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Oral antithrombotics and dentistry: Current state of affairs and guideline proposal

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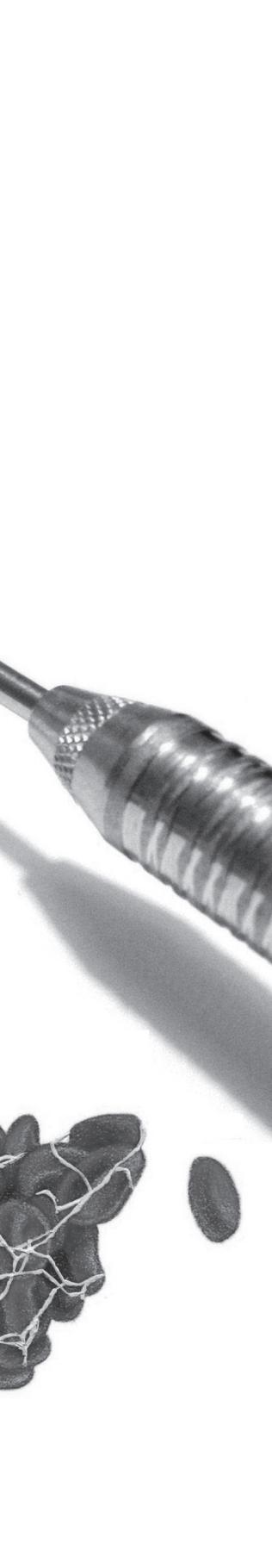
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Chapter 7

Management recommendations for invasive dental treatment in patients using oral antithrombotic medication

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Submitted for publication



ABSTRACT

Objectives. The aims were: 1. To search the scientific literature from 2007-2012 for guidelines and new studies on the dental management of patients using oral antithrombotic medication; 2. To summarize their evidence and recommendations and 3. To propose a clinical practice guideline for general dentists anno 2013.

Study design. Systematic literature search in Medline, EMBASE and Guideline Websites from October 2007- October 2012.

Results. The systematic literature search for guidelines yielded 74 citations (MEDLINE 45, EMBASE 22, and the Guideline websites 7). Of these, only two guideline publications and two systematic reviews met the inclusion criteria. They yielded 32 recommendations.

Conclusions. The evidence and subsequent recommendations from published guidelines all point in the same direction: do not interrupt oral antithrombotic medication, not even dual antiplatelet therapy, in simple dental procedures.

INTRODUCTION

Oral antithrombotic medication (OAM) has since long been used successfully to treat a variety of thrombotic diseases, such as myocardial infarction, stroke, deep venous thrombosis or as a medicine to prevent cardiovascular diseases¹⁻⁴. For decades doctors and patients have worried about the adverse side-effects of these medicines, mainly consisting of bleeding complications, either spontaneously or peri-operatively. Also in dentistry, this has been a major concern for years, resulting in the advice to temporarily discontinue oral antithrombotic medication prior to invasive dental treatments, such as dental extractions⁵⁻⁷.

Since 1998 several publications appeared in medical and dental journals^{5,6,8-10}, suggesting that bleeding complications after dental procedures in patients who did not discontinue their antithrombotic medication, might not be as serious as previously thought. Furthermore, several studies were published suggesting that the risk of thrombosis after discontinuing OAM might outweigh the bleeding risks while continuing OAM. These considerations have led to several clinical practice guidelines (CPG) on this topic¹¹⁻¹⁵.

In 2009 a systematic search for guidelines and critical evaluation of these guidelines was performed which led to the conclusion that with the use of the AGREE instrument only two guidelines met the criteria of “good” CPG’s¹⁶. One was developed in the UK¹⁷ and one at the International World Workshop of the American Academy of Oral Medicine¹⁸.

The aim of this study is to review the dental literature from 2007-2012 and to propose a clinical practice guideline for general dentists anno 2013.

METHODS

We used the search strategies from our previous systematic search for guidelines on invasive dental treatment in patients using OAM as described and published in 2009¹⁹ to obtain additional guidelines, systematic reviews and RCT’s published between October 2007 and October 2012 (Figure 1&2) in Medline and EMBASE.

