

Knowledge and Clinical Practice of Antithrombotic Therapy among Dentists in Chiang Mai, Thailand

Chaiporn Karaket¹, Krit Leemasawat² and Arintaya Phrommintikul²

¹Department of Internal Medicine, Chiangkham Hospital, Phayao

²Cardiovascular Unit, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai

Abstract

This study aimed to survey the knowledge and clinical practice of dentists regarding antithrombotic drug management before dental procedures. All dentists who worked in Chiang Mai, Thailand between February 2014 and December 2014 were invited to answer the questionnaires via mail. The survey items consisted of 20 questions focusing on knowledge and clinical practice regarding antiplatelet therapy, warfarin therapy and guideline recommendations. From 186 invitation mails, 100 dentists (53.8 %) returned the questionnaires. Seventy-two percent of the participants recognized clopidogrel, while only 20 % knew ticagrelor. Over 90 % of the participants did not know the optimal duration of dual antiplatelet therapy after stenting. Approximately half of the participants discontinued aspirin before dental procedures in their patients, and 66.7 % of them required at least 7 days of discontinuation. Three quarters of the participants suspended P2Y₁₂ inhibitors before their procedures, and 87.0 % of them required at least 5 days of discontinuation. Warfarin was discontinued in 71.6 %, 89.4 % and 93.5 % of the patients undergoing low-, moderate- and high-risk procedures, respectively. Approximately half of the participants were willing to perform low-risk dental procedures at the INR level of 2.1-4.0, while most of them preferred to perform moderate- and high-risk dental procedures at INR level of ≤ 2.0 (60.9 % and 72.5 %, respectively). All the participants were aware of the guideline recommendations, but there was a discrepancy between their practice and guideline recommendations to which they referred. The knowledge of antithrombotic therapy among dentists in Chiang Mai, Thailand was limited. A high percentage of dentists practiced differently from guideline recommendations. Some educational interventions should be done to improve the quality and safety of the medical care.

Keywords: Antiplatelet therapy, Antithrombotic therapy, Dental procedure, Survey, Warfarin

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Correspondence to:

Krit Leemasawat. Cardiovascular Unit, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, 110 Intavarorot Rd., Sripum, Mueang district, Chiang Mai 50200, Thailand Tel: 053-936713 Fax: 053-289177 E-mail: krit_lee@yahoo.com

Introduction

Nowadays, antithrombotic drugs are widely used. Aspirin, irreversible cyclooxygenase enzyme inhibitor, is effective for atherothrombotic prevention.^{1,2} It is commonly prescribed in patients with overt cardiovascular disease such as previous myocardial infarction, myocardial ischemia, transient ischemic attack or ischemic stroke, for secondary prevention.³ Dual antiplatelet therapy (DAPT) with aspirin and P2Y₁₂ inhibitors (i.e., clopidogrel, prasugrel and ticagrelor) demonstrates the cardiovascular benefits in patients with acute coronary syndrome or myocardial infarction.⁴⁻¹¹ Furthermore, DAPT shows a dramatic reduction in the incidence of ischemic complications after percutaneous coronary intervention.^{5,12} DAPT is now indicated in patients with acute coronary syndrome (up to 12 months) and patients treated with coronary stenting (at least 1 month after bare-metal stent implantation and 6 months after drug-eluting stent implantation).¹³ Oral anticoagulant (i.e., apixaban, dabigatran, rivaroxaban and warfarin) can reduce the incidence of embolic stroke in patients with non-valvular atrial fibrillation.¹⁴⁻¹⁷ In patients with mechanical heart valves, warfarin also reduces thromboembolic events and prosthetic valves thrombosis.¹⁸ As a result, oral anticoagulant is indicated in patients with non-valvular atrial fibrillation with high thromboembolic risk, patients with rheumatic mitral stenosis with high thromboembolic risk, patients with history of thromboembolism and patients with mechanical heart valves.^{19,20} The number of patient with antithrombotic drug use undergoing dental procedures is increasing continuously. Dentists are now confronting with the dilemma of antithrombotic drug management; how to balance between the thrombotic and bleeding risks.

