

## Antiplatelet Therapy in the Perioperative Period (Systematic review)

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**Abstract: Objectives:** The goal of our work is to discuss different strategies for preoperative management of antiplatelet therapy and the new anti-platelets drugs types. **Background:** cardiovascular events represent the major cause of morbidity and mortality. A key role in the pathogenesis of these events is played by platelets. The activated platelet plays not only an important role in the initiation and progression of atherosclerotic disease<sup>(1)</sup>. **Data sources:** Medline, articles in Medscape, Science Direct, and PubMed were searched. The search was performed on January 2016 and included all articles with no language restriction. **Study selection:** The initial search presented 98 articles. The articles studied antiplatelet therapy in the perioperative period. **Data extraction:** Data from each study were independently abstracted to capture information on study characteristics and interventions. **Data synthesis:** Significant data were collected. Thus, a structured review was performed. **Finding:** Antiplatelet agents represent a particular challenge for the anaesthesiologist when regional anaesthetic techniques are considered. New antiplatelet agents have been developed for patients at high risk of thrombosis, their benefits in terms of mortality and major cardiovascular events have been demonstrated. **Conclusion:** Platelets are essential for primary hemostasis and repair of the endothelium, but they also play a key role in the development of acute coronary syndromes and contribute to cerebrovascular events. Several antiplatelet drugs are available for use in clinical practice and several antiplatelet are under investigation. Antiplatelet and anticoagulants are be useful in the treatment and prophylaxis of arterial thrombotic conditions<sup>(2)</sup>.

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**Keywords:** Platelets, Antiplatelets, Anticoagulants, Hemostasis, Aspirin, Coronary

### 1. Introduction:

Hemostasis is the process that maintains the integrity of a closed, high-pressure circulatory system after vascular damage. It is also a critical event in the arterial diseases associated with Myocardial Infarction (MI) and stroke, and venous thromboembolic disorders accounting for considerable morbidity and mortality<sup>(3)</sup>. Platelets are integral to the initiation of thrombosis. Drugs that affect platelet function are a fundamental part of primary and secondary management of atherosclerotic thrombotic disease. To manage patients receiving antiplatelet drugs during the perioperative period, Understanding of the underlying pathology and rationale for their administration, pharmacology, pharmacokinetics, and drug interactions.<sup>(4)</sup>

### 2. Material and Methods:

#### Search strategy

Search was performed in several databases. It included Medline, articles in Medscape, Science Direct, and PubMed. The search was performed on August 2016, and included all articles published

dealing with antiplatelet therapy in the perioperative period. No restriction according to language.

#### Study selection

All the studies were independently assessed for inclusion. They were included if they fulfilled the following criteria:

Inclusion criteria of the publisher studies

- Articles in no English language were translated.
- Published in peer-reviewed journal.
- Focused on antiplatelet therapy in the perioperative period.
- Discussed the antiplatelet therapy in the perioperative period.
- If a study had several publications on certain aspects we used the latest publication.

The article title and abstract were initially screened. Then the selected articles were read in full and further assessed for eligibility. All references from the eligible articles were reviewed in order to identify additional studies.

#### Data extraction

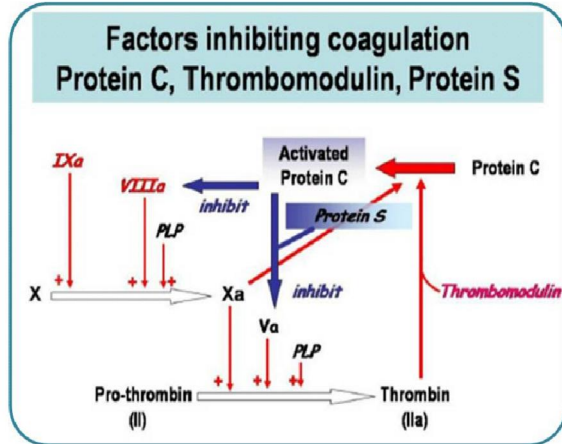
Data from each eligible study were independently abstracted to capture information on study characteristics and interventions.

**Quality Assessment:**

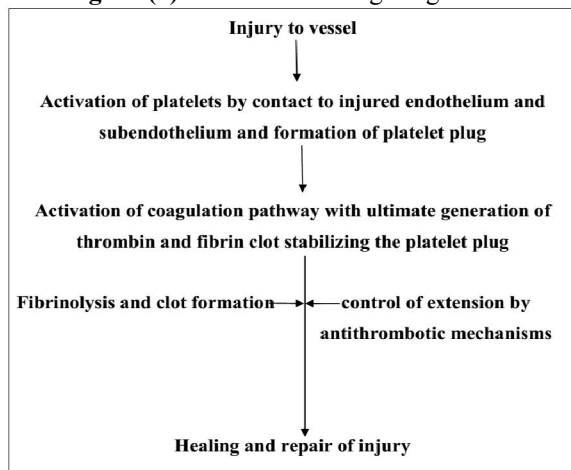
The quality of all studies was assessed. Important factors included, study design, attainment of ethical approval, specified eligibility criteria, appropriate controls, adequate information and specified assessment measures.

**Data Synthesis:**

A structured systematic review was performed.



