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

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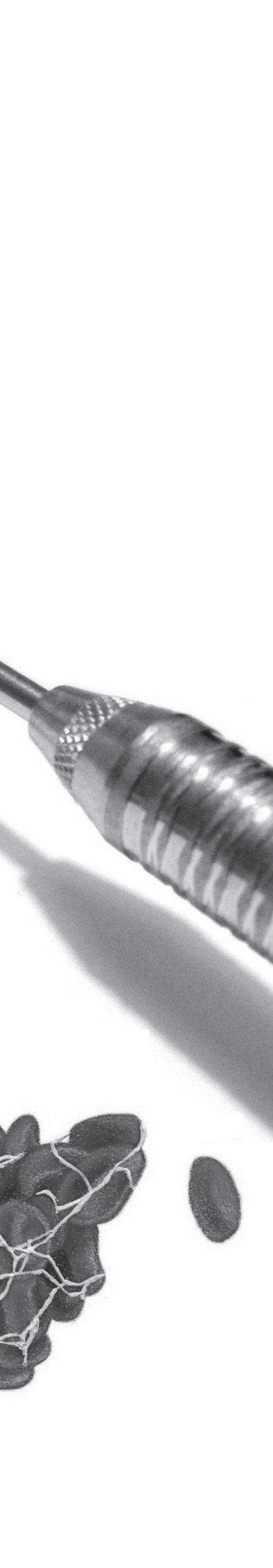
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Chapter 8

General discussion



DISCUSSION

When the research for this thesis started in 2007, the debate on whether or not to interrupt oral antithrombotic medication (OAM) prior to surgical procedures was vivid. Not only in dental surgery, but also in other surgical fields, it was widely accepted to adjust the dose or completely interrupt antithrombotic medication, or bridge it with heparin in a hospital setting, because the bleeding risks were considered to be too high in case of surgery¹.

In the spring of 2007, we had exploratory conversations with two Dutch dentists, three medical general practitioners (GP) and one oral and maxillofacial surgeon on this topic. The dentists stated that they left the choice of interruption of OAM to the GP's which resulted most of the time in the discontinuation of the antithrombotic medications, both thrombocyte aggregation inhibitors, such as acetylsalicylic acid (ASA) as well as Vitamin K Antagonist (VKA's), such as acenocoumarol. Furthermore the dentists experienced that different doctors gave different advice, which led to confusion and insecurity in the dental management of these patients. The GP's in their turn, consulted with medical specialists on this topic and admitted they were not very familiar with dental procedures. The oral and maxillofacial surgeons performed surgery in patients on ASA, but switched patients on VKA to bridging with heparin. All interviewed practitioners concluded that a Clinical Practice Guideline (CPG) on this topic would be advisable (unpublished data).

In 2007 only few CPG's existed on dental topics in the Netherlands. A study by Van der Sanden et al. published in 2003, described the Dutch situation, in which only 50% of Dutch dentists supported the development and implementation of clinical guidelines². In 2003 a literature review that was published in the Dutch Medical Journal (Nederlands Tijdschrift voor Geneeskunde) by Fijnheer et al³, discussed the possibility of continuation of acetylsalicylic acid (ASA) prior to surgical procedures, including dental surgery, especially in cardiac patients. The American College of Chest Physicians Evidence-based CPG, published in 2004⁴ advised tranexamic acid mouthwash without interrupting anticoagulant therapy in patients undergoing dental procedures. In the guideline by the CBO (Centraal Begeleidings Orgaan), published in 2008⁵, dental procedures were not mentioned. Until 2007 no CPG was published

on the topic of antithrombotic medication and invasive dental procedures in the Netherlands. A search through the Dutch dental literature revealed 4 publications in the Dutch Journal of Dentistry (Nederlands Tijdschrift voor Tandheelkunde) published in 1998, 2004 and 2006⁶⁻⁹. In these publications, no clear evidence-based recommendations were given. As described earlier by Van der Sanden et al², CPG's are not very prevalent in dentistry and have had a much longer tradition in medicine, both in the Netherlands as well as elsewhere in the world.

At the Academic Centre for Dentistry Amsterdam (ACTA), we receive many questions of dental practitioners by telephone and email at the Dental Feedback Post, a service for Dutch dentists where they can pose questions they have on medical topics in dentistry. In the years 1999-2006, questions about antithrombotic medication were in the top three of dental inquirers (non-published data). This was one of the reasons to start the current research, to be able to give evidence-based advice and to find an evidence base for a clinical practice guideline. Now in 2013, we have studied and recapitulated the dental and medical literature on this topic and formulated a clinical practice guideline for use by general dental practitioners in the Netherlands and abroad, when treating patients using oral antithrombotic medication (**Appendix 1**). We found four international guidelines¹⁰⁻¹³, and two systematic reviews^{14,15} on this topic, all pointing to the same direction: do not interrupt oral antithrombotic medications when performing minor dental surgery, because the bleeding complications are mild and do not compare with the possible life-threatening complications of a recurrent thrombosis, a possible danger when interrupting oral antithrombotics.