Antithrombotic drug-induced bleeding after dental procedures²¹⁻²³ is a principal concern, leading to antithrombotic drug discontinuation. According to the questionnaire studies in Spain²⁴ and Turkey²⁵, aspirin

and clopidogrel were discontinued in 88 to 93 % of the patients before dental procedures. Moreover, routine interruption of warfarin occurred in nearly a quarter of the patients undergoing low-risk dental procedures.²⁶ The rate of discontinuation of antithrombotic drug in patients undergoing dental procedures is still high, despite the fact that the premature discontinuation of antiplatelet drugs increases the risk of thrombotic events such as myocardial infarction, stent thrombosis or ischemic stroke²⁷⁻³⁴, and the interruption of anticoagulant in patients with high thromboembolic risk sometimes can be fatal.

There are many clinical practice guidelines for the management of antithrombotic drugs during dental procedure.³⁵⁻⁴⁰ However, the recommendations are diverse among guidelines. The perioperative management of patients who receive antithrombotic drugs still presents a dilemma for dentists and consulting physicians. This study aimed to survey the knowledge and clinical practice of dentists in Chiang Mai, Thailand, regarding the antithrombotic drug management before dental procedures.

Materials and Methods

Study design and study population

This study was a descriptive cross-sectional survey, conducted in Chiang Mai, Thailand between February 2014 and December 2014. We invited all dentists who worked in Chiang Mai, Thailand to answer the questionnaires via mail. They were informed of the purpose of the study and the names of corresponding investigators. The dentists who wished to participate in the survey would be asked to complete the questionnaires, then return them by mail. All information was kept strictly confidential. The protocol and study materials were approved by the institutional review board of the Faculty of Medicine, Chiang Mai University.

Questionnaire

The questionnaire consisted of 2 parts, general participant's information and survey. The questions in the survey part aimed to assess the knowledge and clinical

practice about antiplatelet therapy, warfarin therapy and guideline recommendations. There were 20 questions in total, adapted from reference²⁴⁻²⁶ (Table 1).

Table 1 Survey questions (adapted from reference 24-26)

Antiplatelet therapy:

1. Do you know what clopidogrel is?
2. Do you know what ticagrelor is?
3. Do you know what a coronary stent is?
4. Do you know the optimal duration of DAPT after bare metal stent?
5. Do you know the optimal duration of DAPT after drug eluting stent?
6. Do you discontinue aspirin before a dental procedure in your patients? If YES, how many days?
7. Do you discontinue P2Y₁₂ inhibitor before a dental procedure in your patients? If YES, how many days?
8. Do you consult with a physician before discontinuing antiplatelet drugs?
9. Do you know the serious consequences of premature discontinuation of antiplatelet therapy in patients with coronary stents?
10. Do you wait until DAPT is completed before performing a dental procedure, if it is possible?

Warfarin therapy:

11. Do you discontinue warfarin before performing a low-risk dental procedure in your patients? If YES, how many days?
12. Do you discontinue warfarin before performing a moderate-risk dental procedure in your patients? If YES, how many days?
13. Do you discontinue warfarin before performing a high-risk dental procedure in your patients? If YES, how many days?
14. What is the maximum INR that you accept for performing a low-risk dental procedure?
15. What is the maximum INR that you accept for performing a moderate-risk dental procedure?
16. What is the maximum INR that you accept for performing a high-risk dental procedure?
17. Do you consult with a physician before discontinuing warfarin?
18. Do you know the serious consequences of discontinuation of warfarin in patients with prosthetic heart valves?

