Risk of Uncontrolled Bleeding after Oral Surgical Procedures Attributed to Chronic Conditions and Antiplatelet Therapy: a Practice-Based Analysis of Patients Attending a District Hospital in Thailand

ความเสี่ยงต่อภาวะเลือดออกไม่หยุดจากหัตถการผ่าตัดในช่องปาก ของผู้ป่วยที่มีภาวะเรื้อรัง และการใช้ยาต้านเกล็ดเลือด การศึกษา ตามบริบทการให้บริการของโรงพยาบาลชุมชนแห่งหนึ่งในประเทศไทย

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ABSTRACT

Objective: To measure risk of immediate and late-onset bleeding complication after oral surgical procedures in patients with chronic conditions and continued antiplatelet therapy compared to other patients without the antiplatelet therapy.

Methods: This study adopted retrospective cohort data collection approach which analyzed 2,723 Thai adult dental patients–aged 30 years old and over–undergoing oral surgical treatments from October 2011 to September 2015 at Phutthamonthon Hospital. Based on past record of medication and history taking on dental visit, patients were categorized as index group receiving continued low-dose aspirin (≤162 mg/day) and referent group without the antiplatelet therapy. Immediate and late-onset bleeding complication was an outcome. Measurable confounders in this clinical context included age, sex, numbers of teeth extracted, surgical procedures, dental arches (maxilla, mandible), positions of teeth, operators, and major diagnoses of underlying chronic diseases. All data were recorded according to time of the first visit for oral surgical service of each patient within the specified data collection period. To measure risk of uncontrolled bleeding attributed to existing chronic conditions and antiplatelet therapy, risk ratio was estimated by using generalized linear model for risk ratio regression.

Results: Cumulative incidences of bleeding complication were not significantly different between the two groups (index 2.4%, reference 1.7%, p=0.437). After adjusting for potential confounders, estimated risk of uncontrolled bleeding attributed to underlying chronic conditions and antiplatelet therapy of patients in the index was higher than the risk among those in the reference, though not statistically significant (RR=2.3, 95% CI=0.8 to 6.4, p=0.113).

Conclusion: Higher risk of bleeding was identified among patients with underlying chronic conditions and continued antiplatelet therapy in this study. Although the risk was not statistically significant, oral surgical procedures should still be cautiously provided. Attempt to limit trauma extent during procedure and well-prepared hemostatic measures without suspension of antiplatelet therapy were recommended.

Keywords: oral surgery, antiplatelet therapy, aspirin, bleeding risk

บทคัดย่อ

วัตถุประสงค์: เพื่อระบุความเสี่ยงการเกิดภาวะเลือดออกไม่หยุด ทั้งที่เกิดทันทีและภายหลังหัตถการผ่าตัดในช่องปาก ในผู้ป่วยที่มีภาวะเรื้อรังและใช้ยาต้านเกล็ดเลือด โดยไม่หยุดก่อนทำหัตถการเปรียบเทียบกับผู้ป่วยอื่นๆ ที่ไม่มีการใช้ยาต้านเกล็ดเลือด

