

A Systematic Review of Hemorrhage Risk in Patients on the New Oral Anticoagulant Therapy Postdental Implant Placement

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ABSTRACT

Aim: Dental implant placement is potentially invasive and hemorrhagic. Patients on the new oral anticoagulants (NOAC) have a potential risk of hemorrhage postoperative. The present study systematically reviews if NOAC medication presents the potential to increase the bleeding risk after dental implant placement.

Materials and methods: A systematic review was conducted of randomized clinical trials evaluating the risk of hemorrhage after dental implants in patients taking NOAC medication. The literature search was conducted using Cochrane Central Register of Controlled Trials, PubMed, Science Direct without the restriction of language from June 2010 to December 2018. The inclusion criteria were: anticoagulant therapy, dental implant placement and postoperative incidence of bleeding follow-up. The reviewers performed data extraction, bias risk assessment, and determination of the overall quality of evidence for each of the outcomes using the Jadad scale.

Review results: Two articles regarding the incidence of bleeding risk post dental implant placement were included in the review. The first article showed that one patient from the intervention group and two patients from the control group presented slight bleeding the day after the surgery, with the relative risk of 0.919 and the 95% confidence interval of 0.078–10.844. The second article showed that two patients from the intervention group and two patients from the control group presented slight bleeding the day after the surgery, with the relative risk of 0.675 and the 95% confidence interval of 0.090–5.088.

Conclusion: The results suggested that continuing the intake of NOAC during and post procedure has not increased the hemorrhage risk. Hence, drugs modification or alteration was not necessary.

Clinical significance: More well-designed studies are required for future research.

Keywords: Dental implants, Hemorrhage risk, NOAC medication.

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INTRODUCTION

Anticoagulant medication is increasingly used worldwide.¹ In recent years, in the United Kingdom, besides the popular anticoagulant warfarin, new oral anticoagulants therapies have been made available, such as dabigatran, and rivaroxaban.¹ They have been prescribed for patients who presented a high risk or have had a thrombotic event.¹ The high-risk group of patients includes those who have had experienced deep vein thrombosis, pulmonary embolism, stroke or have a cardiac arrhythmia that predisposes patients to clot formation.¹ As the number of NOAC prescriptions has increased in the last few years, the chances of having a patient in the dental surgery and taking them have increased considerably.¹

The recent introduction of NOAC, rivaroxaban, and dabigatran has revealed the need for more scientific reports about their use in conjunction with dental implants. Nocini et al. have highlighted the high rates of cardiovascular disease and the aging population in most countries.² This would lead to a high number of patients taking NOAC and needing dental treatment. Statistics provided by the American Association of Oral and Maxillofacial Surgeons show that 69% of adults ages 35–44 have lost at least one permanent tooth to an accident, gum disease, a failed root canal or tooth decay. Furthermore, by age 74, 26% of adults have lost all of their permanent teeth.³ There were about 100,000–300,000 dental implants placed per year.⁴

Considering the number of dental implant placements per year and the high number of NOAC prescription it was acknowledged that there was a high chance of having a patient in the dental practice taking NOAC medication and wanting dental implant placement.^{1,4}

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Dabigatran was developed as a direct oral inhibitor of thrombin which was transformed by plasma esterases into the active medication known at this point.⁵ The highest plasma concentration was obtained between 1 hour and 2 hours after administration.⁵ The terminal half-life was approximately nine hours after a single dose and twelve to seventeen hours after repeated dosing.⁵ A steady-state level was reached after two or three days of administration.⁶ A third of the drug in the blood circulation was connected to plasma proteins. The drug clearance was achieved in the vast majority by the renal function. The interruption protocol for dabigatran should consider the incidence of hemorrhage and type of surgery.⁷ Thrombin time should be assessed 6–12 hours before surgery if

the risk of hemorrhage was high or if highly difficult surgery was planned.⁷

Rivaroxaban is a direct oral inhibitor of factor Xa. Peak plasma concentrations are reached 2–4 hours after intake.⁸ Rivaroxaban has no direct effect on platelet aggregation, but indirectly inhibits platelet aggregation induced by thrombin.⁸ The half-life for rivaroxaban was regarded in the frame of five and thirteen hours.⁸

By systematically reviewing the available literature, the direct relationship between NOAC medication and prolonged oral hemorrhage following implant placement was analyzed.

The scope of the present article was to research if NOAC medication has the potential to increase bleeding risk after dental implant placement.

MATERIALS AND METHODS

A systematic review was conducted of available literature evaluating the possibility of NOAC medication increasing the hemorrhage risk after dental implants. The literature search was conducted using the Cochrane Central Register of Controlled Trials, PubMed and Science Direct databases without the restriction of language from June 2010 to December 2018. A combination of the following keywords was used: "oral anticoagulant," "new oral anticoagulation" "bleeding risk" and "dental implant".

The inclusion criteria were represented by articles that researched the postoperative incidence of bleeding in patients on NOAC that had dental implant placement.