Guideline recommendations:

19. Are you aware of any guideline recommendations in your clinical practice?
 20. What is your reference guideline?
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Definitions

The definition of the bleeding risk from a dental procedure in this study is adapted from post-operative bleeding in pre-transplant liver failure patients undergoing oral surgery.⁴¹ A low-risk dental procedure is defined as scaling or 1-5 simple extractions, carried out under local anesthesia. A moderate-risk dental procedure refers to 6-10 simple extractions or 1 impacted extraction, in which suture(s) may be needed. A high-risk dental procedure is defined as 11 or more simple extractions

or 2 or more impacted extractions, in which sutures are unavoidably needed. In this study, low international normalized ratio (INR) level, medium INR level and high INR level refer to the INR level of ≤ 2.0 , 2.1-3.5 and >3.5 , respectively.

Statistical analysis

Based on the data of Ministry of Public Health of Thailand, there were 186 dentists, working in Chiang

Mai, Thailand during the survey period. In order to represent the entire population with the confident level of 95 % and the margin of error of 5 %, at least 126 dentists (67.7 %) should be participated in the study. The response rates to survey ranged from 73.5 to 100 % in the previous studies²⁴⁻²⁶. However, mail survey needs both attention and willing to participate. We expected that the response rate to be lower in this study than

in previous reports. All descriptive data were given as number (percentage) and median (IQR), as appropriate. The difference in categorical and continuous data was analyzed with Chi-square test and One-way ANOVA test, respectively. Two-tailed p-value of less than 0.05 was considered statistical significance. The statistical analysis was performed using IBM SPSS Statistics, version 22.

Results

From 186 questionnaires, 100 mails (53.8 %) were returned. The median age of the participants was 36 (IQR 32.0-42.8) years. The ratio of male to female was about 1:2. The median duration of work experience was 12 (IQR 7-17) years. Of the 100 dentists included, 67 (67 %) worked in government hospitals, and 33 (33 %) worked in private hospitals or clinics. Sixty-seven participants (67 %) worked in urban area (Mueang district, Chiang Mai).

Antiplatelet therapy

Table 2 showed the survey results of antiplatelet therapy. Most of the participants (72 %) recognized clopidogrel, while only 20 % knew what ticagrelor was.

Three-fourths of the participants (74 %) knew a coronary stent, but over 90 % of them did not know the optimal duration of dual antiplatelet therapy (DAPT) after stenting. More than half of the dentists in this survey (59.8 %) discontinued aspirin before dental procedures in their clinical practices, and 66.7 % of them required at least 7 days of aspirin discontinuation. Three-fourths of the participants (76.3 %) suspended P2Y₁₂ inhibitors before their procedures, and 87.0 % of them required at least 5 days of P2Y₁₂ inhibitors discontinuation. There was no significant difference in term of knowledge and clinical practice regarding antiplatelet therapy between participants who worked in urban and rural areas.

Table 2 Survey results of antiplatelet therapy

| Questions, n (%)* | Total (n=100) | Urban area (n=67) | Rural area (n=33) | P value |
|---|---------------|-------------------|-------------------|---------|
| Do you know what clopidogrel is? | 72 (72 %) | 47 (70.1 %) | 5 (75.8 %) | 0.64 |
| Do you know what ticagrelor is? | 20 (20 %) | 16 (23.9 %) | 4 (12.1 %) | 0.20 |
| Do you know what a coronary stent is? | 74 (74 %) | 51 (76.1 %) | 23 (69.7 %) | 0.63 |
| Do you know the optimal duration of DAPT after bare metal stent? | 10 (10 %) | 8 (11.9 %) | 2 (6.1 %) | 0.49 |
| Do you know the optimal duration of DAPT after drug eluting stent? | 8 (8 %) | 5 (7.5 %) | 3 (9.1 %) | 1.00 |
| Do you discontinue aspirin before a dental procedure in your patients? | 58 (59.8 %)** | 43 (66.2 %)** | 15 (46.9 %)** | 0.08 |
| Do you discontinue P2Y12 inhibitor before a dental procedure in your patients? | 74 (76.3 %)** | 51 (78.5 %)** | 23 (71.9 %)** | 0.61 |
| Do you consult with a physician before discontinuing antiplatelet drugs? | 96 (96 %) | 65 (97 %) | 31 (93.9 %) | 0.60 |
| Do you know the serious consequences of premature discontinuation of antiplatelet therapy in patients with coronary stents? | 73 (73 %) | 50 (75.8 %) | 23 (69.7 %) | 0.63 |
| Do you wait until DAPT is completed before performing a dental procedure, if it is possible? | 72 (76.6 %)** | 51 (81 %)** | 21 (67.7 %)** | 0.20 |

