Comparative Risk of Bleeding Complication Following Oral Surgical Procedures Between Patients with Continued Aspirin Use Versus Those Without Aspirin Use

ความเสี่ยงของการมีเลือดออก ภายหลังหัตถการผ่าตัดในช่องปาก เปรียบเทียบระหว่างผู้ป่วยที่ไม่หยุดยาแอสไพรินก่อนหัตถการ และผู้ป่วยที่ไม่ใช้ยาแอสไพริน

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ABSTRACT

Objective: To compare risk of bleeding complication following provision of oral surgical procedures in Thai patients with and without aspirin therapy attending public dental service at a district hospital.

Methods: The retrospective cohort approach was adopted using archived routine clinical data of 2,907 consecutive adult patients receiving oral surgical procedures from January 1, 2013 to December 31, 2015 at Huayploo Hospital. The patients were categorized into “index group” receiving continued low-dose aspirin (81 - 300 mg) and “referent group”–not using aspirin. Relative risk of bleeding complication attributed to index group compared to referent group was estimated by generalized linear model for risk ratio regression, controlling for other potential confounders as sex, age, service provider, underlying chronic diseases, involved dental arch, oral surgical procedures, and major dental position in dental arch.

Results: The study found only minor bleeding those could be stopped with local hemostatic measures. The late-onset bleeding was not found. Cumulative incidence of immediate-onset bleeding among patients in the index was 6.6%, which was higher than 0.8% observed in the reference ($p<0.001$).

After adjusting for potential confounders, multivariable analysis estimated that patients in the index group were 6.4 times more likely to have minor bleeding complication to the reference (RR=6.4, 95% CI=2.5 to 16.4, p<0.001).

Conclusion: Clinically significant increase in bleeding risk was observed in patients with underlying chronic condition and uninterrupted aspirin therapy. Nonetheless, oral surgical procedures could be safely performed when close monitoring and local hemostatic measures were well prepared without need to discontinue the aspirin therapy.

Keywords : bleeding, aspirin, oral surgery, oral epidemiology

บทคัดย่อ

วัตถุประสงค์: เพื่อเปรียบเทียบความเสี่ยงของการมีเลือดออก ภายหลังหัตถการผ่าตัดในช่องปากของผู้ป่วยไทย กลุ่มที่ไม่หยุดยาแอสไพรินก่อนหัตถการ เทียบกับกลุ่มที่ไม่ใช้ยาแอสไพริน ที่รับการรักษาโดยกลุ่มงานทันตกรรม โรงพยาบาลชุมชนแห่งหนึ่ง

วิธีการศึกษา: การศึกษารวบรวมข้อมูลจากเหตุไปหาผล ซึ่งเหตุการณ์เกิดในอดีต โดยใช้ข้อมูลทางคลินิกของผู้ป่วยวัยผู้ใหญ่จำนวน 2,907 คน ที่มารับบริการผ่าตัดช่องปากตามลำดับต่อเนื่องกัน ระหว่าง 1 มกราคม พ.ศ. 2556 ถึง 31 ธันวาคม พ.ศ. 2558 ณ โรงพยาบาลห้วยพลู จังหวัดนครปฐม โดยผู้ป่วยจะถูกจำแนกเป็น “กลุ่มศึกษา” ซึ่งไม่หยุดใช้ยาแอสไพรินก่อนหัตถการ และ “กลุ่มเปรียบเทียบ” ซึ่งไม่มีการใช้ยาแอสไพริน ความเสี่ยงสัมพัทธ์ของการมีเลือดออกในกลุ่มศึกษาเทียบกับกลุ่มเปรียบเทียบ วิเคราะห์โดยตัวแบบเชิงเส้นนัยทั่วไป เพื่อประมาณค่าอัตราเสี่ยงที่มีการควบคุมปัจจัยกวนด้าน เพศ อายุ ผู้ให้บริการ ภาวะโรคเรื้อรังขากรรไกรที่เกี่ยวข้อง ชนิดหัตถการผ่าตัดในช่องปาก และตำแหน่งฟัน