Although this seems like a straightforward conclusion, some aspects on the topic of dental treatment of patients on oral antithrombotics are still equivocal: Most of the clinical studies that were done and that formed the base of the published clinical practice guidelines, have been performed in hospital setting and not in general dental practice. This could have caused selection bias¹⁶ in the study population. Since more complicated patients tend to be treated in hospitals than in private practices, the risks of bleeding in anticoagulated patients as found in different clinical studies may even be lower in private dental practice.

The incidence of bleeding after invasive dental procedures in healthy patients is not very well studied and therefore not known. Gornitsky et al. report an estimated

bleeding incidence of 0.2% - 3.3%¹⁷. Retrospectively reviewing all cases of continued bleeding after dental extractions in our university dental clinic from 2000-2009, we found 67 cases of continued bleeding in 38,971 dental extractions, calculating to an incidence of 0.17% (unpublished data). In a study by Reich et al.¹⁸ patients with compromised anticoagulation, such as Von Willebrandt's disease, were studied, and they found an incidence in postoperative bleeding of 9.9%. These figures are important when comparing results from studies in patients using oral antithrombotics, bearing in mind that even healthy individuals can experience extended bleeding after oral surgical procedures. Most studies in anticoagulated patients demonstrate a slightly higher incidence in recurrent or prolonged bleeding than control groups, but rarely lead to hospital admissions or the need for bloodtransfusions¹⁹.

The incidence of recurrence of thrombosis after the discontinuation of oral antithrombotic medication has been investigated in several studies. The discontinuation of aspirin led to an increased occurrence of arterial thrombosis in cardiac patients with an odds ratio of 3.14. In patients with coronary stents, the odds ratio of developing a stent thrombosis after discontinuation of antiplatelet therapy was even as high as 89.78²⁰. These findings led to a science advisory from the American Heart Association in collaboration with the American College of Cardiology, Society for Cardiovascular Angiography and Interventions, the American College of Surgeons, and American Dental Association, with representation from the American College of Physicians in 2007, with a warning, not to prematurely interrupt antiplatelet therapy in patients with coronary stents. A study by Ho et al.²¹ showed that patients who discontinued use of all medications at one month after experiencing a myocardial infarction, had a lower 1-year survival rate (88.5% vs 97.7%) than patients who continued taking at least one medication. Results were consistent when evaluating discontinuation of the use of aspirin separately. Sibon et al.²² studied the frequency of stroke occurring after antiplatelet discontinuation (APD). Only 4.49% of strokes were related to a recent APD discontinuation, but all cases occurred between 6 and 10 days after drug discontinuation. This temporal pattern has biologic plausibility because the inhibited platelets circulate in the blood for about 10 days. Discontinuation of VKA's or other causes for low INR values have caused relapses of venous thrombosis and pulmonary emboli, as shown in multiple clinical studies²³⁻²⁹.

In the Netherlands a clinical practice guideline has been developed by the CBO on the topic of the diagnostics, treatment and prevention of venous and arterial thrombosis⁵. Several high risk patient groups are classified, in which discontinuation of oral Vitamin K antagonists (VKA) will pose a great risk to the patient of experiencing a recurrent thrombosis. Examples are patients with mechanical heart valves or patients with atrial fibrillation and recurrent strokes. In these patients it is of utmost importance that they stay on therapeutic levels of anticoagulation and should not be exposed to unnecessary risks when undergoing simple dental procedures. Even temporarily discontinuation of acenocoumarol, may disrupt the INR equilibrium for several weeks, leading to high or low INR values³⁰.

From the scientific literature we may conclude there is no need to discontinue oral antithrombotic medication when performing minor invasive dental procedures, like one to three dental extractions or apex resection. Unfortunately, no large studies have been done in patients undergoing major invasive dental procedures. No advice can be given to dentists or oral and maxillofacial surgeons, whether such procedures can be performed without bleeding complications. Comparing surgical procedures from other surgical fields, such as cardiac bypass surgery or orthopedic surgery, might give oral and maxillofacial surgeons some relief considering patients using antiplatelet medication: several studies showed substantially large operations were carried out safely in patients using acetylsalicylic acid or clopidogrel and the ACCP guidelines recommend continuing oral antithrombotic medication in certain patients with high risks of recurrent thrombosis¹².