วิธีการศึกษา: การศึกษานี้ใช้รูปแบบการเก็บข้อมูลจากเหตุไปหาผลซึ่งเหตุการณ์เกิดในอดีต (retrospective cohort data collection approach) โดยรวบรวมข้อมูลผู้ป่วยชาวไทย จำนวน 2,723 ราย อายุ 30 ปีขึ้นไป ที่ได้รับหัตถการผ่าตัดในช่องปากในช่วงเดือน ตุลาคม พ.ศ. 2554 ถึง กันยายน 2558 ณ โรงพยาบาลพุทธมณฑล จังหวัดนครปฐม จากข้อมูลผู้ป่วยแต่ละรายที่มารับบริการหัตถการผ่าตัดช่องปากครั้งแรกในช่วงเวลาดังกล่าว สามารถจำแนกผู้ป่วยตามบันทึกการใช้ยาต้านเกล็ดเลือด และข้อมูลการซักประวัติในวันที่ให้บริการทันตกรรมได้เป็นสองกลุ่มคือ กลุ่มศึกษา (index) ที่มีภาวะเรื้อรังหรือมีความเสี่ยงสูงและมีการใช้ยา aspirin ไม่เกิน 162 มก.ต่อวัน โดยไม่หยุดยาก่อนหัตถการ และกลุ่มเปรียบเทียบ (reference) ที่เป็นผู้ป่วยอื่นๆ และไม่มีการใช้ยา aspirin ภาวะเลือดออกไม่หยุดทันทีและหลังหัตถการเป็นผลลัพธ์ทางคลินิกที่สนใจ ตัวแปรกวนที่สามารถวัดได้ของผู้ป่วยตามบริบททางคลินิกของสถานบริการนี้ประกอบด้วย อายุ เพศ จำนวนซี่ฟันที่ถอนหรือผ่า ชนิดหัตถการผ่าตัดช่องปาก ขากรรไกร (maxilla, mandible) ตำแหน่งฟัน ผู้ให้บริการ และภาวะโรคเรื้อรังที่แพทย์เป็นผู้วินิจฉัย ใช้ risk ratio ระบุความเสี่ยงซึ่งวิเคราะห์โดย generalized linear model สำหรับ risk ratio regression

ผลการศึกษา: อุบัติการณ์สะสมของภาวะเลือดออกไม่หยุดเมื่อเปรียบเทียบสองกลุ่มไม่แตกต่างกันทางสถิติ (Index 2.4%, Reference 1.7%, p=0.437) เมื่อควบคุมอิทธิพลของตัวแปรกวนสามารถระบุว่าผู้ป่วยที่มีภาวะเรื้อรัง และใช้ยาต้านเกล็ดเลือดโดยไม่หยุดก่อนหัตถการมีความเสี่ยงต่อการเกิดภาวะเลือดออกไม่หยุดสูงกว่าเมื่อเทียบกับผู้ป่วยอื่นๆ ที่ไม่ใช้ยา aspirin อย่างไม่มีนัยสำคัญทางสถิติ ในบริบทการให้บริการแห่งนี้ (RR=2.3, 95% CI 0.8-6.4, p=0.113)

ข้อสรุป: การศึกษาในบริบทนี้ระบุความเสี่ยงต่อภาวะเลือดออกไม่หยุดที่เพิ่มขึ้นในผู้ป่วยที่มีภาวะเรื้อรังและมีการใช้ยาต้านเกล็ดเลือดโดยไม่หยุดก่อนทำหัตถการผ่าตัดในช่องปากเมื่อเทียบกับผู้ป่วยอื่นๆ แม้จะไม่มีนัยสำคัญทางสถิติแต่หัตถการผ่าตัดช่องปากก็ยังจำเป็นต้องทำอย่างระมัดระวัง โดยพยายามจำกัดการบาดเจ็บของเนื้อเยื่อระหว่างทำหัตถการ และมีการเตรียมมาตรการห้ามเลือดโดยไม่จำเป็นต้องหยุดใช้ยาต้านเกล็ดเลือด

คำสำคัญ: การผ่าตัดในช่องปาก ยาต้านเกล็ดเลือด แอสไพริน ความเสี่ยงภาวะเลือดออกไม่หยุด

Introduction

A growing number of Thai dental patients with underlying chronic diseases and conditions; such as diabetes mellitus, hypertension, dyslipidemia, and others; and being indicated for antiplatelet therapy by medical doctors have been observed by dental professionals providing routine oral surgical services at Phutthamonthon Hospital–a district hospital setting. In consideration of rational dental management for these patients undergoing oral surgical procedures, an issue of hemorrhagic complication attributed to the existing chronic diseases or conditions along with the indication of antiplatelet therapy has been raised.

