Urological Surgery and Antiplatelet Drugs After Cardiac and Cerebrovascular Accidents

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Abbreviations and Acronyms

ACS = acute coronary syndrome
AP = antiplatelet agents
BMS = bare metal stent
CABG = coronary artery bypass graft
DES = drug-eluting stent
MI = myocardial infarction
P-Bx = prostate biopsy
PCI = percutaneous coronary intervention
RRR = relative risk reduction
TURP = transurethral resection of the prostate

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Purpose: The perioperative treatment of patients on dual antiplatelet therapy after myocardial infarction, cerebrovascular event or coronary stent implantation represents an increasingly frequent issue for urologists and anesthesiologists. We assess the current scientific evidence and propose strategies concerning treatment of these patients.

Materials and Methods: A MEDLINE® and PubMed® search was conducted for articles related to antiplatelet therapy after myocardial infarction, coronary stents and cerebrovascular events, as well as the use of aspirin and/or clopidogrel in the context of surgery.

Results: Early discontinuation of antiplatelet therapy for secondary prevention is associated with a high risk of coronary thrombosis, which is further increased by the hypercoagulable state induced by surgery. Aspirin has recently been recommended as a lifelong therapy. Clopidogrel is mandatory for 6 weeks after myocardial infarction and bare metal stents, and for 12 months after drug-eluting stents. Surgery must be postponed beyond these waiting periods or performed with patients receiving dual antiplatelet therapy because withdrawal therapy increases 5 to 10 times the risk of postoperative myocardial infarction, stent thrombosis or death. The shorter the waiting period between revascularization and surgery the greater the risk of adverse cardiac events. The risk of surgical hemorrhage is increased approximately 20% by aspirin and 50% by clopidogrel.

Conclusions: The risk of coronary thrombosis when antiplatelet agents are withdrawn before surgery is generally higher than the risk of surgical hemorrhage when antiplatelet agents are maintained. However, this issue has not yet been sufficiently evaluated in urological patients and in many instances during urological surgery the risk of bleeding can be dangerous. A thorough dialogue among surgeon, cardiologist and anesthesiologist is essential to determine all risk factors and define the best possible strategy for each patient.

Key Words: platelet aggregation inhibitors; myocardial revascularization; stents; blood loss, surgical

More than 2 million patients undergo PCI with stents each year. Since 5% of these patients present for surgery within the following 12 months, perioperative treatment with coronary stents and dual antiplatelet therapy represents an increasingly frequent issue for urologists and anesthesiologists. Most of the time the urologist is the first physician to inform the pa-

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tient about the future operation. However, surgeons are often not sufficiently aware of the high risk of withdrawing antiplatelet agents before surgery in patients after MI or implantation of coronary stents.[1,2] Long-term dual antiplatelet therapy (aspirin and clopidogrel) is particularly important in the perioperative period because it represents the basis for secondary prevention after ACS and MI, and the cornerstone of treatment after PCI with placement of bare metal or drug-eluting stents. We assess the current scientific evidence and evaluate whether it is possible to propose recommendations concerning the treatment of urological patients receiving antiplatelet therapy.

ANTIPLATELET AGENTS

Antiplatelet agents are classified into the 3 categories of acetylsalicylic acid (aspirin), thienopyridines (clopidogrel, prasugrel) and platelet GP-IIb-IIIa inhibitors (eptifibatide, tirofiban, abciximab). This review deals mainly with aspirin and clopidogrel since to our knowledge there is no perioperative experience with prasugrel, and GP-IIb-IIIa inhibitors are only used for ACS and immediately after PCI.

Aspirin irreversibly inhibits thromboxane A_2 and prostacyclin (PGI_2) synthesis. It is effective in doses of 50 to 160 mg a day. There is no evidence that doses greater than 160 mg a day are more efficacious in reducing the cardiovascular risk but they increase the risk of gastric bleeding. After cessation of aspirin, platelet aggregation returns to baseline in 5 days. The long-term benefit of aspirin is a RRR of recurrent vascular events of 38% after MI and 25% after stroke.[3]

Clopidogrel is a pro-drug oxidized by hepatic cytochromes into an active metabolite which has a plasma elimination half-life of 8 hours and inhibits irreversibly platelet aggregation in a dose dependent fashion (daily dose 75 mg). At 7 days after cessation 80% of platelets have recovered normal aggregation. There are no major differences in terms of bleeding between aspirin and clopidogrel when administered alone. The benefit of dual therapy (aspirin and clopidogrel) compared to aspirin alone has been clearly demonstrated. The 1-year RRR is 31% after PCI and stent.[4] Beyond 1 year the benefit of dual therapy is less pronounced (RRR 23%) but it is better than aspirin alone after PCI and DES. The rate of MI and death is 3.1% in patients still on clopidogrel at 2 years vs 7.2% in those who discontinue clopidogrel at 6 months.[5]

EVIDENCE ACQUISITION

A PubMed search was conducted for articles published during the last 10 years using the key words antiplatelet agents withdrawal, perioperative antiplatelet agents and coronary stents, perioperative antiplatelet agents after cerebrovascular accidents, antiplatelet agents and management of surgical bleeding, antiplatelet agents substitution and surgery. A total of 778 articles were found and 167 matching the focus of this review were selected, including controlled trials, observational series, meta-analyses and guidelines from major medical associations.

Evidence indicates that early discontinuation of antiplatelet therapy is associated with a worse outcome in patients after cardiac or cerebrovascular accidents.[5–9] However, most of the data supporting maintenance of antiplatelet therapy in the perioperative period are from case series and nonrandomized retrospective or prospective studies because of the obvious ethical difficulties in performing a placebo controlled, randomized trial when the tested substance is possibly a matter of safety. The recent recommendations formulated by panels of experts are essentially based on precautionary principles and an empirical balance between the risk of vessel thrombosis when antiplatelet agents are stopped and the risk of surgical hemorrhage when they are maintained.[10–12] Our review demonstrates whether the risk of coronary thrombosis outweighs the risk of surgical hemorrhage when antiplatelet agents are withdrawn before surgery.

ANTIPLATELET AGENTS AND CORONARY REVASCULARIZATION

As long as coronary stents are not fully covered by a cellular layer they behave like unstable plaques and require dual antiplatelet therapy. The metal frame of BMSs is covered by smooth muscle cells within 6 weeks and by a normal endothelial layer within 3 months but only 13% of DESs are completely covered by endothelium at 3 months and no more than 56% are covered at 3 years.[13]

Several retrospective series demonstrated high complication rates when surgery was performed early after PCI.[14–16] The combined rate of MI and death is 10% to 38% within 4 weeks after BMS but decreases to 3.8% and 2.8% when surgery is performed at 2 and 3 months, respectively (fig. 1). After DES the rate of adverse cardiac events is more continuous (5.9% up to 12 months) and decreases to 3.3% beyond 1 year but the mortality rate is high (average 35%).[17]

BMSs are threatened by an overgrowth of the neoendothelium, which leads to a restenosis rate of 12% to 25% at 6 to 12 months. To prevent this phenomenon DESs slowly elute antiproliferative agents. The rate of restenosis decreases to 6.5% at