gave written informed consent to be included in the study.
2. Patients who were not on any concurrent therapy such as birth control pills, hormone replacement therapy, other anticoagulation; or any drug such as NSAIDs that could interact with the aspirin.
3. Patient who required minimum two teeth extractions with comparable socket size.
4. Patients on dual anti-platelet therapy.
5. Only local residents were considered.

Exclusion Criteria

1. Pregnant females and lactating mothers.
2. Patients who underwent radiation therapy or history of radiation therapy in the head and neck region within the last two years.
3. Patients who were not willing to participate in the study or come for follow-up.
4. Those with a preoperative bleeding time of more than 20 minutes, a history of bleeding disorders, alcoholism, and minors.
5. Chronic liver disease.
6. Local disease with the tendency of excessive bleeding.
7. Patients who were on anticoagulants like warfarin.

The Patients Were Divided Into 2 Groups:

Group 1- 32 dental extractions were done under local anesthesia without discontinuing the dual antiplatelet therapy. (Study Group)

Group 2- 32 dental extractions were done under local anesthesia with dual anti- platelet drugs stopped 5 days before the procedure after consulting with the patient's physician (control group).

During the preoperative period, all patients underwent clinical and radiologic evaluations, vitals, and estimations of bleeding time (duke method: 2-6 min.) on the day of extraction in both study group and control group. In the control group bleeding time was taken after stopping the dual anti platelet drugs for 5 days.

Gel foam was placed and suturing with 3-0 silk suture was done in all patients in both the groups. Pressure pack was placed in the extraction socket for 1 h in both the groups, and a post-operative instructions sheet with an emergency contact number was provided to the patient. Patients were discharged 1 h after extraction after evaluating for any signs of bleeding. Bleeding was evaluated 1 hour, 8 hours, 12 hours, and 24 hours postoperatively. All the patients were requested to contact immediately if any bleeding occurs. The presence or absence of bleeding, oozing, and active bleeding were evaluated in postoperative patients.

Blood that totally reddens the pack but does not fill the mouth with blood was regarded to be oozing. Active bleeding was defined as when the socket was bleeding enough to frequently fill the mouth with blood. If bleeding persisted, it was controlled with various local hemostatic measures, such as a use of local hemostatic agents like, 5% Tranexamic acid.

The data was tabulated on an excel sheet and was analyzed using SPSS version 2.0. the chi-square test was used to calculate the bleeding at 1 hr, 8 hr, 12 hr, 24hr, and active bleeding among the two groups.

RESULTS

There were total of 18 female patients, and 46 male patients who were on dual anti platelet therapy. Out of these 18 female patients, 9 were included in study group and 9 were in control group. Out of 46 male patients 23 patients were included in each study & control group. The age of all patients ranged between [55-75] with a mean of 65. Bleeding time of all the patients was recorded which was within normal limits.

Total number of extractions performed were 128 which included which 32 molars, 60 premolars and 36 anterior teeth. Table 1 shows the bleeding at 1 hour post op in the study and the control group. The result shows statistically no significant difference in the two groups ($p > 0.05$). Table 2 shows the bleeding at 8 hour post op in the study and the control group. The result shows that there was no bleeding in all the cases in study and control group. Hence, no statistical association. Table 3 shows the bleeding at 12 hour post op in the study and the control group. The result shows that there was nil bleeding in all the cases in study and control group. Hence, no statistical association. Table 4 shows the bleeding at 24 hr post op in the study and the control group. The result shows that there was nil bleeding in all the cases in study and control group. Hence, no statistical association. Table 5 shows the active bleeding status in the study and the control group. The result shows that there was no active bleeding in all the cases in study and control group. Hence, no statistical association.

Table 1 Bleeding At 1 Hour Post Operatively

Group	Bleeding 1 hour post op in form of oozing		p-value
	Absent	Present	
Study	27	5	0.230
Control	30	2	

Table 2 Bleeding At 8 Hr Post Op

Group	Bleeding at 8 hr post op- oozing		p-value
	Absent	Present	
Study	32	0	-
Control	32	0	

Table no. 3 Bleeding at 12-hour post op

Group	Bleeding 12-hour post op- oozing		p-value
	Absent	Present	
Study	32	0	-
Control	32	0	

Table no. 9 Bleeding at 24 hr post op

Group	Bleeding 24hr post op- oozing		p-value
	Absent	Present	
Study	32	0	-
Control	32	0	

Table no. 10 Active Bleeding

Group	Active bleeding		p-value
	Absent	Present	
Study	32	0	-
Control	32	0	

DISCUSSION

Cardiovascular illnesses like atherosclerosis, thrombosis, and acute coronary syndromes are becoming more common in tandem with an increase in life expectancy. About 800,000 people each year pass away from CVD, which includes coronary heart disease (CHD)¹²; most of these people had underlying atherosclerosis. Around 7.9 million individuals in the United States have experienced a heart attack, around 7 million adults have experienced a stroke¹³, and around 16 million adults in the United States have been diagnosed with CHD¹².