According to relevant evidences currently reported in scientific literature, controversy regarding the risk of uncontrolled bleeding still exists. A latest meta-analysis has concluded that bleeding time could be prolonged and hemorrhagic complication could be exacerbated due to long-term use of aspirin.[1] Nonetheless, the study did not recommend suspension of the aspirin use before dental extraction but to enhance hemostatic measures.[1] Such recommendation that low-dose aspirin therapy should not be discontinued for minor oral surgical procedures[1] was still consistent with other clinical studies[2,3] and recent review articles.[4-10] It should be remarked, anyway, that the meta-analysis[1] included only randomized and non-randomized controlled trials[1]; excluding evidences from observational studies. In contrast; a recent review[11], a few clinical trials[12,13], and other observational studies[14-17]; indicated no clinically significant increase in risk of hemorrhagic complication after invasive oral surgical procedures in patients either on single or dual antiplatelet therapy. A study focused on the risk of bleeding after periodontal treatment in patients on antithrombotic therapy had determined that the treatment could be provided safely in such patient domain.[18]

Nevertheless, evidence regarding the risk of hemorrhagic complication from 'real world' practice of oral surgical care was still scarce and none of those previously-summarized studies was conducted to indicate the risk in Thai dental patients. The risk of hemorrhagic complication attributed to the pre-existing chronic diseases or conditions along with the indication of antiplatelet therapy in Thai patients remained the knowledge gap to be investigated. To assess the current practice paradigm allowing provision of oral surgical procedures in patients with chronic conditions and continued antiplatelet therapy–assuming relatively similar risk of hemorrhage as that of other patients–was still important for evidence-based patient management and patient

safety. The purpose of this study was therefore to measure the risk of immediate and late-onset bleeding complication attributed to underlying chronic conditions and continued antiplatelet therapy of Thai patients undergoing oral surgical procedures.

Methods

This study retrospectively analyzed all Thai adult dental patients undergoing oral surgical treatments from October 2011 to September 2015 at Phutthamonthon Hospital, a 30-bed district hospital under authority of Ministry of Public Health in Nakhon Pathom, Thailand. Eligible patients were those registered in the hospital registry and could be verified by civil registration system as having permanent residences in the main serviced area–Phutthamonthon District–and adjacent areas in other districts; including Nakhon Chai Si and Sam Phran Districts of Nakhon Pathom, and Thawiwatthana District of Bangkok. The inclusion based on permanent residence was in attempt to ensure a level of homogeneity of patients whom result of this study could be generalized to. Eligible patients aged 30 years old and over were included in analysis according to common regimen of adult low-dose aspirin therapy–not exceeding 162 mg/day (81 mg., 1-2 tablets)–for primary prevention of cardiovascular diseases and secondary prevention of thromboembolic events in this setting. Only single antiplatelet treatment by using aspirin was considered in this study, since dual antiplatelet therapy by additional use of clopidogrel was rarely indicated in this facility. The study finally included 2,723 patients in analysis.

This study adopted retrospective cohort data collection approach, ascertaining major exposure and related confounders which well preceded the outcome. Regarding major exposure ascertainment, aspirin use was assured by tracking computerized record of previous prescription by medical doctors within the same year before dental treatment date and reascertained by routine history taking on visit date. According to their records of medication and history taking on dental visit, patients were categorized as index group receiving uninterrupted aspirin therapy and referent group receiving no antiplatelet therapy [Index: patients at high risk of cardiovascular diseases or with existing chronic diseases and all receiving aspirin; Reference: all other patients without aspirin therapy]. This categorization was based on treatment protocol in this setting that aspirin therapy was not interrupted prior to dental surgical procedures. This study was thus not designed to measure relative risk of continued versus interrupted antiplatelet therapy, which was not clinically relevant by practice in this setting.

Oral surgical procedures were classified into 3 categories: a) removal of plaque and calculus by means of full-mouth scaling and localized alveoloplasty by the use of bone files or bone rongeur forceps; b) simple extraction or removal of a single tooth without elevation of periosteal flap–including simple extraction of erupted third molar if applicable, and compound procedures including removal of a few teeth (not exceeding 3 teeth) which might involve minor alveoloplasty; c) surgical removal of partially-erupted impacted teeth which might require elevation of periosteal flap and removal of adjacent alveolar bone during surgery–service of surgical removal of embedded tooth was not available at this facility. Most patients were treated in the morning service session, except for those appointed for surgical