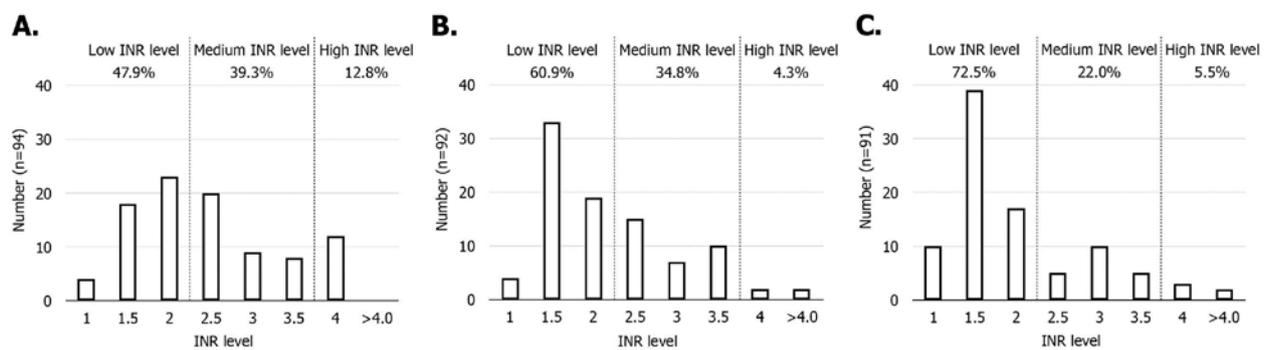
Warfarin therapy

Most of the dentists in this survey preferred to discontinue warfarin before performing their procedures (Table 3), and over 95 % of them suspended warfarin at least 3 days. Approximately half of the participants (52.1 %) were willing to perform low-risk dental procedures at the INR level of 2.1 to 4.0 (Fig. 1). Most of participants

preferred to perform moderate- and high-risk dental procedures at low INR level (60.9 % and 72.5 %, respectively). There was no significant difference regarding the knowledge and clinical practice on warfarin therapy between participants who worked in urban and rural areas.

Table 3 Survey results of warfarin therapy

| Questions, n (%)* | Total (n=100) | Urban area (n=67) | Rural area (n=33) | P value |
|---|---------------|-------------------|-------------------|---------|
| Do you know what clopidogrel is? | 72 (72 %) | 47 (70.1 %) | 5 (75.8 %) | 0.64 |
| Do you know what ticagrelor is? | 20 (20 %) | 16 (23.9 %) | 4 (12.1 %) | 0.20 |
| Do you know what a coronary stent is? | 74 (74 %) | 51 (76.1 %) | 23 (69.7 %) | 0.63 |
| Do you know the optimal duration of DAPT after bare metal stent? | 10 (10 %) | 8 (11.9 %) | 2 (6.1 %) | 0.49 |
| Do you know the optimal duration of DAPT after drug eluting stent? | 8 (8 %) | 5 (7.5 %) | 3 (9.1 %) | 1.00 |
| Do you discontinue aspirin before a dental procedure in your patients? | 58 (59.8 %)** | 43 (66.2 %)** | 15 (46.9 %)** | 0.08 |
| Do you discontinue P2Y12 inhibitor before a dental procedure in your patients? | 74 (76.3 %)** | 51 (78.5 %)** | 23 (71.9 %)** | 0.61 |
| Do you consult with a physician before discontinuing antiplatelet drugs? | 96 (96 %) | 65 (97 %) | 31 (93.9 %) | 0.60 |
| Do you know the serious consequences of premature discontinuation of antiplatelet therapy in patients with coronary stents? | 73 (73 %) | 50 (75.8 %) | 23 (69.7 %) | 0.63 |
| Do you wait until DAPT is completed before performing a dental procedure, if it is possible? | 72 (76.6 %)** | 51 (81 %)** | 21 (67.7 %)** | 0.20 |