1. guideline* or practice guideline (241.975)
2. recommendation* (129.340)
3. standard* of care (244.041)
4. practice standard* OR professional standard (1675)
5. algorithm OR clinical algorithm* (206.863)
6. practice algorithm (10.184)
7. clinical guideline* (5.833)
8. expert* consensus (8.286)
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 743.740)
10. anticoagulant* (193.641)
11. aspirin (50.447)
12. coumadin (19.098)
13. coumarin* (14.480)
14. warfarin (18.744)
15. clopidogrel (7.666)
16. oral anticoagulant* (4.638)
17. ticlopidine (7.293)
18. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 (246.917)
19. dentistry (411.475)
20. dental treatment* (5.540)
21. dental surgery (65.562)
22. dental extraction* (1.324)
23. dental scaling (3.906)
24. dentoalveolar procedure* (12)
25. dental implant* (23.947)
26. 19 or 20 or 21 or 22 or 23 or 24 (428.805)
27. 9 and 18 and 25 and 26 (158)
28. limit 27 to human (145)
29. limit 28to English OR Dutch language (129)
30. limit to date Oct 2007-October 2012 (45)

Figure 1. Medline search strategies (October 28th, 2012)

# 25 #24 AND ([cochrane review]/lim OR [controlled clinical trial]/lim OR [meta analysis]/lim OR [randomized controlled trial]/lim OR [systematic review]/lim	44
#24 #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23	219,781
#23 dental AND implant* AND [2005-2012]/py	41,566
#22 dentoalveolar AND procedure* AND [2005-2012]/py	604
#21 dental AND scaling AND [2005-2012]/py	1,353
#20 dental AND extraction* AND [2005-2012]/py	12,210
#19 dental AND ('surgery'/exp OR surgery) AND [2005-2012]/py	91,736
#18 dental AND treatment* AND [2005-2012]/py	76,612
#17 'dentistry'/exp OR dentistry AND [2005-2012]/py	123,752
#16 #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15	195,707
#15 'ticlopidine'/exp OR ticlopidine AND [2005-2012]/py	5,458
#14 'oral'/exp OR oral AND anticoagulant* AND [2005-2012]/py	40,826
#13 'clopidogrel'/exp OR clopidogrel AND [2005-2012]/py	25,821
#12 'warfarin'/exp OR warfarin AND [2005-2012]/py	29,769
#11 coumarin* AND [2005-2012]/py	39,104
#10 'coumadin'/exp OR coumadin AND [2005-2012]/py	28,953
#9 'aspirin'/exp OR aspirin AND [2005-2012]/py	65,524
#8 anticoagulant* AND [2005-2012]/py	186,803
#7 #1 OR #2 OR #3 OR #4 OR #5 OR #6	637,170
#6 algorithm OR clinical AND algorithm* AND [2005-2012]/py	39,686
#5 practice AND standard* OR professional AND ('standard'/exp OR standard) AND [2005-2012]/py	218,811
#4 practice AND standard* OR professional AND ('standard'/exp OR standard) AND [2005-2012]/py	218,811
#3 standard* AND of AND care AND [2005-2012]/py	412,918
#2 recommendation* AND [2005-2012]/py	89,971
#1 guideline* OR practice AND guideline AND [2005-2012]/py	161,358

Figure 2. EMBASE search strategy (October 28th, 2012)



Subsequently, we systematically searched for additional guidelines, systematic reviews and RCT's published between October 2007 and October 2012 as described earlier. We collected the levels of evidence and levels of recommendations.

Inclusion/exclusion criteria

Guidelines were included if they were developed for the dental management of patients using antiplatelet or oral anticoagulation medication on the basis of consensus or evidence-based methods. If the guidelines had been updated the latest version was included. Guidelines based on commentaries and narrative reviews were excluded. Only guidelines written in English or Dutch were reviewed. Systematic reviews were included if the patient population was either on antiplatelet therapy or on vitamin K antagonists, had invasive dental procedures performed, were analyzed for bleeding and/or thrombosis outcomes and included RCT's or cohort studies of sufficient scientific quality.

RESULTS

The systematic literature search for guidelines from October 2007- October 2012 yielded 74 citations (MEDLINE 45, EMBASE 22, and the Guideline websites 7) (Figure 1&2). Of these, only 2 guideline publications met the inclusion criteria^{20,21}. Furthermore, one systematic review and meta-analysis was published in 2009 on dental procedures in patients using warfarin, which reviewed all studies that appeared until June 2008²². Napenas et al performed a systematic review on dental procedures in patients using single or dual antiplatelet therapy, which included all published studies until September 2011²³. We collected the levels of evidence (Table 1) and levels of recommendations (Table 2) as described and provided by the authors^{20,21}. In table 1 and table 2 we added the results from our former study¹⁹, in which two international guidelines were found to be AGREE-able^{17,18}.