removal of impacted teeth in the afternoon. All maxillary teeth were extracted under local anesthetic injection in labial or buccal aspects on the outer side and palatal aspect on the inner side of teeth. Posterior alveolar nerve block together with buccal and lingual anesthetic infiltration was administered for extraction of mandibular teeth. Use 1.8 ml of 2% lidocaine solution with epinephrine 1:100,000 was typical for all extractions or surgical removal which ensured the same hemostatic effect of epinephrine. Wound management was primarily undertaken by instructing patients to bite tightly on gauze packing. Immediate and late-onset bleeding complication was outcome of interest. Immediate hemorrhage was determined by clinical manifestation of uncontrolled bleeding along with decisions of operators to control bleeding by either suturing or use of sterile compressed sponge (Gelfoam®) or both. Late-onset complication was determined by returning to hospital for management of bleeding anytime thereafter. All patients were informed to revisit the dental office if any complications occurred. For those who underwent extractions and surgical removal of impacted teeth, appropriate instruction was given right after local anesthetic administration.

Variables considered as potential confounders in this clinical context included age, sex, numbers of teeth extracted, procedures, dental arches (maxilla, mandible), positions of teeth (anterior, premolar, molar), operators, and major clinical diagnoses of underlying disease (diabetes mellitus, hypertension, cardiovascular diseases). Data of all variables–exposure, outcome, and potential confounders–were recorded according to the time of the first visit for oral surgical service of each patient within the specified period of data collection. By the restriction to the first dental visit for each patient; later change in general health condition (e.g., from non-disease status to disease status), subsequent disease progression, and cumulative effect of medication overtime were not considered. The relevant data were obtained from electronic health record (EHR) of the hospital information system (HOSxP).

Descriptive statistics were used to summarize clinical characteristics of patients in each group. To measure risk of uncontrolled bleeding attributed to antiplatelet therapy and chronic condition, risk ratio was specified as effect measure and estimated by generalized linear model for risk ratio regression. Explanatory modeling strategy was adopted to estimate effect of the major exposure on the outcome with control of the measurable confounders mentioned earlier through the model.

This study protocol was approved by Ethical Review Committee for Human Research, Faculty of Public Health, Mahidol University.

Results

Proportions of male to female patients in the two groups were not significantly different ($p=0.586$). Mean age of patients in the index group (61.4±10.2) was significantly higher than that of the patients in the reference (50.2±12.4), $p<0.001$. Major diagnoses of chronic diseases including diabetes mellitus and hypertension were significantly in much greater proportions among those in the index group (diabetes mellitus: index 66.5%, reference 7.2%, $p<0.001$; hypertension: index 25.8%, reference 14.8%, $p<0.001$). A few cases with diagnoses of cardiovascular diseases were found similarly in both groups ($p=0.069$). Mean number of extracted teeth was higher in the index ($p<0.001$). Positions involved in surgical

treatments were significantly different between groups (p=0.001). Proportions of oral surgical procedures in the two comparing groups were also significantly different (<0.001). None of the patients in the index group received localized alveoloplasty and surgical removal of impacted tooth. Proportions of cases categorized by service providers–dentist and dental hygienist–were relatively the same in both groups (p=0.284). (Table 1)

Table 1 Clinical characteristics of adult patients underwent minor oral surgical procedures

Clinical characteristics	Index group n=248		Referent group n=2,475		P-value
	n	%	n	%	
Sex					
Male	103	41.5	981	39.6	0.586†
Female	145	58.5	1,494	60.4	
Age					
Mean ± S.D.	61.4	10.2	50.2	12.4	<0.001‡
Min. – Max.	32	85	30	93	
30-49	30	12.1	1,273	51.4	
50-69	162	65.3	1,002	40.5	
≥70	56	22.6	200	8.1	
Major chronic disease					
Diabetes mellitus					
Yes	165	66.5	178	7.2	<0.001†
No	83	33.5	2,297	92.8	
Hypertension					
Yes	64	25.8	367	14.8	<0.001†
No	184	74.2	2,108	85.2	
Cardiovascular disease					
Yes	2	0.8	3	0.1	0.069†
No	246	99.2	2,472	99.9	
Number of extracted teeth					
Mean ± S.D.	1.0	0.6	0.8	0.6	<0.001‡
0 (in cases of scaling and alveoloplasty)	39	15.7	617	24.9	
1	180	72.6	1,649	66.6	
2	26	10.5	189	7.6	
3	3	1.2	20	0.9	
Main position of teeth involved					
Full mouth	5	2.0	36	1.5	0.001†
Anterior teeth	91	36.7	971	39.2	
Premolar	70	28.2	439	17.7	
Molar	82	33.1	1,029	41.6	
Oral surgical procedure					
Scaling	37	14.9	600	24.2	0.001†
Localized alveoloplasty	0	0.0	1	0.1	
Extraction	211	85.1	1,852	74.8	
Surgical removal of impacted tooth	0	0.0	22	0.9	
Service provider					
Dentist	213	85.9	2,057	83.1	0.284†
Dental hygienist	35	14.1	418	16.9	