INR, international normalized ratio.

Figure 1 The maximum acceptable INR level for (A) low-, (B) moderate-, and (C) high-risk dental procedures

Guideline recommendations

All participants (100 %) were aware of guideline recommendations, and the clinical practice guideline of Dental Health Division, Department of Health, Bangkok³⁹ was the most frequently used as a reference (76.3 %). However, the discrepancy between the participants' practice and guideline recommendations to which they referred was observed. Approximately one-third of the participants (35.3 %) who used the clinical practice guideline of Dental Health Division, Department of Health, Bangkok³⁹ as a reference continued aspirin without interruption before their procedures, while the guideline recommended to stop aspirin before their procedures. Moreover, only half of the dentists (50.6 %) were willing to perform low-risk dental procedures at the recommended INR level.

Discussion

Our study was the first cross-sectional survey among dentists who worked in Chiang Mai, Thailand regarding knowledge and clinical practice of antithrombotic management in patients undergoing dental procedures. Unfortunately, the response rate (53.8 %) was much lower than our expectation. These results might not represent the entire population of dentists in Chiang Mai, Thailand. However, the results of our study could somehow reflect the current situation regarding knowledge and clinical practice of dentists in term of antithrombotic management.

Since clopidogrel has been available in Thailand and throughout the world for decades, most of the dentists recognize clopidogrel well. The rate of awareness of clopidogrel in this study (72 %) was similar to that of the previous reports (60-90.6 %).^{24,25} Ticagrelor, a novel P2Y₁₂ inhibitor, was approved by Food and Drug Administration of Thailand 1 year prior to this survey, so only 20 % of the participants knew what it was. Four years ago, none of the dentists in Turkey survey²⁵ recognized ticagrelor. Prasugrel, another novel P2Y₁₂

inhibitor, was available in Thailand shortly before the survey period. We predict that the rate of recognition would be very low, so we decide not to include prasugrel in our questionnaire. To familiarize with a new medication does take time, especially for the outsiders. However, the imbalance between the growing of new antithrombotic drug use and the restriction of drug recognition could be troublesome. When novel P2Y₁₂ inhibitors and NOACs are not recognized, dentists will perform their procedures as usual, and no prompt bleeding management will be prepared. This situation could lead to serious post-operative bleeding complications, especially in moderate- and high-risk dental procedures. Thus, dentists should regularly make an effort to update their knowledge.

Most evidence-based guidelines recommend that patients who are undergoing a minor dental procedure should continue aspirin without interruption prior to the procedure.^{35,38,40} In this survey, more than half of the participants still suspended aspirin treatment before their procedures. However, the rate of aspirin suspension is lower than that of the previous report.²⁵ The recommendations for DAPT management^{35,38-40} are controversial, since the risk of serious post-operative bleeding is very high and may outweigh the risk of thromboembolism. In the current situation, P2Y₁₂ inhibitors are usually discontinued before dental procedures. In our study, most of the participants (74 %) knew about a coronary stent. The result is similar to that of the previous studies (83-100 %).^{24,25} Most of the participants (73 %) were aware of the serious consequences when antiplatelet therapy was discontinued prematurely in patients with coronary stents. However, most of them (79.2-92 %) did not know the optimal duration of DAPT after stenting, and DAPT discontinuation was still frequently observed in their practice (76.3 % in our study and 89.9 % in the study in Turkey²⁵). In our opinion, filling this gap of knowledge could minimize DAPT interruption, since most of the dentists in our survey (76.6 %) preferred to wait until DAPT was completed before performing their dental procedures.

