ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/cardiosci.2018-63266

Should Antiplatelet Drugs Stopped Before Dental Extraction?

Antiplatelet İlaçlar Diş Çekiminden Önce Kesilmeli midir?

Nur ALTIPARMAK[a],
Sıdıka Sinem AKDENİZ[a],
Burak BAYRAM[a],
Kenan ARAZ[a]

[a]Department of
Oral and Maxillofacial Surgery,
Baskent University Faculty of Dentistry,
Ankara, TURKEY

Received: 12.10.2018
Received in revised form: 11.01.2019
Accepted: 29.01.2019
Available online: 05.02.2019

Correspondence:
Nur ALTIPARMAK
Baskent University Faculty of Dentistry,
Department of
Oral and Maxillofacial Surgery, Ankara,
TURKEY/TÜRKİYE
nuraltiparmak@hotmail.com

ABSTRACT Objective: The aim of this study was to evaluate the incidence of postoperative bleeding after dental extraction in patients without interruption of single or dual antiplatelet therapy. **Material and Methods:** The study comprised a total of 195 consecutive subjects who underwent dental extractions performed by the same qualified dentist in Baskent University Department of Oral and Maxillofacial Surgery between the date of February and May 2016. Patients were divided into three groups (n=65 in each group): dual antiplatelet therapy (acetylsalicylic acid and clopidogrel), first control (no antiplatelet or anticoagulant therapy) and second control group (antiplatelet therapy ceased for 3-10 days prior to dental extraction). **Results:** There was no significant difference in sex distribution, mean age, or in the types or number of teeth extracted between the groups. The incidence of postoperative bleeding was higher in the study group than in the control groups, but the difference was not significant. In the study group, the incidence of postoperative bleeding was higher in patients on dual therapy than in those on acetylsalicylic acid alone or clopidogrel alone; however, the differences were not significant. **Conclusion:** The findings of the present study suggest that there is no need to stop single or dual antiplatelet therapy prior to dental extraction.

Keywords: Bleeding; dental extraction; antiplatelet drugs; hemorrhage

ÖZET Amaç: Bu çalışmanın amacı antiplatelet ilaç tedavisinin kesilmediği durumlarda diş çekimi sonrası postoperative kanama insidansının değerlendirilmesidir. **Gereç ve Yöntemler:** Bu klinik çalışmaya, Şubat-Mayıs 2016 tarihleri arasında Başkent Üniversitesi Ağız Diş Çene Cerrahisi Anabilim Dalı'nda aynı nitelikli dişhekimi tarafından diş çekimi uygulanan toplam 195 kişi dahil edilmiştir. Hastalar herbir grupta 65 kişi olacak şekilde üç gruba ayrılmıştır. Kombine ilaç tedavisi (asetil salisilik asit ve klopidogrel), ilk kontrol grubu (antiplatelet tedavi görmeyen bireyler) ve ikinci kontrol grubu (antiplatelet tedaviye diş çekilmesinden 3-10 gün önce ara veren hastalar). **Bulgular:** Gruplar arasında cinsiyet dağılımı, yaş ortalaması, dişlerin çekim tipleri veya sayısı açısından anlamlı bir fark yoktu. Postoperatif kanama insidansı çalışma grubunda kontrol grubuna göre daha yüksekti, ancak fark anlamlı değildi. Çalışma grubunda, postoperatif kanama insidansı, ikili ilaç tedavisi alan hastalarda tek başına asetil salisilik asit veya klopidogrel kullanan hastalara göre daha yüksekti. Ancak farklılıklar istatistiksel olarak anlamlı değildi. **Sonuç:** Bu çalışmanın bulguları, diş çekimi öncesinde antiplatelet (dual veya tek) tedaviyi durdurmaya gerek olmadığını düşündürmektedir.

Anahtar Kelimeler: Kanama; diş çekimi; antiplatelet ilaç; hemoraji

Patients suffering from cerebrovascular and cardiovascular thromboembolic diseases are encountered very frequently for oral and maxillofacial operations. Antiaggregant medications, such as acetylsalicylic acid and clopidogrel, which prohibits platelet aggregation are frequently prescribed to decrease the risk of thromboembolism in these patients.