The exclusion criteria were studies that presented other dental procedures or the patients included in the article were administered other antithrombotic medication. Also if patients were not followed up after the procedure for a sufficient amount of time, any guidelines, expert opinions, animal studies, case reports or reviews were considered in the exclusion criteria.

Three reviewers performed data extraction, bias risk assessment, and determination of the overall quality of evidence for each of the outcomes using the Jadad scale.

The methodological quality of clinical trials was assessed by the Jadad scale in terms of the presence of randomization, masking, and accountability of all patients including withdrawals, as described in the literature.

RESULTS

Initially, 217 studies were identified with our search strategy (Flow chart 1) using the keywords mentioned in the methodology. The inclusion and exclusion criteria were applied to obtain the relevant studies which contained NOAC medication and dental implant placement as the researched focus. There were a number of 215 articles excluded due to the fact of being guidelines, expert opinions, case reports or articles that did not assess the hemorrhage risk after dental implant placement on patients on NOAC. Following the screening process, two full-text articles were selected (Flow chart 1) and included in the assessment. Due to the heterogeneity of the key parameters, aggregation of statistical data was not possible. Therefore, a descriptive analysis of the selected studies was conducted. The clinical studies identified are shown in Table 1.

Gómez et al. compared the postoperative hemorrhage for groups who were taking rivaroxaban with patients not medicated after dental implant placement.⁹ They have conducted a randomized clinical trial in an outpatient setting. Patients in the intervention group had been in treatment with rivaroxaban for over six months before the dental implant surgery. There was

no significant difference between the two groups of patients regarding the incidence of bleeding risk. The relative bleeding risk of 0.919 with a 95% confidence interval of 0.078–10.844 was obtained. The same local hemostatic measures were applied to both groups. The authors concluded that patients can undergo dental implant placement procedures without changing their rivaroxaban medication intake.

Gomez et al. assessed the postoperative bleeding risk for two groups. In the first group were included the patients who were taking dabigatran and in the second group those who were not medicated.¹⁰ They have conducted a randomized clinical trial in an outpatient setting. Patients in the intervention group had been in treatment with dabigatran for over six months before the dental implant surgery. The relative bleeding risk of 0.675 with a 95% confidence interval of 0.090–5.088 was obtained. There was no significant difference between the two groups of patients regarding the incidence of bleeding risk. The same local hemostatic measures were applied to both groups. The authors concluded that patients can undergo dental implant placement procedures without changing their dabigatran medication intake.

The results associated with the incidence of bleeding after dental implants placement have shown acceptable reliability with both studies.

DISCUSSION

The recent introduction of new oral anticoagulant medications, rivaroxaban, and dabigatran, has revealed the need for more scientific reports about their use in conjunction with dental implant placement.¹¹ Dental implants have become a worldwide known procedure which has gained huge popularity due to its good prognostic and success longevity.¹²

The dental implant surgery was regarded as a procedure that was likely to have caused bleeding post-treatment by the Scottish Dental Clinical Effectiveness Programme.¹³ This in conjunction with anticoagulant medication raised a scientific question upon procedural boundaries of dental implants.

The patient had administered rivaroxaban and dabigatran for a sufficient amount of time before surgery and the medication was administered during and after surgery. In both studies, the implant placement was conducted in an outpatient facility. In both cases, there were multiple sites for implant placement.

The incidence of bleeding in patients taking rivaroxaban and dabigatran therapy following dental implant placement

Flow chart 1: Prisma flow diagram

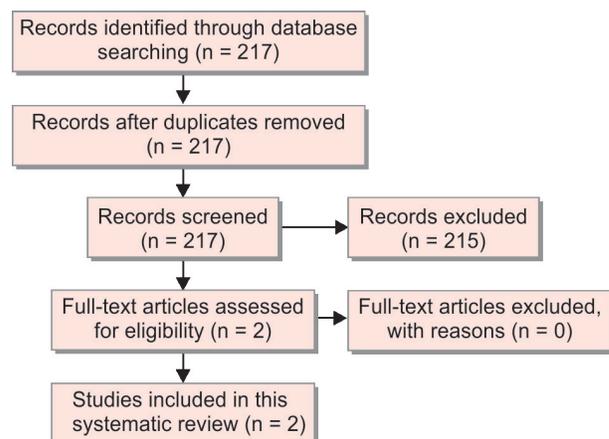


Table 1: Clinical studies identified in the systematic research

Author and year	JADAD score	Type of research	Intervention group/ control group	Hemostatic measures	Result
Gómez-Moreno et al. ⁹	2	Randomized clinical trials	18 taking rivaroxaban/ 39 healthy subjects	Nonabsorbable sutures gauzes impregnated with tranexamic acid 5%	1 from intervention group and 2 from the control group presented slight bleeding the day after the surgery. Relative risk of 0.919 95% confidence interval of 0.078–10.844
Gómez-Moreno et al. ¹⁰	2	Randomized clinical trials	29 taking dabigatran/ 49 healthy subjects	Nonabsorbable sutures gauzes impregnated with tranexamic acid 5%	2 from intervention group and 2 from the control group presented slight bleeding the day after the surgery. Relative risk of 0.675 95% confidence interval of 0.090–5.088

has not been statistically significantly higher than in the control groups. Reviewing the incidence of bleeding after dental implant placement, it has been clear that the bleeding risk has not increased if local hemostatic procedures were taken.