The recommendations and underlying levels of evidence that were extracted from these guidelines, systematic reviews and one RCT are summarized in table 3. The gathered recommendations were formulated into a clinical practice guideline proposal (Table 4).

Table 1. Definition of the levels of evidence as described by subsequent CPG's:

***Levels of evidence used by Aframian et al¹⁸:**

Level A: based on multiple randomized controlled trials

Level B: based on data from a single randomized trial or nonrandomized studies

Level C: expert opinion

***Levels of Evidence of the Brazilian Society of Cardiology²¹**

A. Evidence in several populations from multiple randomized clinical trials or meta-analyses;

B. Evidence in a limited group of populations from single randomized clinical trial or non-randomized clinical studies;

C. Evidence in very limited group of populations from consensus and experts' opinions, case reports and series.

***Classification of evidence levels used by Perry et al.¹⁷:**

Ia Evidence obtained from meta-analysis of randomized controlled trials

Ib Evidence obtained from at least one randomized controlled trial

IIa Evidence obtained from at least one well-designed controlled study without randomization

IIb Evidence obtained from at least one other type of well-designed quasi-Experimental study

III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

Table 1. Continued

*Classification of evidence levels used by Douketis et al.²⁰:

Grade of Recommendation	Benefit vs Risk and Burden	Methodologic Strength of Supporting Evidence	Implications
Strong recommendation, high-quality evidence (1A)	Benefits clearly outweigh risk and burdens or vice versa.	Consistent evidence from randomized controlled trials without important limitations or exceptionally strong evidence from observational studies.	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change our confidence in the estimate of effect.
Strong recommendation, moderate-quality evidence (1B)	Benefits clearly outweigh risk and burdens or vice versa.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise) or very strong evidence from observational studies.	Recommendation can apply to most patients in most circumstances. Higher-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate.
Strong recommendation, low- or very-low-quality evidence (1C)	Benefits clearly outweigh risk and burdens or vice versa.	Evidence for at least one critical outcome from observational studies, case series, or randomized controlled trials, with serious flaws or indirect evidence.	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate.
Weak recommendation, high-quality evidence (2A)	Benefits closely balanced with risks and burden.	Consistent evidence from randomized controlled trials without important limitations or exceptionally strong evidence from observational studies.	The best action may differ depending on circumstances or patient or societal values. Further research is very unlikely to change our confidence in the estimate of effect.
Weak recommendation, moderate-quality evidence (2B)	Benefits closely balanced with risks and burden.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies.	Best action may differ depending on circumstances or patient or societal values. Higher-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate.
Weak recommendation, low- or very-low-quality evidence (2C)	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Evidence for at least one critical outcome from observational studies, case series, or randomized controlled trials, with serious flaws or indirect evidence.	Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate.

Table 2. Definition of the grades of recommendations

****Class of recommendations used by Aframian et al.¹⁸**

Class	I:	benefit of patients clearly outweighs any risks, procedure SHOULD be performed
Class	II:	conflicting evidence and/or a divergence of opinion about the usefulness of a procedure or treatment
	Ila:	Benefit seems to outweigh the risk, weight of evidence is in favor of usefulness. IT IS REASONABLE to perform the procedure
	Ilb:	Benefit seems to outweigh the risk, usefulness is less well established. IT IS NOT UNREASONABLE to perform the procedure
Class	III:	Risk outweighs the benefit, IT MAY BE HARMFUL AND IS UNHELPFUL. Procedure should NOT be performed

****Classification of grades of recommendations used by Perry et al.¹⁷**

- A. Requires at least one randomized controlled trial as part of a body of literature of overall good quality and consistency addressing specific recommendation. (*Evidence levels Ia, Ib*).
- B. Requires the availability of well conducted clinical studies but no randomized clinical trials on the topic of recommendation. (*Evidence levels IIa, IIb, III*).
- C. Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (*Evidence level IV*).

****Classification of degree of recommendations used by Brazilian Society of Cardiology²¹**

Degree of Recommendation I - Benefit >>> Risk; the treatment/procedure must be indicated/administered;

Degree of Recommendation IIa - Benefit >> Risk; the choice for the treatment/procedure may help the patient;

Degree of Recommendation IIb - Benefit > Risk; it is not defined if the treatment/procedure can help the patient;

Degree of Recommendation III - Risk > Benefit; the treatment/procedure must not be performed since it does not help and may be harmful for the patient.