ผลการศึกษา: พบการมีเลือดออกที่ไม่รุนแรง และสามารถควบคุมได้ด้วยมาตรการห้ามเลือดเฉพาะที่ ไม่พบการมีเลือดออกที่เกิดขึ้นช้าภายหลังหัตถการ อุบัติการณ์สะสมของการมีเลือดออกที่เกิดขึ้นทันทีในผู้ป่วยกลุ่มศึกษาเท่ากับร้อยละ 6.6 ซึ่งสูงกว่าร้อยละ 0.8 ที่พบในกลุ่มเปรียบเทียบอย่างมีนัยสำคัญทางสถิติ (p<0.001) เมื่อปรับอิทธิพลของตัวแปรกวน ผู้ป่วยในกลุ่มศึกษาจะเสี่ยงต่อการมีเลือดออกหลังทำหัตถการประมาณ 6.4 เท่า เมื่อเทียบกับกลุ่มเปรียบเทียบ อย่างมีนัยสำคัญทางสถิติ (RR=6.4, 95% CI=2.5 to 16.4, p<0.001)

สรุป: การศึกษาในบริบทนี้ ระบุความเสี่ยงต่อการมีเลือดออกที่เพิ่มขึ้นในผู้ป่วยที่มีภาวะเรื้อรัง และไม่หยุดยาแอสไพรินก่อนทำหัตถการผ่าตัดในช่องปาก แต่อย่างไรก็ตามหัตถการดังกล่าวสามารถทำได้อย่างปลอดภัยด้วยความระมัดระวัง การติดตามผู้ป่วยอย่างใกล้ชิด และมีการเตรียมมาตรการห้ามเลือดที่ดี โดยไม่จำเป็นต้องหยุดยาแอสไพริน

คำสำคัญ : การมีเลือดออก แอสไพริน การผ่าตัดในช่องปาก ระบาดวิทยาโรคช่องปาก

Introduction

Decision to provide oral surgical procedures to patients without interruption of antiplatelet therapy has recently been driven by several evidences reported in scientific literatures. A review summarizing evidences from many primary studies provided a consensus that simple extraction could be performed safely without need to discontinue antiplatelet therapy since prolonged postoperative bleeding was uncommon.[1] Another recent review immensely supported this notion by its conclusion that invasive dental procedures did not significantly impose greater risk of postoperative bleeding complication in patients with single or dual antiplatelet therapy.[2] Several clinical studies, including clinical trial and analytical studies (e.g., prospective cohort study), also suggested that the risk of uncontrolled bleeding would not be increasingly modified by continuation of the therapy.[3-7]

Nonetheless, a recent meta - analysis contrastively concluded that long - term use of aspirin could potentially lengthen bleeding time and exacerbate postoperative bleeding.[8] A review also added to this contradiction by suggesting that postoperative bleeding risk following minor oral surgery should not be assumed equal for different individuals with antiplatelet therapy and individualized risk assessment should be considered to balance risk of postoperative bleeding and thromboembolic complication from discontinuation of antiplatelet therapy.[9] Discontinuation of antiplatelet therapy was additionally suggested to be considered on case - by - case basis since different patients would carry different risk of bleeding and thrombosis.[10]

Based on these reviewed evidences, controversy regarding risk of bleeding complication modified by uninterrupted antiplatelet therapy still existed. A major issue was whether risk of bleeding complication could be rationally assumed equivalent when dental patients with underlying chronic condition and indicated use of low - dose aspirin prophylaxis were compared to general dental patients - who might be relatively healthier - without need of such antiplatelet therapy. This issue has been appealing for investigation since interruption of antiplatelet therapy was no longer encouraged in current practice and clinical consideration went far beyond comparing effect of continued antiplatelet therapy to its discontinuation within the homogenous domain of patients with indicated use of such therapy. Furthermore, evidences from practice - based analysis, which would reflect bleeding risk in reality, of Thai patients attending dental care at district hospitals - which are major public dental service providers throughout the country - were scarce. This study therefore aimed to measure comparative risk of immediate - and late - onset bleeding complication following provision of oral surgical treatments in Thai patients with and without antiplatelet therapy attending public dental service at a district hospital.