Previous studies have shown that routine dental extractions can be completed without the interruption of these medications by hemorrhage control with the use of local hemostatic agents when required.[1,2] Nonetheless, according to the results provided by surveys carried out across the country, it shows that over 50% of hematologists and oral and maxillofacial surgeons recommend stopping taking antiplatelet medications by the time the patient goes under aforementioned procedures.[1-3] Murphy et al. stated that prior to dental extraction, 90% of these medications are interrupted by responsible clinicians.[4] Alcock et al. stated that the decision to bring antiplatelet therapy to an end as it appeared in almost half of their sample group, was not influenced by perioperative cardiac or cerebrovascular risk stratification.[5] The results from the literature indicate that there is insufficient awareness among clinicians regarding the treatment protocol for patients using antiplatelet medication, especially prior to routine dental extractions.[6]

When the literature is reviewed, there are very few studies comparing the hemorrhage rate after dental extractions performed on patients who kept receiving antiplatelet therapy versus a control group consisting of individuals who ceased antiplatelet therapy. Moreover, there are very few studies focusing on the difference between patients who received monotherapy and patients who received dual therapy.[7,8]

We hypothesized that there would not be any breakthrough or delayed bleeding after the dental extractions performed on patients who kept receiving antiplatelet therapy with acetylsalicylic acid or acetylsalicylic acid plus clopidogrel. Developing and implementing a standard therapy protocol prior to dental extraction for these patients is very important, as this continues to be a challenging decision for clinicians. In this study, the authors intended to clarify whether the cessation of antiplatelet agents is required prior to dental extraction, despite the risk of thromboembolism that may result in death, or whether intraoperative or postoperative hemorrhage could be managed with local measures.

MATERIAL AND METHODS

PATIENTS AND METHODS

This present study was approved by the Baskent University Institutional Review Board and Ethics Committee (with project no D-KA 18/31, Approval Date: 23.10. 2018). The study was carried out in the Department of Oral and Maxillofacial Surgery of Baskent University, located in Ankara, Turkey.

One-hundred and ninety-five patients, who received treatment from equally experienced oral and maxillofacial surgeons between February and May 2016, were a part of this study. All of the patients put a signature to a consent form in detail before participating in this study. The variables analyzed in this study were as follows: Patients' age, gender, their background of antiplatelet therapy (such as asetil salisilik asit treatment, clopidogrel treatment, or dual therapy), their number of extracted teeth, and difficulties experienced in the extraction procedure (whether simple or complex).

The patients participating in the study were grouped into three as stated by their antiplatelet drug regimen during the dental extraction. Sixty-five patients were receiving antiplatelet therapy (single/dual) for various cardiac diseases (Group 1) and they did not interrupt the antiplatelet therapy before the dental extractions. Group 2 comprised 65 healthy patients who were not taking any antiplatelet drugs or were not receiving anticoagulant therapy and on whom dental extractions were performed as normal. Group 3 comprised 65 patients on antiplatelet therapy who were advised to stop their medication prior to dental extraction by their hematologist or cardiologist. In Group 3, 25 patients were receiving dual therapy and 40 patients were receiving monotherapy.

SURGICAL PROCEDURE

All dental extractions were performed under local anesthesia using 1:100,000 articaine as the local anesthetic agent. The extractions were performed without trauma as possible, and any granulation tissue was curetted. If additional surgical procedures, such as raising a flap, sectioning of the tooth

roots, or bone removal were required, the extraction was considered complex. The extraction sockets were sutured only when required using 3-0 resorbable sutures. The routine hemostatic protocol after extraction involved packing the extraction socket with oxidized cellulose (Clinisponge, Yucel Medikal, Istanbul, Turkey) prior to having the patient bite a dry gauze pad. If any hemorrhage condition was detected despite the dry gauge compression, the socket was repacked with additional oxidized cellulose and tranexamic acid solution (Transamine 10% A/H, Actavis Ilaclari AS, Istanbul, Turkey) was applied. Patients were sent home after 30 minutes of observation. They were informed that leakage type bleeding for the 24-hour period following the extraction is considered normal after all extractions; however, in the case of more severe bleeding (e.g., a mouthful of blood) they were advised to present immediately to an emergency service.