Table 3: Review of the recommendations from guidelines and systematic reviews on patients undergoing dental surgery using oral antithrombotic drugs (aspirin, clopidogrel, warfarin and new oral anticoagulants, such as dabigatran and rivaroxaban).

	Level of evidence*	Recommendations Class or Grade or Degree**
1. Continuation of anticoagulant drugs		
When the International Normalized Ratio (INR) is less than 3.5 do not modify or discontinue warfarin therapy for simple single dental extractions ¹⁸ .	level A	Class I
When INR is 3.5 or more and complicated or invasive oral surgery procedures are planned, discuss with physician ¹⁸ .	Level A	Class I
Consult physician of patient on Low Molecular Weight Heparin (LMWH) for advise on continuing, altering or stopping of medication before dental procedure ¹⁸ .	Level C	
Do not discontinue or modify the regular dose of warfarin for patients undergoing minor dental procedures(up to 5 dental extractions/6 dental implants) ²² .	Level 1A	Class I
Do not alter or stop single or dual antiplatelet therapy for invasive dental treatment (single or multiple tooth extractions, deep scaling and probing, biopsies, flap surgery, gingivectomy, alveoloplasty) ¹⁸ .	Level 1A	Class I
Do not interrupt low-dose aspirin therapy (100 mg or less) for outpatient dental procedures ¹⁸ .	Level B	Class I
Oral anticoagulants should not be discontinued in the majority of patients requiring out-patient dental surgery, including extraction ¹⁷ .	Level Ib	Grade A
Continue vitamin K antagonists (VKAs) with an oral prohemostatic agent in patients who require a minor dental procedure ²⁰ .		Grade 2C
Continue ASA around the time of minor dental procedures in patients who are receiving ASA for the secondary prevention of cardiovascular disease ²⁰ .		Grade 2C
Do not discontinue OAC before simple surgeries (extraction ≤ 3 teeth, gingival surgery, periodontal scaling) in patients with INR<3.0 ²¹ .	Level C	
Do not discontinue use of aspirin for dental procedures ²¹ .	Level B	
2. Antibiotics		
A single dose of prophylactic antibiotics will not need an alteration of anticoagulation regimen ¹⁷ .	level IV	Grade C
No need to change anticoagulation regimen when single dose of prophylactic antibiotic is used ²¹ .	Level C	Degree I

3. Preoperative measures		
Check INR prior to dental surgery 72 hours before dental surgery in patients that have stable INR's ¹⁷ .	Level Ib	Grade A
Check INR at least 24 hours before the dental procedure ²¹ .	Level I C	Degree I
Evaluation of INR 72 hours before the procedure is acceptable in stable patients ²¹ .	Level C	Degree I
Discuss with physician in charge when INR \geq 3.0 and the planned procedures are more extensive ²³ .	Level C	
Assess the patients complete medical history ²¹ .	Level C	Degree I
Schedule larger number of visits when there is extraction of more than 3 teeth ²¹ .	Level C	Degree I
Plan the surgeries earlier in the day and in the beginning of the week ²¹ .	Level C	Degree I
4. Operative measures		
Inform the patients that minor bleeding or oozing from gingival mucosa may be more common when not interrupting VKAs during dental procedures ²⁰ .		Grade 2C
Minimize surgical trauma ²¹ .	Level C	Degree I
Reduce areas of periodontal surgery and scaling and root planning (per quadrant) ²¹ .	Level C	Degree I
6. Postoperative pain control		
Do not prescribe NSAID's and Cox-2 inhibitors as analgesic ¹⁷ .	Level III	Grade B
Consider using gelatin sponges, fibrin glue, fibrin adhesive dressing, oxidized cellulose or epsilon-amino caproic acid mouthwash ¹⁸ .	level B	Class I
Give patients on oral anticoagulation (OAC) a 2-day regimen of postoperative 4.8% Tranexamic Acid Mouthwash (TAM) ¹⁸ .	level A	Class I
Give patients who do not interrupt VKAs a 5-mL oral dose of tranexamic acid, 5-10 min before the dental procedure and 3 to 4 times daily for 1 to 2 days after the procedure ²⁰ .		Grade 2C
Remove non-absorbable sutures after 4-7 days ²¹ .	Level C	Degree I
Compress with gauze for 15-30 minutes after the surgical procedure ²¹ .	Level C	Degree I
Use coagulating agents, such as gelatin sponges, oxidized regenerated cellulose, synthetic collagen or tranexamic acid mouthwash in 4.8% aqueous solution during and 7 days after the surgery, using 10 ml, 4 times a day for 2 minutes ²¹ .	Level C	Degree I
8. Referral		
Refer patients whose INR is unstable ¹⁷ .	Level Ib	Grade A