Local measures, such as sutures, gauzes, and 5% tranexamic acids should be the main hemostatic procedures following dental implant placement in a patient under anticoagulant medication.^{14,15} Following this clinical procedure any unwanted hemorrhagic events could be avoided. A proper follow-up of the patient healing process would be ideal to assess and prevent any further issues.

The risk of bias was that in both studies there was no discussion regarding patients' comorbidities. Conditions, such as liver disease, chronic renal failure, and hematological diseases can increase the bleeding risk or can be the main cause for any hemorrhagic events post-treatment. A thorough general pre-surgery assessment should be conducted to identify any chronic pathologies that can have a direct effect on the coagulation and hemorrhagic risk. Another bias was identified as the operators were not blinded during the procedures and at the review appointment. It was not mentioned if the different sites could have affected the bleeding risk as some location might be more prone to hemorrhage than others. The limited amount of time since NOAC medication has been made available and the specific dental treatment researched decreased the available number of articles studied.

CONCLUSION

The level of the available evidence was low so that no strong clinical recommendations could be formulated. Future studies should focus on the bleeding risk for patients having dental implants placement and taking anticoagulant medication.

REFERENCES

1. Becker DE. Antithrombotic drugs: pharmacology and implications for dental practice. *Anesth Prog* 2013;60(2):72-80.
2. Nocini PF, Castellani R, Zanotti G, et al. The use of computer-guided flapless dental implant surgery (NobelGuide) and immediate function to support a fixed full-arch prosthesis in fresh-frozen homologous patients with bone grafts. *J Craniofac Surg*. 2013;24:e551-e558.
3. Oral and maxillofacial surgeons: the experts in face, mouth and jaw surgery [Internet] Rosemont (IL): American Association of Oral and Maxillofacial Surgeons; [cited 2014 Apr 21].
4. Gupta A, Dhanraj M, Sivagami G. Status of surface treatment in endosseous implant: a literary overview. *Indian J Dent Res*. 2010;21:433-438.
5. Stangier J, Rathgen K, Stähle H, et al. The pharmacokinetics, pharmacodynamics and tolerability of dabigatran etexilate, a new oral direct thrombin inhibitor, in healthy male subjects. *Br J Clin Pharmacol* 2007;64(3):292-303.
6. Ageno W, Gallus AS, Wittkowsky A, et al. Oral anticoagulant therapy: antithrombotic therapy and prevention of thrombosis, 9th ed: American college of chest physicians evidence-based clinical practice guidelines. *Chest* 2012 Feb.
7. Van Ryn J, Stangier J, Haertter S, et al. Dabigatran etexilate – a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity. *Thromb Haemost* 2010;103(6):1116-1127.
8. Kubitzka D, Becka M, Voith B, et al. Safety, pharmacodynamics, and pharmacokinetics of single doses of BAY 59-7939, an oral, direct factor Xa inhibitor. *Clin Pharmacol Ther* 2005;78(4):412-421.
9. Gómez-Moreno G, Aguilar-Salvatierra A, Fernández-Cejas E, et al. Dental implant surgery in patients in treatment with the anticoagulant oral rivaroxaban. *Clin Oral Implants Res* 2016;27(6):730-733.
10. Gómez-Moreno G, Fernández-Cejas E, Aguilar-Salvatierra A, de Carlos F, Delgado-Ruiz RA, Calvo-Guirado JL. Dental implant surgery in patients in treatment by dabigatran. *Clin Oral Implants Res*. 2018 Jun;29(6):644-648.
11. Nice . <https://www.nice.org.uk/advice/ktt16>. [Online]. Available from: <https://www.nice.org.uk/advice/ktt16> [Accessed January 2019]. https://www.aaid.com/about/press_room/dental_implants_faq.html.

12. American academy of implant dentistry. [Online]. Available from: https://www.aaid.com/about/press_room/dental_implants_faq.html [Accessed January 2019].
13. Sdceporguk. [Online]. Available from: <http://www.sdcep.org.uk/wp-content/uploads/2015/09/SDCEP-Anticoagulants-Guidance.pdf> [Accessed January 2019].
14. Perry DJ, Noakes TJ, Helliwell PS. Guidelines for the management of patients on oral anticoagulants requiring dental surgery. *Br Dent J* 2007;203:389-393.
15. Forbes CD, Barr RD, Reid G, et al. Tranexamic acid in control of haemorrhage after dental extraction in haemophilia and Christmas disease. *Br Med J* 1972;2(5809):311-313.

