Perioperative use of dual antiplatelet therapy for patients with coronary artery stents

Percutaneous coronary intervention is an accepted part of management of coronary artery disease. An estimated 2 million patients will undergo percutaneous coronary intervention per year worldwide, and of those up to 90% will have a coronary artery stent inserted (Steinhul et al, 2002). Of these roughly 5% will then present for non-cardiac surgery within the first 12 months after percutaneous coronary intervention (Vicenzi et al, 2006).

It is important that anaesthetists understand the perioperative dilemma between continuing the antiplatelet therapy and risking surgical bleeding, and stopping it and risking life-threatening acute stent thrombosis.

The two main types of coronary artery stents are bare metal stents and drug-eluting stents. Bare metal stents were first introduced in 1987 in response to failures with balloon angioplasty. They were used to prevent elastic recoil of the lumen and vessel occlusion. Unfortunately they caused neointimal hyperplasia and restenosis in 12–20% of patients within 6 months, and up to 80% in certain subgroups such as diabetics and those with chronic renal failure (Hoffman and Mintz, 2000).

Drug-eluting stents were developed to combat this problem of restenosis. The first generation used a thin polymer coating the stent, which inhibits the vascular smooth cell proliferation and neointimal hyperplasia. Unfortunately although they do reduce rates of restenosis, they delay the formation of endothelium and so leaving uncovered metal struts. Because of this they remain thrombogenic for an unknown length of time. In-stent thrombosis is prevented by the use of dual antiplatelet therapy (i.e. aspirin and clopidogrel). Current recommendations state that dual antiplatelet therapy should be continued for a minimum of 12 months for drug-eluting stents and 6 weeks for bare metal stents (Chassot et al, 2007), but in some institutions if there are risk factors present for in-stent thrombosis dual antiplatelet therapy will be continued indefinitely (*Table 1*) (Carrozza, 2006).

With dual antiplatelet therapy the overall risk of stent thrombosis is now around 1%, but this catastrophic event has a mortality rate of up to 45% (Iakovou et al, 2005).

If aspirin and clopidogrel are stopped abruptly there can be a rebound effect with increased platelet adhesiveness (Beving et al, 1996). This, together with the systemic inflammatory syndrome and acute phase reaction to the surgery itself (Chassot et al, 2007), gives an increased risk of thrombosis. The exact risk of perioperative stent thrombosis is unknown but a prospective study in patients with coronary artery stents undergoing non-cardiac surgery, showed a 4.9% mortality rate and a 44.7% morbidity rate (most adverse events were cardiac in nature) (Vicenzi et al, 2006).

Chassot et al (2007) reviewed the use of antiplatelet therapy drugs in surgery. They found that on average surgical blood loss increased by 2.5–20% with patients taking aspirin, this increased to 30–50% if they were taking both aspirin and clopidogrel. This increase in bleeding was not associated with any increased surgical mortality except during intracranial surgery and possibly transurethral prostate surgery. They argue that the overall risks of withdrawing dual antiplatelet therapy are greater than if they are continued.

Table 1. Risk factors for in-stent thrombosis

Inappropriate stopping of dual antiplatelet therapy
Stents inserted in left main stem or at a bifurcation
Multiple or overlapping stents
In-stent restenosis
Left ventricular dysfunction
Renal failure
Diabetes

The exact perioperative management of these patients has not yet been identified. Strategies include stopping dual antiplatelet therapy and using a bridging therapy before surgery, e.g. low molecular weight heparin, unfractionated heparin or tirofiban (a short-acting glycoprotein IIa/IIIb inhibitor) (Vicenzi et al, 2006; Broad et al, 2007). More evidence is needed to define the optimal approach to managing these patients.

Conclusions

Anaesthetists will see this dilemma more often. It requires a multidisciplinary approach with close discussions between the surgeon, anaesthetist and cardiologist on a case by case basis. It is important to recognize those patients who are at risk of stent thrombosis and balance these risks against the risk of surgical bleeding. **BJHM**

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Beving H, Zhao C, Albage A, Invert T (1996) Abnormally high platelet activity after discontinuation of acetylsalicylic acid treatment. *Blood Coagul Fibrinolysis* **7:** 80–4

Broad L, Lee T, Conroy M, Bolsin S, Orford N, Black A, Birdsey G (2007) Successful management of patients with a drug-eluting coronary stent presenting for elective, non-cardiac surgery. *Br J Anaesth* **98:** 19–22

Carrozza JP Jr (2006) Duration of clopidogrel therapy with drug-eluting stents. *J Interven Cardiol* **19**(Suppl): S40–S46

Chassot PG, Delabays A, Spahn DR (2007) Perioperative antiplatelet therapy: the case for continuing therapy in patients at risk of myocardial infarction. *Br J Anaesth* **99:** 316–28

Hoffman R, Mintz GS (2000) Coronary in-stent restenosis –predictors, treatment and prevention. *Eur Heart J* **21:** 1739–49

Iakovou I, Schmidt T, Bonizzoni E et al (2005) Incidence, predictors, and outcomes of thrombosis after successful implantation of drug eluting stents. *JAMA* **293:** 2126–30

Steinhul SR, Berger PB, Mann JT III, Fry ETA, DeLago A, Wilmer G, Topol RJ; for the CREDO investigators (2002) Clopidogrel for the reduction of events during observation. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomised controlled trial. *JAMA* **288:** 2411–20

Vicenzi MN, Meislitzer T, Heitzinger B, Halaj M, Fleisher LA, Metzler H (2006) Coronary artery stenting and non-cardiac surgery-a prospective outcome study. *Br J Anaesth* **96:** 686–93

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