*Levels of evidence are explained in Table 1

**Degrees of recommendation are explained in Table 2

DISCUSSION AND CONCLUSIONS

Since the publication in 2007 of two evidence-based guidelines in the UK and USA^{17,18}, some additional evidence has emerged from one systematic review on antiplatelet therapy²³ and dental procedures and one meta-analysis on VKAs²². Both systematic reviews conclude in concordance with the earlier published guidelines that “continuing the regular dose of warfarin therapy does not seem to confer an increased risk of bleeding when compared with discontinuing or modifying warfarin dose in patients undergoing minor dental procedures”²² and “that there is no indication to alter or discontinue antiplatelet therapy before invasive dental procedures”²³.

Several considerations still have to be taken into account: most studies that were included in the systematic reviews were performed in hospital settings and not in outpatient settings. Neither were they performed in patients with comorbid conditions which might influence bleeding after invasive dental procedures. Several medications are known to influence the coagulation system, like non-steroid anti-inflammatory drugs, or drugs that have a potentiating interaction with VKA's, like antifungal agents such as miconazole, which can increase INR values and might enhance bleeding. Furthermore, local factors, like the degree of inflammation of oral mucosa, might play a role in the risks of developing bleeding after dental surgical procedures. More studies are needed to investigate these additional factors.

The preparation of clinical practice guidelines has received a lot of scientific attention in recent years. Lately, the Board on Health Care Services from the Institute of Medicine in the United States published the latest opinions on good CPG making²⁴. The common opinion is that guidelines need to be conceived in a formal and transparent way, taking into account factors like quality of guidelines as measured by the AGREE instrument (scope and purpose of the guideline, stakeholder involvement, rigor of development, clarity and presentation, editorial independence). Much attention has been given to the fact that certain evidence can lead to different recommendations, depending on the composition of the guideline committee. One example is the differences in recommendations from the guidelines for the prevention of bacterial

endocarditis from both the UK and USA: In 2008 the National Institute of Health and Clinical Excellence (NICE)^{25,26} and American College of Chest Physicians (ACCP)²⁷ each made a guideline in which the American guideline advises to prescribe antibiotics in certain groups of patients undergoing invasive dental treatments, whilst the UK guideline advises against all antibiotic prophylaxis to prevent bacterial endocarditis in dental patients.

One of the quality indicators of good guidelines is that they are built on sound scientific evidence, which can lead to clear recommendations. Unfortunately, recommendations are very much dependent on the background of guideline committee members and possible conflicts of interest. These conceptions gave rise to the development of GRADE (Grading of Recommendations Assessment, Development and Evaluation)^{28,29}. Using the GRADE can help gaining insight into the guideline process and into the way recommendations are derived from evidence or even lack of evidence. In the present article we have only summarized the recommendations based on evidence. In a definitive CPG the independence of the guideline makers should be clearly stated and GRADE should be used to clarify the way how evidence led to the recommendations. GRADE is one method that tries to tackle this problem, and helps guideline makers to get insight into the underlying considerations and make them more explicit when doing recommendations, by including the quality of the evidence and strength of the recommendations. This method has been adopted by well established guideline making institutions, such as NICE, WHO and Cochrane Collaboration and CBO in the Netherlands³⁰. Another important issue is the opinion of the patients. The patients views should be implemented into the CPG to warrant that point of views from their perspectives should be incorporated into the CPG.

Two surveys have been undertaken in the Netherlands, one amongst general dentists¹⁹ and one in oral and maxillofacial surgeons (OMS's)³¹, both showing that dentists and OMS's have very variable management strategies in patients using antiplatelet medicines, like aspirin, as well as in patients using vitamin K inhibitors (VKA's), like acenocoumarol, a warfarin-like antithrombotic mainly used in the Netherlands. Both dentists and OMSs did express the need for a Dutch CPG on this topic. The accumulated evidence and recommendations from this study can be helpful to compose such guideline. Unfortunately, international guidelines cannot

be accepted unchanged, but have to be adapted to local circumstances and needs of both patients, dentists and medical specialists.