To our knowledge, the risk of significant surgical bleeding is very low in patients on warfarin with a stable INR in the range of 2.0 to 4.0^{36,37,42} whereas the risk of thrombosis is increased when warfarin is temporarily discontinued. As a consequence, it is generally recommended to check INR level within 72 hours of surgery and not to discontinue warfarin in most of the patients undergoing low-risk dental procedures.^{36,37,40} Surprisingly, in our study, 71.6 % of the participants routinely discontinued warfarin before performing low-risk dental procedures despite the awareness of serious consequences. The previous survey in Michigan²⁶ showed a much lower rate of discontinuation (23.6 %). However, approximately half of the dentists were willing to perform low-risk dental procedures at the recommended INR level in both studies (52.1 % in our study and 66.4 % in the study in Michigan²⁶). Some dentists might not feel comfortable to perform the operations in patients fully anticoagulated with warfarin. Bridging therapy with heparin or low-molecular weight heparin, purposely minimizing the duration of subtherapeutic anticoagulation, could potentially be an alternative strategy. Unfortunately, it was not cost-effective and might increase the risk of bleeding complications in patients undergoing low-risk dental procedures.^{43,44} Most of the dentists in our survey preferred to perform moderate- and high-risk dental procedures at subtherapeutic INR level, similar to the previous survey.²⁶ This practice may be defensible, since there is still lack of data regarding the management strategy of anticoagulation therapy for moderate- and high-risk dental procedures. Moreover, the emergence of novel oral anticoagulants (NOACs) (i.e., apixaban, dabigatran and rivaroxaban) leads to an additional controversy in the clinical practice. The safety data of NOACs in patients undergoing dental surgery are still limited. Dentists, together with consulting physicians, should carefully balance between bleeding risk and thrombotic risk, in order to provide the best medical care.

Our own clinical practice guideline should be updated in an evidence-based manner to avoid confusion among guideline recommendations and to help dentists provide the best medical care. However, the implementation of those recommendations into clinical practice is also another important issue. It is a complex pathway, involving multidisciplinary medical personnel and resource management. Dentists and all stakeholders play a vital role to develop and implement the plans. Almost all the dentists in our survey and in previous studies^{24,25} consulted the physicians or cardiologists for antithrombotic management before their procedures. Physician consultation is a valuable tool⁴⁵ and one of the key mechanisms to implement clinical guideline. However, traditional one-way communication is not the best method of consultation. Sometimes the physician's recommendation conflicts with the dentist's professional decision, especially when one relies on clinical experience rather than medical evidence. Two-way discussion, based on medical evidence and guideline recommendations, is a solution for decision making.

There are some limitations of this study. Firstly, the number of participants was relatively small. Our survey might not represent the results of the entire dentists working in Chiang Mai, Thailand. However, the results still provided necessary information for further studies and interventions. Secondly, our survey was conducted in a single region. The results cannot be generalized, since knowledge and clinical practice may be different in other regions of Thailand, as well as in other parts of the world. Lastly, most of the questions in our survey were "yes-no" questions which unavoidably forced bias into the interpretation when the answers were not absolutely yes or no. Faithfulness and reliability of perception were also the limitations of questionnaire research design. Moreover, it is undeniable that physician's suggestions potentially have an effect on dentist's response in the clinical practice.

Conclusion

The knowledge of antithrombotic therapy among dentists in Chiang Mai, Thailand is limited, especially for novel antiplatelet agents and the optimal duration of DAPT after stenting. Moreover, a high percentage of dentists practice differently from what the current evidence-based guidelines recommend. Some educational interventions should be done to improve the quality and safety of the medical care.

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