Methods

This study employed retrospective cohort data collection approach by retrospectively ascertaining patients' clinical characteristics and procedural details of oral surgical interventions which preceded and potentially influenced occurrence of prolonged immediate - and late-onset bleeding. All 2,907 consecutive adult dental patients - aged 20 years old and over - undergoing oral surgical procedures at Huayploo Hospital from 1 January 2013 to 31 December 2015 were included. The inclusion of all consecutive patients has previously been illustrated in a clinical study.[11] By considering clinical factors of each patient at the first visit for minor oral surgical treatment in the specified accrual period of data collection, probability of outcome occurrence (bleeding) was therefore similarly evaluated between comparison groups. Issues related to subsequent visits; including intrapersonal correlation of bleeding risk, cumulative effect of antiplatelet therapy over time, dynamic change of systemic condition (e.g., shift from healthy to diseased status), and later disease progression; were thus beyond the scope of this analysis.

Regarding study setting, Dental Department of Huayploo Hospital - a 60 - bed district health facility in Nakhon Chaisri, Nakhon Pathom - provided public dental services under authority of Ministry of Public Health. Thai patients in this analysis were verified through hospital registry which based its registration on personal identification in official civil registration system. This analysis was therefore planned to generalize its result to Thai patients attending care at this facility and other similar settings with comparable patient domain. Adult low - dose aspirin (81 - 300 mg) was a regimen commonly indicated for prevention of thrombotic event in patients with chronic diseases (e.g., diabetes mellitus, cardiovascular disease) in this setting. The aspirin therapy - a major exposure of interest - was ascertained through electronic record of physician's prescription in the relevant period prior to oral surgical procedure and was reassured by routine history taking prior to procedure on the dental visit. Present and absence of aspirin use was specified as patient cohort's point of departure, dividing the pool of patients into two comparison groups: index and reference. Index group included patients with aspirin therapy while referent group included the counterpart without aspirin use. In other words, patients with underlying chronic condition and indicated use of low - dose aspirin prophylaxis (index group) were compared to general dental patients - who might be relatively healthier - without need of such antiplatelet therapy (referent group). This was due to the fact that interruption of antiplatelet therapy prior to oral surgical procedures was no longer practiced in this context by the time of this study. This study was therefore not designed to directly measure comparative bleeding risk of uninterrupted versus interrupted antiplatelet therapy.

Oral surgical procedures included in this analysis were not restricted only to dental extractions. The procedures ranged initially from

the mildly invasive category including full - mouth scaling and polishing. The more invasive treatments included simple and complicated dental extraction - tooth removal without and with elevation of periosteal flap respectively - and root planing. Intensely invasive procedures in the analysis included alveolar ostectomy and surgical removal of impacted tooth with elevation of periosteal flap. Prolonged postoperative bleeding was defined as bleeding that continued in spite of the pressure pack given for 15 - 30 minutes post - surgery. It was controlled with various local hemostatic measures.

Factors potentially confounded risk ratio estimation in this context included sex, age, service provider, diabetes mellitus, hypertension, cardiovascular disease, stroke, COPD and asthma, involved dental arch, oral surgical procedure and major dental position in dental arch. Informations regarding these factors were retrieved from electronic health records in hospital information system.

Patients' clinical characteristics and details of oral surgical procedures were summarized using descriptive statistics. Independent samples t-test and exact probability test were applied to determine statistically significant differences in continuous and categorical variables respectively between index and referent groups. Risk ratio was effect measure to determine risk of bleeding complication attributed to chronic condition and uninterrupted aspirin therapy. Explanatory modeling strategy was adopted to estimate effect attributed to exposure of interest after adjusted for other potential confounders. Risk ratio was estimated using generalized linear model for risk ratio regression.

The proposal of this study was declared and submitted to the Director of Huaysloo Hospital. The permission of using patients' data was authorized on the basis of ethical issues and routine to research for developing services of the hospital.