All patients were checked by telephone call 24 hours after the procedure and 7 days after the operation at the clinical follow-up, and conditions such as the emergence of any bleeding that was delayed, the gauze pressure pack's sufficiency in stemming the bleeding, and any professional aid needs were evaluated. Some patients may interpret seeing red or pink saliva or a blood clot in the extraction socket as a sign of persistent bleeding, whereas this may not have been the case and could have led to false reporting of postoperative bleeding. To minimize this variable, the patients were informed that red or pink saliva is an expected postoperative finding.

STATISTICAL ANALYSIS

The patients' demographics, dose, and type of antiplatelet medication, the reason for dental extraction, type of extractions as simple or complex, number of extracted teeth, and postoperative bleeding data were collected and statistically compared for all three groups. Group 1 was also divided into the following three subgroups according to the type of antiplatelet therapy being used: acetylsalicylic acid alone, clopidogrel alone, and dual therapy. The degree of hemorrhage, extraction difficulty and a number of teeth extracted were also analyzed and compared between these subgroups. The relationships between the subgroup (acetylsalicylic acid, clopidogrel, and dual therapy) and bleeding, the dental extraction's type, together with the number of teeth extracted were examined using the chi-squared test. The relationships between the main groups (continued antiplatelet therapy, healthy control, and discontinued antiplatelet medication therapy) and the dental extraction's type, the number of teeth extracted, the reason for extraction, and genders were also investigated using the chi-squared test. All the tests were carried out with the usage of SPSS 20.0 (IBM Corp., 2011; Armonk, NY, USA) with a 95% confidence interval.

RESULTS

There was no considerable difference according to the statistics in the average age and in the gender distribution between the first, the second and the third groups ($p>0.05$)

When the incidence of hemorrhage was compared between the three main groups, hemorrhage was observed in 6.2% of patients belonging to the Group 1, 4.6% of patients belonging to the Group 2, and 4.6% of patients belonging to the Group 3. There was no statistically significant difference in the occurrence of hemorrhage amongst the groups ($p>0.05$) (Table 1).

In Table 2, the statistical correlation of the type of extraction protocol, the number of extracted teeth, and the reasons for extraction was

TABLE 1: The statistical comparison of hemorrhage rates of study and control groups.

		Hemorrhage		
		No	Yes	Total
Patients undergo antiplatelet therapy Group I	n	61	4	65
	%	93,8%	6,2%	100,0%
Healthy Group II	n	62	3	65
	%	95,4%	4,6%	100,0%
Quit therapy Group III	n	62	3	65
	%	95,4%	4,6%	100,0%
Total	n	185	10	195
	%	94,9%	5,1%	100,0%
p=0.09				

TABLE 2: The Correlation between the type of extraction protocol, numbers of the extracted tooth and reason of tooth extraction of all groups.

			Groups			Total	p
			Patients undergo Antiplatelet Therapy	Healthy	Quit Therapy		
Tooth Extraction Type	Complicated	n	4	5	5	14	0.926
		%	6:2%	7.7%	7.7%	7.2%	
	Simple	n	61	60	60	181	
		%	93.8%	92.3%	92.3%	92.8%	
	Total	n	65	65	65	195	
		%	100.0%	100.0%	100.0%	100.0%	
The number of extracted tooth	1	n	51	51	51	153	0.987
		%	78.5%	78.5%	78.5%	78.5%	
	2	n	11	12	12	35	
		%	16.9%	18.5%	18.5%	17.9%	
	3	n	3	2	2	7	
		%	4.6%	3.1%	3.1%	3.6%	
	Total	n	65	65	65	195	
		%	100.0%	100.0%	100.0%	100.0%	
Reason of extraction	Decay- Root resorbtion	n	26	37	37	100	0.083
		%	40.0%	56.9%	56.9%	51.3%	
	Periodontitis	n	39	28	28	95	
		%	60.0%	43.1%	43.1%	48.7%	
	Total	n	65	65	65	195	
		%	100.0%	100.0%	100.0%	100.0%	

given amongst the three groups. There was no considerable difference according to the statistics in the dental extraction difficulty between the groups.