† Exact probability test, ‡ Independent samples t-test

Cumulative incidences of bleeding complication in the period of October 2011 to September 2015 was not significantly different between the two groups (index 2.4%, reference 1.7%, p= 0.437). After adjusting for potential confounders, generalized linear model estimated the risk of bleeding complication attributed to underlying chronic conditions and antiplatelet therapy of patients in the index group to be 2.3 times more likely than the risk of those in the reference, though not statistically significant. (Table 2)

Table 2 Occurrence of bleeding complication and comparative risk attributed to antiplatelet therapy and underlying chronic conditions

Outcome features	Index group n=248		Referent group n=2,475		Risk ratio	95% CI	P-value
	n	%	n	%			
Bleeding event	6	2.4*	41	1.7*	1.5†	0.6, 3.4†	0.379†
					2.3‡	0.8, 6.4‡	0.113‡
Hemostatic measures indicating bleeding event							
Need suturing	5	2.0	28	1.1			
Need Gelfoam®	1	0.4	8	0.3			
Need both	0	0.0	4	0.2			

* Cumulative incidence of bleeding complication among patients attending care from October 2011 to September 2015;
† Crude estimates; ‡ Estimates adjusted for sex, age, number of extracted teeth, dental arch being treated, main position of teeth involved, oral surgical procedure, diabetes mellitus, and hypertension by risk ratio regression

Discussion

In this practice-based study, higher risk of hemorrhagic complication after oral surgical procedures in Thai dental patients with underlying chronic conditions and uninterrupted aspirin therapy compared to other patients was identified, though not statistically significant. This finding was consistent with another observational study[3] which estimated risk ratio of bleeding complication in patients on aspirin alone versus patients without antiplatelet therapy in Greece (RR=6.3, 95%CI 0.6 to 68.4, p=0.2). The estimated risk ratios in both studies were clinical evidences which still called for awareness to cautiously provide surgical procedures for such patient domain and this key message should not be ignored by statistical insignificance. In addition, the study[3] consistently found prolonged bleeding in need of proper hemostatic treatment in 2.4% of patients on aspirin. Based on these practice-based evidences, it was therefore recommended that service providers should attempt to limit extent of tissue trauma during surgical procedures. Hemostatic measures should be planned for prompt action if immediate bleeding occurred. Surveillance of late-onset hemorrhagic complication by

patients could be achieved through well-given postoperative instruction and emergency contact information.

Cumulative incidences of bleeding complication of both groups in this study were not significantly different (Index=2.4%, Reference=1.7%, p=0.437 by exact probability test). Such incidences were relatively minute, given a long accrual period. Finding of the limited incidence of bleeding complication was consistent with other observational studies.[3,15,17] Local hemostatic measures, such as suturing, were consistently found sufficient to control bleeding complication once occurred.[3,15,17] None of the patients receiving scaling or alveoloplasty in this study developed bleeding complication. Such finding was in accordance with previous study indicating that scaling could be safely provided for patients on aspirin.[18] Severe or life-threating bleeding complication attributed to chronic condition and aspirin use was neither found in this study nor other articles reviewed herein.[1-18]

It must be noted that result of this study did not determine the direct effect of antiplatelet therapy on the risk of bleeding complication. As mentioned in the method, since suspension of antiplatelet therapy during oral surgical procedures was no longer practiced in this setting, patients with relatively the same underlying chronic condition who discontinued the use of aspirin during oral surgical procedures could not be obtained. Patients in the referent group of this study were thus generally healthier than those in the index group. Nonetheless, this should not be viewed as bias in control selection since the focus of this study was centered around evaluating the current practice paradigm allowing provision of oral surgical procedures in patients of the index group, assuming relatively similar risk of hemorrhage as that of other patients.