When science is pretty straightforward, what is the problem then? Dentists in the Netherlands have since long been educated and instructed to discontinue oral antithrombotic medication before invasive dental procedures. In the years 1998-2006, the *Netherlands Journal of Dentistry* (*Nederlands Tijdschrift voor Tandheelkunde*) published four articles on the topic of cardiologic patients and antithrombotic medication⁶⁻⁹. Several recommendations were given, mostly emphasizing the risk of bleeding in anticoagulated patients. No wonder many dentists fear mostly the bleeding complications of antithrombotic medication. This was also illustrated in our survey studies in Dutch dentists and oral and maxillofacial surgeons, published in this thesis, in which the risk of bleeding was estimated higher than the risk of thrombosis.

Bleeding after dental procedures is a complication a dentist will be confronted with himself soon after the procedure, whereas thrombosis usually occurs several days after the dental procedure with prior discontinuation of oral antithrombotics, and hospitalization of the patient with the thrombotic sequelae may be missed by the dentist. Dentists therefore need to be informed about the actual risks of bleeding and thrombosis and the backgrounds of this issue and should not routinely advise patients to stop taking their medication when an invasive dental procedure is planned. By using an evidence-based practice guideline, dentists may be aided in making more rational decisions in these complex patients.

Dentists in the Netherlands are traditionally educated as “pure” dentists. Studying in dental school puts their focus mainly on dental subjects, although medical topics find their way into dental school more often because of the growing group of medically complex patients seeking dental care. When dentists have medical questions about their dental patients, they often seek advice from physicians. In our survey in Dutch dentists, more than 70% of dentists stated they ask advice from primary care physicians and nearly 70% of dentists call on medical specialists regularly for advice about patients using oral antithrombotic medication. Unfortunately, many physicians and medical specialists have little knowledge on dental subjects and are not acquainted with dental procedures¹⁹. Interviews with several Dutch primary care physicians confirm this assumption (unpublished data). This concludes to the necessity to not only inform dentists about this issue, but also notify medical doctors and specialists, like cardiologists and neurologists, that it is usually not necessary to interrupt oral antithrombotic medication in their patients after suffering from a myocardial infarction or stroke when visiting a dentist. Multidisciplinary guidelines are therefore advisable. In the Netherlands several initiatives have been undertaken, such as the composition of a Landelijke Eerstelijns Samenwerkingsafpraak (LESA) in which a multidisciplinary team of “first line” caretakers, such as representatives of the NHG (Dutch general medical practitioners association), KNMP (Royal Dutch Society for the advancement of pharmacy), FNT (Dutch Federation of thrombosis services) and NMT (Dutch Society for the advancement of dentistry) have worked together to produce a working document for all general medical practitioners, dentists, pharmacists and thrombosis services, to streamline the care for patients

using oral antithrombotic medication. (**Appendix2**). Since the publication of the LESA in 2011, it has indeed led to several agreements between local groups of dentists, general physicians, pharmacists and thrombosis services about practical issues regarding mutual patients using antithrombotic medications. The LESA can be found digitally on the website of the NMT (www.tandartsennet.nl).

Recently (November 2012) the issue of the multidisciplinary approach of patients using oral antithrombotic medication by medical specialists was addressed in the Landelijke Standaard Ketenzorg Antistolling voor de eerste- en tweedelijnszorg (National Standard Chain of Care on Antithrombotics for first and second line caretakers) (www.medicatieoverdracht.nl). Next step will be the announcement and publication and subsequent implementation of these agreements to general dentists and physicians, to be of practical use to them and to ultimately improve patient care and safety. Will Dutch dentists adopt this CPG, since Van der Sanden et al.² found that in 2003 only 50% of Dutch dentists supported clinical guidelines? In the survey studies published in this thesis, 87% of dentists and 73% of oral and maxillofacial surgeons were positive towards the development and implementation of a CPG on this topic.

Medicine, dentistry and oral anticoagulants are subject to continuous change and new developments. In 2012 new oral anticoagulant (NOAC) medicines have been introduced in the Netherlands and are registered for prevention of venous thrombosis after hip surgery and recently approved for the prevention of cerebral thrombosis in atrial fibrillation patients. The efficacy and safety of these NOAC's (apixaban, dabigatran and rivaroxaban) have been found to be comparable with acenocoumarol. The advantage is that they can be taken as a single daily oral dose and that monitoring at the Thrombosis Service is not necessary. The expectation is that soon many more patients will switch to these NOAC's. Unfortunately, no studies have been performed in patients using these NOAC's while undergoing invasive dental procedures. Clinical studies in dental patients using NOAC's are urgently needed. Nevertheless, we have included advice for dentists on these new medications in our 2013 CPG, although based on limited available information.

The suggested recommendations provided in the ACTA guideline 2013 (Appendix 1 of this thesis) will need a final step of official approval by a guideline committee

of the Dutch Dental Association, preferably with the GRADE methodology³². This may lead to an official national dental guideline on “Dental invasive procedures in patients using oral antithrombotic medication” for which this thesis may be one of the scientific foundations.

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