Table 3 showed the statistical comparison of hemorrhage situation of the subgroups of Group 1. There was no statistically significant difference in the occurrence of hemorrhage amongst the subgroups ($p>0.05$).

DISCUSSION

Before extracting teeth in patients receiving antiplatelet drug therapy, it is first necessary to decide whether these agents should be interrupted. Interrupting antiplatelet therapy may increase the risk of thromboembolism while undertaking dental extractions without interrupting antiplatelet therapy may result in severe hemorrhage. While some clinicians argue that these agents must be interrupted for a defined period of time before dental extraction, others defend undertaking dental extractions without any change in the medication regime. The present paper investigated this controversial clinical subject and found that continuing antiplatelet agents, such as acetylsalicylic acid and clopidogrel, preoperatively to dental extraction results in the same bleeding potential as interrupting these agents before the dental extraction.

Acetylsalicylic acid and clopidogrel can be used alone as monotherapy or can be combined in dual therapy. Although it is known that the dual use of these agents significantly decreases the risk of thromboembolism, it has also been stated that patients receiving dual therapy have a significant risk of hemorrhage during dental surgical procedures.[7] In this present study, hemorrhage rate was similar among the subgroups as one patient on acetylsalicylic acid subgroup, one patient on clopidogrel subgroup, and two patients on dual therapy subgroup.

TABLE 3: Statistical comparison of the sub-groups of Group 1.

			Subgroup			Total	p
			Clopidogrel	Acetylsalicylic acid	Dual		
Hemorrhage	No	n	23	15	23	61	0,856
		%	95,8%	93,8%	92,0%	93,8%	
	Yes	n	1	1	2	4	
		%	4,2%	6,3%	8,0%	6,2%	
	Total	n	24	16	25	65	
		%	100.0%	100,0%	100,0%	100,0%	
	2	n	83,3%	68,8%	80,0%	78,5%	
		%	3	5	3	11	
	3	n	12,5%	31,3%	12,0%	16,9%	
		%	1	0	2	3	
	Total	n	4,2%	0,0%	8,0%	4,6%	
		%	24	16	25	65	
		n	100,0%	100,0%	100,0%	100,0%	

Extraction sockets were packed with gelatin sponges after granulation tissue was curetted following the dental extractions, and a dry gauze compress was applied for 10 minutes in this study as a standard protocol described in literature.[9,10] The proportion of patients in which hemostasis was achieved for each patient group was as follows: 93.8% of those who continued antiplatelet therapy before the extraction, 95.4% of those who interrupted the therapy, and 95.4% of the healthy control group. Additional use of gelatin sponges and suturing to converge the wound edges were sufficient to control hemorrhage in the remaining patients.

The possible complications that may result from the interruption of antiplatelet agents in patients receiving antiplatelet therapy are much more significant than the potential hemorrhagic complications that may result from undergoing dental extraction without the interruption of these agents. Moreover, the discontinuance of antiplatelet therapy followed by oral operation may increase the risk of permanent disability or death. It is recommended by the American College of Chest Physicians (ACCP) that usage of acetylsalicylic acid should be stopped 7 to 10 days before the operation.[11] Nevertheless, 48 hours after stopping acetylsalicylic acid, non-acetylated cyclooxygenase can be found in up to 20% of the platelet pool, and these platelets release thromboxane A2 to activate other platelets which fail to make their own, and as a result, the deformity in the primary hemostasis is recovered.[12] 50% of the patients suffering from platelet aggregation are healed in 3 days, and 80% of them are healed in 4 days.[13] Therefore, if it is required, acetylsalicylic acid discontinuation may be drawn to 3–5 days in opposition to the ACCP recommendation which is 7-10 days before the operation takes place. Although different time intervals have been recommended for stopping the antiplatelet therapy before the procedures, the consequences which stopping the antiplatelet therapy brings to these patients must always be taken into account. Non-fatal myocardial infarction risk significantly increases in patients with a history of cerebrovascular or cardiovascular diseases and in those who stop taking acetylsalicylic acid in low doses when compared with patients who continue their antiplatelet therapy.[14]

A previous literature review showed that there is a very limited number of studies evaluating the hemorrhage risk at the same times as major or minor operations take place, even if it's a simple dental extraction.[7,15-17] Eighty-two patients who underwent a single or multiple dental extraction operations were evaluated by Krishan et al.[17] The

researchers reported that they did not encounter any prolonged hemorrhage, and they concluded that it is unnecessary to interrupt antiplatelet therapy before simple dental extractions.