In the final version of a CPG clinical questions for which no clinical studies have been undertaken, are relevant. For example: Is it safe to treat patients with OAC with dental implants, which dental procedures are considered more invasive and what should be the management then? How should dentists treat patients using the new generation of oral antithrombotic medicines, like rivaroxaban and dabigatran? Turpie et al.³² advise to not interrupt rivaroxaban in procedures with a low risk of bleeding, such as simple tooth extraction. They also advise to avoid interventions at peak rivaroxaban activity, that is 2-4 hours after dosing. Although there is no antidote to the NOAC's, these medications have a short half-life of 5-9 hours and their anticoagulating effect will wear off much sooner than VKA's, although the effect can last longer in elderly patients³².

Furthermore, the problem of implementing evidence and evidence based CPG into practice, remains a problem. Several studies have shown that since 2007, general dentists and oral and maxillofacial surgeons throughout the Western world, remain advising patients to interrupt their oral antithrombotic medication for simple dental treatments, posing these patients to increased thrombosis risks³³.

In this article we presented the scientific evidence and subsequent recommendations from the literature until October 2012 that can be used as a sound base for an up-to-date clinical practice guideline on the management of dental patients using oral antithrombotic medications and undergoing simple dental procedures²³. We excluded recommendations without scientifically evident sources and produced a four step management advise for general dentists (table 4).

The evidence and subsequent recommendations all point in the same direction: do not interrupt oral antithrombotic medication, not even dual antiplatelet therapy, in simple dental procedures.

Table 4. Proposal for a 2013 clinical practice guideline for general dental practitioners

Recommendations to *general dental practitioners* when planning invasive dental treatment for patients using *oral antithrombotic medication* and undergoing *simple dental treatment* (single or multiple dental extractions up to 3 teeth; up to 3 dental implants, scaling and root planing, probing, flap surgery, apex resection, alveoloplasty):

1. Continuation of oral antithrombotic medication (OAM)*

- a. Do not interrupt single or dual TAR* (such as ASA*, clopidogrel and carbasalate calcium).
- b. Do not interrupt VKA's* if the INR* is less than 3.5.
- c. Do not interrupt NOAC's* (direct thrombin inhibitors or Xa-inhibitors, like apixaban, dabigatran and rivaroxaban).

Note: A single dose antibiotics for prophylaxis does not need alteration of anticoagulation regime, miconazole is contra-indicated when VKA* or NOAC* are taken.

2. Preoperative measures:

- a. Inform the patients that minor bleeding or oozing from gingival mucosa may be more common when not interrupting OAM* during dental procedures
- b. Check INR* in patients using VKA* at least 24 hours before the dental procedure, or – if the patients INR* is stable – 72 hours prior to dental surgery; refer patients whose INR* is unstable.
- c. Advise patients on NOAC* not to take medication 1-3 hours immediately before dental treatment.
- d. Assess the patients' complete medical history and discuss with physician in charge if renal or liver disorders are suspected; when INR* ≥ 3.5 and/or the planned procedures are more extensive.
- e. Schedule larger number of visits when there is extraction of more than 3 teeth and plan the surgeries earlier in the day and in the beginning of the week

3. Perioperative measures:

- a. Minimize surgical trauma and reduce areas of periodontal surgery and scaling and root planning (per quadrant).
- b. Aim at primary closure of surgical wounds, including extraction wounds, using absorbable sutures.

4. Postoperative measures:

- a. Compress with gauze for 15-30 minutes after the surgical procedure, use coagulating agents, such as gelatin sponges, oxidized regenerated cellulose, synthetic collagen or tranexamic acid mouthwash in 4.8% aqueous solution during 1-2 days after the surgery, using 10 ml, 4 times a day for 2 minutes.
- b. Remove non-absorbable sutures, if used, after 4-7 days.
- c. Do not prescribe NSAID's* and Cox-2 inhibitors as an analgesic.
- d. Provide the patient with oral and written instructions about the expected postoperative course and measures they can take if bleeding occurs.

**Abbreviations: OAM: Oral Antithrombotic Medication; TAR: Thrombocyte aggregation inhibitor; ASA: Acetylsalicylic Acid; VKA: Vitamin K Antagonist; INR: International Normalized Ratio; NOAC: New Oral AntiCoagulant; NSAID: Non-Steroid Anti-Inflammatory Drug.*

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