Atherosclerotic CVD can be decreased with preventive care and lifestyle changes^{13,14}. Practice guidelines highly advise taking aspirin and clopidogrel drugs as one of the numerous

preventative therapies that can significantly help individuals with ischemic vascular disease^{15,16}

Platelets play a chief role in thrombosis via a mechanism where arachidonic acid is formed from membrane phospholipids by cyclooxygenase-1 and thromboxane synthase, thrombin is created by the coagulation pathway, and adenosine diphosphate is released from dense granules on the surface of activated platelets. The activation of the glycoprotein IIb and IIIa receptors leads to the intercellular signaling events that lead to platelet aggregation, which is then mediated by the binding of the dimeric fibrinogen molecule to the activated receptors¹⁷. These three essential G-protein-coupled receptors, the P2Y₁₂ receptor, thromboxane receptor, and protease-activated receptor, are influenced by adenosine diphosphate, thromboxane A₂, and thrombin which causes thrombosis.

Two antiplatelet drugs, aspirin (ASA) and clopidogrel (CLO) have emerged as doctors' top choices among the wide range of antithrombotic drugs because of their reliable efficacy and inexpensive cost¹⁸.

Thromboxane A₂, a crucial component in platelet activation and aggregation, is inhibited by ASA via inactivating the enzyme cyclooxygenase¹⁷. Thienopyridines, like CLO, permanently block the adenosine diphosphate receptor (P2Y₁₂), which is required for the activation of the receptor GPIIb/IIIa complex in platelet aggregation and cross-linking of platelets by fibrin¹⁹. To take advantage of its synergistic activity in the prevention of thrombotic complications, many patients today get a combination of aspirin and clopidogrel, or dual antiplatelet treatment (DAPT)¹⁸.

Stopping antiplatelet medication could have catastrophic repercussions including thrombosis in the coronary or cerebral arteries, which, according to statistics, results in 25% of fatalities and 40% of permanent disability cases²⁰. Papanicolaou et al (2017)³⁶ ST-Elevation Myocardial Infarction (STEMI) may occur along with the cardiogenic shock and in these cases even heparin bridging was unsuccessful increasing the risk of perioperative thrombosis when the antiplatelet therapy is stopped. If antiplatelet therapy is not stopped, dental surgery or tooth extraction may result in prolonged and difficult-to-stop postoperative bleeding. Hemorrhage and hematoma may impede the patient's airway if they are not properly managed, endangering their lives. Medical professionals always struggle with the decision of whether or not to stop antiplatelet therapy in the case of patients on chronic antiplatelet therapy who are qualified for tooth extraction.

There has been various research done in the literature regarding whether to stop dual antiplatelet therapy or not. Olga Olmos-Carrasco et al²¹ conducted a study in 2014 to determine how often individuals on two antiplatelet medications who need dental extractions experience hemorrhagic problems. Type of extraction, number of teeth extracted, number of roots extracted, and presence of inflammation were the predictive variables. Dental extractions that result in hemorrhagic complications that continue longer than 30 minutes are treated utilizing local hemostatic techniques in 8.3% of patients receiving dual antiplatelet medication. The findings of this study provide evidence in favor of the security of dental extraction without withdrawing dual platelet treatment. Alexander Gröbe⁶ did oostomies in total 64 patients, Prashant Babaji²² 2018 did extractions in 150 patients and provided evidence in support that there is no need to stop dual antiplatelet treatment.

Tomasz Tokarek et al²³ designed an online questionnaire that was provided to all 3000 registered members of the Dental Association through email out of which 352 dentists responded to assess their knowledge regarding the use of

antiplatelet and anticoagulant treatment as supplementary material. Questions that were included in the questionnaire were the sociodemographic and clinical profile of respondents and decisions of dentists regarding DAPT and anticoagulant treatment in patients coming for dental extractions. They concluded that extractions were more commonly done in patients on aspirin but dual therapy was discontinued before extractions more frequently.