Fourty-three patients of single or dual (n=29) antiplatelet therapy were evaluated by Napenas et al. and it was found out that after invasive procedures which are periodontal operations, tooth extractions, subgingival scaling, and root planning, little to no oral bleeding occurred. 181 patients supplemented with acetylsalicylic acid or received clopidogrel monotherapy (n=176) or dual therapy (n=5) in the process of dental extraction were evaluated by Olmos-Carrasco et al. and it was concluded that periodic bleedings longer than 30 minutes occurred in 8.3% of the patients.[15,16] Our results appear as no contradictory to the previous listed studies. In contrast Lillis et al. was stated that the risk of instant bleeding in patients who were taking two different antiplatelet drugs simultaneously was fairly higher after performing the dental extraction (acetylsalicylic acid and Clopidogrel®) compared to the control group not taking any antiplatelet agents.[18]

Although most studies in the literature revealed that the risk of considerable bleeding could be eliminated while performing operations such as dental extractions on patients who were receiving antiplatelet therapy, there isn't actually a standardized code to improve the management of such patients.[19] It has been recommended that each patient should be assessed individually after evaluating the risks of thromboembolism and hemorrhage so that an appropriate decision can be made on whether to interrupt antiplatelet medication.[19] Another study drew attention to stopping antiplatelet medication prior to dental surgical procedures do not completely eliminate the risk of postoperative bleeding.[20] Our results were comparable with these clinical observations and it can be emphasized that the most important approach to obtain hemostasis is using effective local hemorrhage control methods after dental extraction.

The results of this clinical study improved that ceasing antiplatelet therapy before simple or complicated dental extraction does not have any considerable effect on the postoperative hemorrhage complications. Dental extractions can be performed in patients who continue mono or dual antiplatelet therapy without increasing the risk of immediate or delayed bleeding after the extraction. Although some local factors, such as periodontal or periapical pathology, can be responsible for bleeding following dental extraction, the risk is small and can be managed by appropriate local hemostatic measures.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Nur Altıparmak;* ***Design:*** *Nur Altıparmak, Sıdıka Akdeniz;* ***Control/Supervision:*** *Burak Bayram, Kenan Aral;* ***Data Collection and/or Processing:*** *Nur Altıparmak, Burak Bayram, Kenan Aral;* ***Analysis and/or Interpretation:*** *Sıdıka Sinem Akdeniz, Nur Altıparmak;* ***Literature Review:*** *Sıdıka Sinem Akdeniz, Nur Altıparmak;* ***Writing the Article:*** *Sıdıka Sinem Akdeniz, Nur Altıparmak;* ***Critical Review:*** *Sıdıka Sinem Akdeniz, Nur Altıparmak;* ***References and Fundings:****Sıdıka Sinem Akdeniz, Nur Altıparmak;* ***Materials:*** *Nur Altıparmak.*

