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REVIEW

Novel oral anticoagulants in plastic surgery

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Summary Novel oral anticoagulants (NOACs) have emerged as a good alternative to warfarin in the prevention of stroke for patients with atrial fibrillation. NOAC use is increasing rapidly; therefore, greater understanding of their use in the perioperative period is important for optimal care.

Studies and reviews that reported on the use of NOACs were identified, with particular focus on the perioperative period. PubMed was searched for relevant articles published between January 2000 and August 2015.

The inevitable rise in the use of NOACs such as rivaroxaban (Xarelto™), apixaban (Eliquis™), edoxaban (Lixiana™) and dabigatran (Pradaxa™) may present a simplified approach to perioperative anticoagulant management due to fewer drug interactions, rapidity of onset of action and relatively short half-lives. Coagulation status, however, cannot reliably be monitored and no antidotes are currently available. When planning for discontinuation of NOACs, special consideration of renal function is required. Advice regarding the management of bleeding complications is provided for consideration in emergency surgery. In extreme circumstances, haemodialysis may be considered for bleeding with the use of dabigatran.

NOACs will increasingly affect operative planning in plastic surgery. In order to reduce the incidence of complications associated with anticoagulation, the management of NOACs in the perioperative period requires knowledge of the time of last dose, renal function and the bleeding risk of the planned procedure. Consideration of these factors will allow appropriate interpretation of the current guidelines.

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Careful management of anticoagulant drugs in the perioperative period demands assessing the balance of risk between thromboembolism and perioperative bleeding.[1] In particular to plastic surgery, bleeding may risk the survival of flaps and grafts.[2] A new generation of anticoagulant drugs — novel oral anticoagulants (NOACs) — are now prescribed routinely; however, many surgeons and departments have not yet established perioperative management guidelines. A recent international survey revealed a limited knowledge base amongst clinicians regarding the perioperative management of NOACs.[3] Herein, we describe NOAC drugs, identify evidence-based guidelines in current use and finally present our own algorithm for their perioperative management for NOACs prescribed on a prophylactic basis. For acute therapeutic dosages prescribed for deep vein thrombosis (DVT) and pulmonary embolism (PE), we would recommend discussion with the original prescribing physician and local haematology services.

Novel oral anticoagulants

The mainstay of anticoagulant therapy for thromboembolic conditions over many decades has been through vitamin K antagonists. Experience with these traditional vitamin K antagonists (warfarin) is vast, and units have established protocols regarding use in the perioperative period. However, a narrow therapeutic index, high incidence of interaction and the need for regular monitoring make warfarin a potentially difficult drug to manage. In response to this, new, target-specific oral anticoagulants have been developed with early evidence indicating an equivalent benefit with a better safety profile.[4]

Four NOACs are currently licenced for use in the UK, the most recent, edoxaban, having been approved for use in the UK in July 2015. The European Society of Cardiology (ESC) guidelines recommend their use in non-valvular atrial fibrillation, with a class IA level of evidence.[5] In the UK, the National Institute for health and Care Excellence (NICE) has approved them for use in stroke and thromboembolism prevention in patients with atrial fibrillation.[6–8] In addition, they are licenced for thromboprophylaxis following hip and knee replacement surgery and in the treatment of PE. They fall into two broad categories according to their mode of action: rivaroxaban (Xarelto™; Bayer Healthcare, Leverkusen, Germany), apixaban (Eliquis™; Bristol-Myers Squibb, New York, NY, USA) and edoxaban (Lixiana™, Daiichi Sankyo UK, Buckinghamshire, UK) target factor Xa within the coagulation cascade, whilst dabigatran (Pradaxa™; Boehringer Ingelheim Pharmaceuticals, Ingelheim am Rhein, Germany) directly inhibits thrombin further downstream in the cascade as illustrated in the abbreviated cell-based coagulation model in Figure 1. A short therapeutic half-

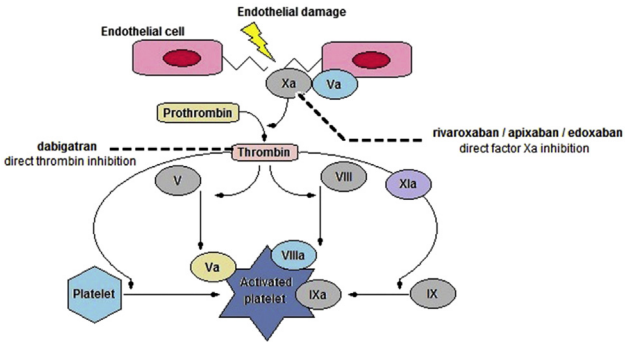

Figure 1 NOAC effects on the cell-based coagulation model. Within the second 'amplification' phase, a procoagulant signal amplified small amounts of activated thrombin, resulting in the activation of platelets, ultimately leading to fibrin clot formation. Both classes of NOAC inhibit this activation: rivaroxaban, apixaban and edoxaban by blocking factor Xa, and dabigatran by inhibiting thrombin's action. Adapted from Wisler JM, Becker RC. Oral factor Xa inhibitors for the long-term management of ACS. Nat Rev Cardiol 2012; 9: 392–401.