Book review

Antiplatelet therapy in ACS and A-Fib

Advances in Cardiology, vol. 47, *Antiplatelet therapy in ACS and A-Fib*. Editor(s) V.L. Serebruany and D. Atar. Published by Karger AG, Basel. 2012. 170 pp, price \$167.00. ISBN 978-3-318-02168-4

This book is part of the *Advances in Cardiology* series, and specifically looks at the current status of antiplatelet therapy in two important cardiac diseases, namely acute coronary syndrome (ACS) and atrial fibrillation (A-Fib).

The first chapter gives a potted summary of the usefulness and place of antiplatelet therapy in ACS and A-Fib; essentially concluding (rightly) that modern antiplatelet regimens have an important and ever-increasing place in ACS treatment, whereas their usefulness in A-Fib is now considered very limited indeed (whereas, by contrast, anticoagulation is now considered a much superior treatment option in A-Fib). These themes are explored in detail in subsequent chapters, which deal successively with aspirin, clopidogrel, prasugrel and ticagrelor. There then follows a chapter on dipyridamole, exploring not so much its antiplatelet actions but its antithrombotic, anti-inflammatory, free-radical-scavenging and other pleiotropic effects; but one comes away from this chapter rather thinking, does any of this translate into anything clinically meaningful?

There then follows a chapter on the protease-activated receptor (PAR)-1 inhibitors and their potential usefulness in treatment of ACS. Whilst this has seemed very attractive as a novel therapeutic option, since the book came into print two relevant and important major trials have been published, namely the TRACER and the TRA 2P-TIMI 50 studies [1, 2]. In the former trial, which was a large, randomized, double-blinded trial comparing the PAR-1 inhibitor vorapaxar with placebo in addition to standard therapy in patients with ACS, no significant reduction was seen in the composite end-point of cardiovascular death, myocardial infarction, stroke, recurrent ischaemia with rehospitalization or urgent coronary revascularization, whilst there was increased risk of major bleeding. In the latter trial, which was a similar study but performed in patients with stable atherosclerosis, vorapaxar reduced the primary end-point of cardiovascular death, myocardial infarction or stroke by 13%, whilst there was a 66% increase in moderate-to-severe bleeding, including intracranial haemorrhage, which necessitated premature termination of this trial at 2 years by the data and safety monitoring board. These data call into question the future of this approach.

The next chapter, entitled 'Genetic Considerations', suggests that pharmacogenetic testing may be the way

forward for clopidogrel use in ACS, given the fact that its pharmacokinetics exhibit huge interpatient variability, much of which is genetically determined. Again, however, events seem to have overtaken since the appearance of this book. A large meta-analysis has concluded that, although there is an association between clopidogrel loss-of-function genotypes (*CYP2C19* alleles) and responsiveness to the drug, there is no significant association of the genotype with cardiovascular events [3]. Moreover, the newer P2Y₁₂ antagonists prasugrel and ticagrelor show little or no pharmacogenetic interindividual variation and are, in many centres, used in preference to clopidogrel for ACS these days owing to their greater efficacy and more predictable pharmacokinetics.

Following this, there are some very useful chapters on antiplatelet approaches for prevention of stent thrombosis, mitigation of bleeding risk and stroke prevention. Finally, the place of antiplatelet agents in A-Fib, possibly in combination with novel anti-thrombotic agents, is considered.

Overall, the book is a useful resource for the clinician, and is presented in an easily digestible form. The main caveat is that some of it – especially the chapters on PAR-1 antagonists and clopidogrel pharmacogenetics – is now already out of date; but such is the problem with any book of this sort, given the lead time needed to publication.

Competing Interests

There are no competing interests to declare.

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