REFERENCES

1. Aframian DJ, Lalla RV, Peterson DE. Management of dental patients taking common hemostasis-altering medication. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103 Suppl S45):e1-11. [Crossref] [PubMed]
2. Madrid C, Sanz M. What influence do anticoagulants have on oral implant therapy? A systematic review. Clin Oral Implants Res. 2009;20 Suppl 4:96-106. [Crossref] [PubMed]
3. Lim W, Wang M, Crowther M, Douketis J. The management of anticoagulated patients requiring dental extraction: a cross-sectional survey of oral and maxillofacial surgeons and hematologists. J Thromb Haemost. 2007;5(10):2157-9. [Crossref] [PubMed]
4. Murphy J, Twohig E, McWilliams SR. Dentists' approach to patients on anti-platelet agents and warfarin: a survey of practice. J Ir Dent Assoc. 2009;56(1):28-31.
5. Alcock RF, Naoum C, Aliprandi-Costa B, Hillis GS, Brieger DB. The peri-operative management of anti-platelet therapy in elective, non-cardiac surgery. Int J Cardiol. 2013;167(2):374-7. [Crossref] [PubMed]
6. Daruwalla SF, Sidana S. Current evidence-based management of patients on anti-platelets and anticoagulants in dental practice: a questionnaire-based survey of interns and staff. J Contemp Dent. 2014;4(1):22-6. [Crossref]
7. Sadhasivam G, Bhushan S, Chiang KC, Agarwal N, Vasundhar PL. Clinical trial evaluating the risk of thromboembolic events during dental extractions. J Maxillofac Oral Surg. 2016;15(4):506-11. [Crossref] [PubMed] [PMC]
8. Lu SY, Tsai CY, Lin LH, Lu SN. Dental extraction without stopping single or dual antiplatelet therapy: results of a retrospective cohort study. Int J Oral Maxillofac Surg. 2016;45(10):1293-8. [Crossref] [PubMed]
9. Davis BR, Sándor GK. Use of fibrin glue in maxillofacial surgery. J Otolaryngol. 1998; 27(2):107-12.
10. Baykul T, Alanoglu EG, Kocer G. Use of Ankaferd Blood Stopper as a hemostatic agent: a clinical experience. J Contemp Dent Pract. 2010;11(1):E088-94.
11. Meves SH, Neubauer H, Overbeck U, Endres HG. Is there an ideal way to initiate antiplatelet therapy with asetil salisilik asit? A crossover study on healthy volunteers evaluating different dosing schemes with whole blood aggregometry. BMC Res Notes. 2011;4(1):106. [Crossref] [PubMed] [PMC]
12. Sonksen JR, Kong KL, Holder R. Magnitude and time course of impaired primary hemostasis after stopping chronic low and medium dose asetil salisilik asit in healthy volunteers. Br J Anaesth. 1999;82(3):360-5. [Crossref] [PubMed]
13. Ferrari E, Benhamou M, Cerboni P, Marcel B. Coronary syndromes following asetil salisilik asit withdrawal: a special risk for late stent thrombosis. J Am Coll Cardiol. 2005;45(3): 456-9. [Crossref] [PubMed]
14. Rodríguez LA, Cea-Soriano L, Martín-Merino E, Johansson D. Discontinuation of low dose aspirin and risk of myocardial infarction: case-control study in UK primary care. BMJ. 2011;343(19):4094. [Crossref] [PubMed] [PMC]
15. Napeñas JJ, Hong CH, Brennan MT, Furney SL, Fox PC, Lockhart PB. The frequency of bleeding complications after invasive dental treatment in patients receiving single and dual antiplatelet therapy. J Am Dent Assoc. 2009;140(6):690-5. [Crossref]
16. Olmos-Carrasco O, Pastor-Ramos V, Espinilla-Blanco R, Otiz-Zárate A, García-Avila I, Rodríguez-Alonso E, et al. Hemorrhagic complications of dental extractions in 181 patients undergoing double antiplatelet therapy. J Oral Maxillofac Surg. 2015;73(2):203-10. [Crossref] [PubMed]
17. Krishnan B, Shenoy NA, Alexander M. Exodontia and antiplatelet therapy. J Oral Maxillofac Surg. 2008;66(10):2063-6. [Crossref] [PubMed]
18. Lillis T, Ziakas A, Koskinas K, Tsirlis A, Giannoglou G. Safety of dental extractions during uninterrupted single or dual antiplatelet treatment. Am J Cardiol. 2011;108(7): 964-7. [Crossref] [PubMed]
19. Mingarro-De-León A, Chaveli-López B, Gavaldá-Esteve C. Dental management of patients receiving anticoagulant and/or antiplatelet treatment. J Clin Exper Dent. 2014;6(2):155-61. [Crossref] [PubMed] [PMC]
20. van Diermen DE, van der Waal I, Hoogstraten J. Management recommendations for invasive dental treatment in patients using oral antithrombotic medication, including novel oral anticoagulants. Oral Surg Oral Med Oral Pathol Oral Radiol. 2013;116(6):709-16. [Crossref] [PubMed]