This study was done to evaluate the effect of dual antiplatelet therapy on bleeding after tooth extractions. Our study compared the bleeding following tooth extractions in patients on dual antiplatelet therapy (aspirin and clopidogrel)- study Group with those who stopped these drugs 5 days prior to tooth extraction after consultation with the physician. The bleeding time of patients in both groups was calculated using the Duke method on the same day of extraction (Table 1 and Table 2).

The bleeding time of patients who continued the dual antiplatelet drugs came out to be on the higher side when compared with those in which this therapy was discontinued but still within the normal limits. Little et al²⁴ claimed that unless the BT lasted longer than 20 minutes, aspirin-affected platelets did not cause a serious bleeding issue.

According to Raul Altman²⁵ et al 2012 found an increase in bleeding time in 52 patients who were on dual anti platelet drugs and bleeding risk increased by 1.74% with each 1min increase in BT. In contrast to our findings, Leavitt and colleagues²⁶ concluded that patients using dual anti-platelet drugs and those not taking them did not have different bleeding rates. Lawrence et al²⁷, Ferraris, and Swanson²⁸ claimed that there is no need to stop aspirin before doing dental retractions especially if the bleeding time and platelet diathesis is within the normal limits.

A review of the literature revealed that the majority of experts supported discontinuing aspirin medication^{18,29,24,25} in favor of these according to B. Krishnan et al³⁰. Dental extractions in patients on uninterrupted DAPT can be done safely. Resorting to the temporary withdrawal of DAPT due to a fear of excessive bleeding is unnecessary. After 1 hour of dental extraction, oozing was seen in five patients in Group I and two subjects in Group II. Both groups did not have any major uncontrolled bleeding following dental extraction. Immediately following extractions gel foam was placed followed by suture placement in all patients in both groups (The coagulation pathway is unaffected by gelfoam; instead, it has a more physical hemostatic effect).

Oozing was seen in patients undergoing extraction of multi-rooted teeth. This was in harmony with the study done by Olga Olmos-Carrasco et al²¹ who stated that the presence of 3-root extractions increases the probability of hemorrhage. Contrary to this study, there is no correlation between the type of extraction and the severity of the hemorrhage, according to Canigral and Silvestre³¹.

The results are in harmony with, Theodoros Lillis et al³², George Varghese K et al³³ stated that the use of merely local hemostatic techniques, and extractions can be done safely on patients who are taking single or two antiplatelet medications without interfering with the therapy. On the other hand, in a study by Bajkin et al¹⁵ after several extractions while on DAPT, the patient experienced postoperative hemorrhage, necessitating readmission, suturing, and wound compression.

None of the patients reported delayed post-operative bleeding i.e., 24 hours after the extraction. The results of our study agree with Napeñas et al³⁴ who observed that none of their 29 patients on dual antiplatelet therapy experienced bouts of persistent bleeding. On contrary, a study on 155

patients by Cardona-Tortajada et al³⁵ who were on antiplatelet drugs reported bleeding in 17% of patients 24 hours following the extraction.

Patients were monitored for at least 1 hour after the extraction in the clinic itself. On the contrary in a study by Cardona-Tortajada et al³⁵ they were monitored for 10 minutes only whereas in a study by Theodoros Lillis 2011³², patients were monitored for only 30 minutes.

In our study, there is a minimal incidence of bleeding in the form of oozing in 5 patients in the study group and 2 patients in control group as local hemostatic measures were taken in every patient

The magnitude of the intended surgical surgery, the nature and severity of the disorder, and the patient's antiplatelet therapy must all be taken into consideration when treating patients who require oral surgical procedures. The degree of danger will depend on how well local hemostasis can be managed and how much access can be gained to the surgical site. The most crucial ones are to reduce trauma, prevent flaps, utilize suture-friendly surgical procedures, cauterize, take all the required steps to maintain hemostasis well, and remove all granulation tissue from areas of persistent inflammation.

More intensive studies with large sample sizes are required to draw important conclusions. The short sample size is an important limitation of this study.

CONCLUSION

Dental extractions can be safely done without stopping the dual antiplatelet drugs especially when the bleeding time is within the normal limits and appropriate local hemostatic measures are taken.

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