Results

Majority of patients in both groups were females (Index 57.9%, Reference 63.5%) and the proportions of patients by sex were statistically significant (p=0.047). Index group - specific mean age was significantly greater than that of the referent group [Mean (S.D.): Index = 65.3 (9.3), Reference = 47.9 (15.3); <0.001]. The minimum age of patients taking adult low - dose aspirin in this context was 28. Up to 96.4% of patients in the index had at least one chronic disease while only 17.5% was observed among those in the reference (p<0.001). Fore major chronic diseases; including diabetes mellitus, hypertension, cardiovascular disease, and cerebrovascular disease; that antiplatelet therapy was commonly indicated to prevent thrombotic event were found in considerably greater proportions among patients in the index compared to those in the reference (p<0.001). Asthma and chronic obstructive pulmonary disease were found in comparable proportions in the two comparison groups (p=0.628). (Table 1)

Table 1 Clinical characteristics of adult patients receiving oral surgical procedures (n=2,907)

Clinical characteristics	Index group n=335 (11.5%)		Referent group n=2,572 (88.5%)		P-value
	n	%	n	%	
Sex					
Male	141	42.1	938	36.5	0.047†
Female	194	57.9	1,634	63.5	
Age (Overall Mean± S.D. = 49.9 ± 15.8)					
Mean±S.D.	65.3	9.3	47.9	15.3	<0.001‡
Min.–Max.	28	87	20	94	
20-59	92	27.5	1,952	75.9	
≥60	243	72.5	620	24.1	
Chronic disease					
Diabetes mellitus					
Yes	235	70.2	163	6.3	<0.001†
No	100	29.8	2,409	93.7	
Hypertension					
Yes	261	77.9	346	13.5	<0.001†
No	74	22.1	2,226	86.5	
Cardiovascular disease					
Yes	75	22.4	6	0.2	<0.001†
No	260	77.6	2,566	99.8	
Stroke					
Yes	29	8.7	16	0.6	<0.001†
No	306	91.3	2,556	99.4	
Asthma or COPD*					
Yes	6	1.8	37	1.4	0.628†
No	329	98.2	2,535	98.6	
Free of above chronic diseases					
Yes	12	3.6	2,121	82.5	<0.001†
No (having ≥ 1 above disease)	323	96.4	451	17.5	

†Exact probability test, ‡Independent samples t-test *COPD = chronic obstructive pulmonary disease

The oral surgical procedures in the two groups were performed either by dentists or dental hygienists in the comparable proportions (p=0.907). The major procedure among patients in the index was dental extraction (50.4%) while the most common procedure among those in the reference was full - mouth scaling (43.7%). Larger proportions of patients in the reference received complicated dental extractions (15.2%) - e.g., extraction with flap incision and alveolar bone removal - and surgical removal of impacted tooth (2.2%) compared to the index group - in which none of the patients underwent impacted tooth surgery. Overall proportions of minor oral surgical procedures underwent by patients in the two comparison groups were significantly different (p<0.001). Extent of surgical procedures was also different (p<0.001). Considerably greater proportion of patients in the index group underwent procedures which involve specifically at least 1 tooth (68.1%) compared to such proportion in the reference (53.1%). Among patients who underwent procedures which involved specifically at least 1 tooth - excluding consideration on patients receiving procedures which involved full-mouth or localized ridge, the average number of teeth involved in the index was 1.4 with standard deviation of ±0.04 which was greater than the average number in the reference [Mean (±S.D.) = 1.2 (±0.01)], and this was significantly different as indicated by independent samples t-test (p<0.001). Furthermore, major position of teeth involved was also different between the two group (p<0.001). Procedures which specifically involved at least 1 tooth were mostly in the molar position as predominantly observed in the reference (63.5%) and in smaller portion in the index (39.0%). Distribution of procedures by dental arch involvement was also different between the two groups (p<0.001), since most of the procedures in the referent group involved full mouth extent (all quadrants) while the majority of procedures in the index contrastively involved wither maxilla (36.7%) or mandible (38.8%). (Table 2)