This study has benefited to provide information on risk of hemorrhagic complication in Thai patients undergoing oral surgical procedures from the real practice. The use of risk ratio regression which adopted explanatory modeling strategy–with control of measurable confounders or alternative explanation for the outcome occurrence–was an initiative to apply epidemiological approach to determine clinical effect for further decision making to provide optimal patient care. Further study on influence of other antiplatelet or anticoagulant therapies on bleeding complication following oral surgical procedures should be undertaken. Practice-based study on larger population was also suggested.

Conflict of interest

Authors declared that there was no conflict of interest.

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References

1. Zhao B, Wang P, Dong Y, et al. Should aspirin be stopped before tooth extraction? A meta-analysis. Oral Surg Oral Med Oral Pathol Oral Radiol 2015;119(5):522-30.
2. Girotra C, Padhye M, Mandlik G, et al. Assessment of the risk of hemorrhage and its control following minor oral surgical procedures in patients on anti-platelet therapy: a prospective study. Int J Oral Maxillofac Surg 2014;43(1):99-106.

3. Lillis T, Ziakas A, Koskinas K, et al. Safety of dental extractions during uninterrupted single or dual antiplatelet treatment. Am J Cardiol 2011;108(7):964-7.
4. Brennan MT, Wynn RL, Miller CS. Aspirin and bleeding in dentistry: an update and recommendations. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104(3):316-23.
5. Verma G. Dental extraction can be performed safely in patients on aspirin therapy: a timely reminder. ISRN Dentistry 2014;2014:1-11.
6. Mingarro-de-Leon A, Chaveli-Lopez B, Gavalda-Esteve C. Dental management of patients receiving anticoagulant and/or antiplatelet treatment. J Clin Exp Dent 2014;e155-61.
7. Doonquah L, Mitchell A. Oral surgery for patients on anticoagulant therapy: current thoughts on patient management. Dent Clin N Am 2012;56(1):25-41.
8. Carrizo A, Carrasco D. Oral surgery in patients under antithrombotic therapy. Narrative review. J Oral Res 2015;4(1):58-64.
9. Aframian D, Lalla R, Peterson D. Management of dental patients taking common hemostasis-altering medications. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103:S45.e1-e11.
10. Wahl M. Dental surgery and antiplatelet agents: bleed or die. Am J Med 2014;127(4):260-7.
11. Napeñas JJ, Oost FC, DeGroot A, et al. Review of postoperative bleeding risk in dental patients on antiplatelet therapy. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;115(4):491-9.
12. Campbell J, Alvarado F, Murray R. Anticoagulation and minor oral surgery: Should the anticoagulation regimen be altered?. J Oral Maxillofac Surg 2000;58(2):131-5.
13. Verma G, Tiwari A, Chopra S. Aspirin and exodontia: a comparative study of bleeding complications with aspirin therapy. Int J Dent Sci Res 2013;1(2):50-3.
14. Partridge C, Campbell J, Alvarado F. The effect of platelet-altering medications on bleeding from minor oral surgery procedures. J Oral Maxillofac Surg 2008;66(1):93-7.
15. Broekema F, van Minnen B, Jansma J, et al. Risk of bleeding after dentoalveolar surgery in patients taking anticoagulants. Br J Oral Maxillofac Surg 2014;52(3):e15-e9.
16. Canigral A, Silvestre F, Canigral G, et al. Evaluation of bleeding risk and measurement methods in dental patients. Med Oral Patol Oral Cir Bucal 2010;15:e863-8.
17. Madan G, Madan S, Madan G, et al. Minor oral surgery without stopping daily low-dose aspirin therapy: a study of 51 patients. J Oral Maxillofac Surg 2005;63(9):1262-5.
18. Morimoto Y, Niwa H, Minematsu K. Hemostatic management for periodontal treatments in patients on oral antithrombotic therapy: a retrospective study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108(6):889-96.