**Figure (1):** Factors inhibiting coagulation.



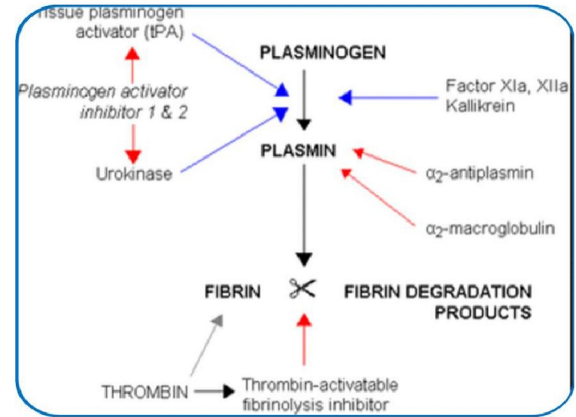
**Figure (2):** Algorithm illustrating the fundamental operation of coagulation pathway.

**4. Discussion:**

Platelets are essential for primary hemostasis and repair of the endothelium, but they also play a key role in the development of acute coronary syndromes and contribute to cerebrovascular events. In addition, they participate in the process of forming and extending atherosclerotic plaques<sup>(5)</sup>.

The platelet is integral to the initiation of thrombosis. Drugs that affect platelet function are a fundamental part of primary and secondary

management of atherosclerotic thrombotic disease including stroke, acute myocardial infarction (AMI), acute coronary syndrome (ACS), angina, percutaneous coronary intervention (PCI), cardiac surgery, primary and secondary cardiovascular disease prevention, peripheral vascular diseases, and thrombotic disorders such as atrial fibrillation<sup>(6 & 7)</sup>.



**Figure (3):** The fibrinolytic pathway.

Several antiplatelet drugs are available for use in clinical practice and several are under investigation. Antiplatelet and anticoagulants are useful in the treatment and prophylaxis of arterial thrombotic conditions, but must be carefully administered without increasing the risk of bleeding to an unacceptable level<sup>(8)</sup>.

The main use of platelet function tests has been traditionally to identify the potential causes of abnormal bleeding, to monitor pro-haemostatic therapy in patients with a high risk of bleeding and to ensure normal platelet function either prior to or during surgery. However, they are increasingly being utilized to monitor the efficacy of antiplatelet and anticoagulants therapy and to potentially identify platelet hyperfunction to predict thrombosis<sup>(9)</sup>.

The perioperative management of patients receiving anticoagulations and antiplatelets agents can be problematic. It is important that the benefit of surgery is first weighed against the risk of altering the anticoagulation regimen. Where doubt exists, there should be a discussion involving the physician managing the anticoagulation, the surgeon and the anesthetist about the risks and benefits of continuing the anticoagulation or the antiplatelets agents. It may also be wise to involve the patient in the decision-making process and to consider an individual plan for complex situations<sup>(10)</sup>.

A multidisciplinary approach helps to manage the perioperative anticoagulation therapy safely and effectively. Patients who are receiving antiplatelets and anticoagulants drugs during the perioperative period requires understanding the underlying

pathology and rationale for their administration, pharmacology, pharmacokinetics and drug interactions. Pharmacodynamics and pharmacokinetics knowledge may allow practitioners to anticipate difficulties associated with drug withdrawal and administration in the perioperative period including the potential for drug interactions<sup>(11)</sup>.

Assessment of continuing or discontinuing these drugs should be made bearing in mind the proposed surgery and its inherent risk for bleeding or thrombotic complications as well as decisions relating to appropriate use of general or some form of regional anesthesia. In the patient requiring urgent surgery, the options to treat an elevated INR are fresh frozen plasma and prothrombin concentrate complex. Vitamin K takes 1-2 days to achieve the target INR and is considered an adjunct in this setting<sup>(12)</sup>.

In the case of semi-urgent surgery, vitamin K can reverse the INR in 1-3 days. Oral administration is preferred, and the dose is based on the INR at presentation. In elective procedures, Coumadin can be discontinued 5 days prior to surgery to achieve a target INR of 1.3 or less. Usage of unfractionated heparin or low molecular weight heparin is indicated in patients with a high or intermediate risk of thrombo-embolism. In patients requiring surgery with a high risk of bleeding, there may be a role for a temporary inferior vena cava filter. In general, Coumadin can be restarted on the first post-operative evening at the maintenance dose. Bridging therapy may be used in postoperatively until the INR is therapeutic<sup>(13)</sup>.

### Conclusion:

Platelets are essential for primary hemostasis and repair of the endothelium. The main use of platelet function tests has been traditionally to identify the potential causes of abnormal bleeding. Anesthesiologists should be cautious in dealing with different types of antiplatelet drugs in withdrawal and continuation in relation to surgical operations<sup>(14)</sup>.

Antiplatelet (as aspirin for an example) administration should be stopped only 3-4 days preoperatively, while clopidogrel discontinuing for 5-7 days preoperatively. Ticlopidine stopped 14 days as the longest antiplatelet should be stopped. Shortest time for stoppage belongs to Tirofiban, only stopped for 8 hours<sup>(15)</sup>.

Today, there are two new antiplatelet agent groups which have been developed for patients at high risk of thrombosis, their benefits in terms of mortality and major cardiovascular events which have been demonstrated<sup>(16)</sup>.

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