Table 2 Service providers and details of minor oral surgical procedures (n=2,907)

Clinical characteristics	Index group n=335 (11.5%)		Referent group n=2,572 (88.5%)		P-value
	n	%	n	%	
Service provider					
Dentist	180	53.7	1,370	53.3	0.907†
Dental hygienist	155	46.3	1,202	46.7	
Minor oral surgical procedure					
a. Scaling	92	27.5	1,124	43.7	<0.001†,*
b. Extraction	169	50.4	877	34.1	
c. Complicated extraction	41	12.2	392	15.2	
d. Root planning	12	3.6	80	3.1	

Table 2 Service providers and details of minor oral surgical procedures (n=2,907) (cont.)

Clinical characteristics	Index group n=335 (11.5%)		Referent group n=2,572 (88.5%)		P-value
	n	%	n	%	
e. Surgical removal of impacted tooth	0	0.0	55	2.2	
f. Alveolar ostectomy	3	0.9	3	0.1	
g. Multiple procedures	18	5.4	41	1.6	
Extent of surgical procedures					
Involve full-mouth or localized ridge	107	31.9	1,207	46.9	<0.001†
Involve specifically ≥1 tooth	228	68.1	1,365	53.1	
In detail: 1 tooth involved	172	51.3	1,167	45.3	<0.001‡
2 teeth involved	38	11.4	164	6.4	
3 teeth involved	14	4.2	22	0.9	
4 teeth involved	2	0.6	7	0.3	
5 teeth involved	2	0.6	4	0.2	
6 teeth involved	0	0.0	1	0.0	
Major position of teeth involved					
Anterior	79	34.7	223	16.3	<0.001†
Premolar	60	26.3	272	19.9	
Molar	89	39.0	867	63.5	
Anterior and molar	0	0.0	1	0.1	
Premolar and molar	0	0.0	2	0.2	
Involved dental arch					
Full mouth (all quadrants involved)	77	23.0	964	37.5	<0.001†
In both arches (some quadrants)	5	1.5	36	1.4	
Maxilla only (1st or 2nd or both)	123	36.7	791	30.8	
Mandible only (3rd or 4th or both)	130	38.8	781	30.4	

†Exact probability test, ‡Independent samples t-test,

*Estimated through categorizing procedures into 5 categories: a., b., c., d.+e.+f., and g.

None of the bleeding events in this study was late - onset type. Regarding the immediate-onset bleeding complication which were minor, cumulative incidence of bleeding complication that needed local hemostatic measures among patients in the index was 6.6%, which was significantly higher than 0.8% observed in the reference (p<0.001). Univariable risk ratio

regression revealed that patients in the index were approximately 8 times more likely to have bleeding complication following oral surgical procedures compared to those in the reference. Multivariable risk ratio regression with explanatory modeling strategy was employed to provide risk estimate adjusted for confounding effects of potential confounders including sex, age, service provider, diabetes mellitus, hypertension, cardiovascular disease, stroke, COPD and asthma, involved dental arch, oral surgical procedure, and major dental position in dental arch. This multivariable analysis revealed that patients in the index group were 6.4 times more likely to have bleeding complication following oral surgical procedures compared to the reference. All 43 bleeding events were well controlled by simple local hemostatic measures. Hemostatic measures which were routinely practiced and used to ascertain occurrence of bleeding complication in this study included suturing only or suturing with additional use of sterile absorbable gelatin sponge (Gelfoam®). (Table 3)

Table 3 Cumulative incidence of bleeding complication and relative risk attributed to continued aspirin therapy and patients' underlying chronic conditions

Clinical outcome	Index group n=335		Referent group n=2,572		Risk ratio	95% CI	P-value
	n	%	n	%			
bleeding complication	22	6.6*	21	0.8*	8.0†	4.5, 14.5†	<0.001†
					6.4‡	2.5, 16.4‡	<0.001‡
Hemostatic measures indicating bleeding complication							
Suture only	17	5.1	14	0.5			
Suture & Gelfoam®	5	1.5	7	0.3			

* Cumulative incidence of bleeding complication among consecutive patients from January 2013 to December 2015;

† Crude estimates; ‡Estimates adjusted for sex, age, service provider, diabetes, hypertension, cardiovascular disease, stroke, COPD & asthma, involved dental arch, procedure and dental position in arch by risk ratio regression

Discussion

This practice - based analysis of bleeding risk following oral surgical procedures provided evidence which contradicted the notion that the risk could be assumed equivalent when Thai dental patients with underlying chronic conditions and indicated use of low - dose aspirin prophylaxis were compared to the general dental patients - who might be relatively healthier - without need of such antiplatelet therapy. This finding was thus consistent with the meta-analysis[8] which indicated that antiplatelet therapy could prolonged

postoperative bleeding and the concept that different individuals would carry different bleeding risk which should not be assumed averagely equivalent[9,10,12] was well confirmed by this study. Consistent finding that underlying systemic condition and continued aspirin therapy increased bleeding risk was also observed in a previous study in Thai patients.[13]

Regarding the risk of bleeding complication by different procedures, all 43 bleeding events (1.5%) from total of 2,907 individuals in this study were found only during tooth removal: simple extraction (29 events), complicated extraction (13 events), and surgical removal of impacted tooth (1 event). In the index group, 22 bleeding events (cumulative incidence of 6.6%) were observed on simple extraction (18 events) and complicated extraction (4 events). In the reference, 21 bleeding events (cumulative incidence of 0.8%) were observed on simple extraction (11 events), complicated extraction (9 events), and surgical removal of impacted tooth (1 event). Finding of bleeding events correspondingly restricted to dental extraction was different from a previous prospective study[14] which suggested that bleeding complication did not depend on type of surgical procedure. Procedures such as alveoloplasty and flap surgery could also cause bleeding complication.[14] None of bleeding events was determined during full mouth scaling or root planing. This finding confirmed a previous recommendation that scaling was relatively safe in patients with antiplatelet therapy.[15]

By the context of this study, we found that oral surgical procedures could be safely performed in patients with long-term aspirin use. The immediate-onset bleedings were minor and could be stopped by local hemostatic measures. Clinical practice guideline stated that the operators should know other underlying diseases those might be at higher risk of prolonged bleeding following oral surgical procedures: liver impairment, and/or alcoholism, renal failure, thrombocytopenia, hemophilia, any concurrent medication affecting hemostasis such as anticoagulants or anti - inflammatory drugs. In case of scaling and root planning, small area of the dental arch should be done first - such as one sextant- for evaluating of bleeding risk before quadrant or arch therapy. In case of extraction, 1-3 teeth must be considered first[10] before other invasive oral surgical procedures such as impact or periodontal surgery were done.

We found minor bleeding complication of patients with long - term aspirin use following extraction and complicated extraction. The wounds those involved both soft and hard tissue. The higher frequency of bleeding events might be associated with short (15-30 minutes) postextraction monitoring, whereas other studies were monitored for >30 minutes and then treated appropriately, if needed. The operators in this study therefore used more local hemostatic measures such as suturing or suturing with Gelfoam® in the aspirin group. This caused immediate-onset bleeding rate as 6.6 %. These complications were limited in the immediate

postoperative time frame, occurring within the safe environment of a dental clinic, and were controlled with local hemostatic measures. Importantly, the incidence of late-onset bleeding which might be more dangerous did not occur.

The study thus consistently suggested as other literatures[16-21] that oral surgical procedures could be performed safely in patients with underlying disease and uninterrupted aspirin therapy when close monitoring and local hemostatic measures were well prepared. Cautious performing of the procedures and attempt to limit extent of surgical trauma would also be beneficial in preventing postoperative bleeding complication.

Conclusion

Clinically significant increase in bleeding risk was observed in patients with underlying chronic condition and uninterrupted aspirin therapy. Nonetheless, oral surgical procedures could be safely performed when close monitoring and local hemostatic measures were well prepared without need to discontinue the aspirin therapy.

Conflict of interest

None declared.

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