Advances in the treatment of STEMI

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Improvements in ST Elevation Myocardial Infarction (STEMI) management have occurred at a brisk pace and has resulted in better outcomes for patients.

There has been ongoing advances in the quality of care from Coronary Care Unit (CCU) monitoring to fibrinolytic therapy and combination medical therapy with antiplatelet and anticoagulant therapy to Primary Percutaneous Coronary Intervention (PPCI). These advances have contributed to a decrease in the 30 day mortality from 30% in the 1970s to less than 5% today.[1]

At the same time, we find ourselves in the throes of a major epidemiological shift within the developing world, with cardiovascular deaths expected by 2030 to outnumber the combined deaths from HIV/AIDS, tuberculosis, malaria and maternal deaths in Sub-Saharan Africa (World Health Organization 2030 Predictions).

Overall, STEMI statistics in the developing world are rising dramatically coupled with the fact that patients are younger and associated with a five times higher mortality as compared to the developed world.[2] Currently, there are no clear explanations for these shifts.

PATHOPHYSIOLOGY OF STEMI

The currently accepted model is that STEMI occurs as a result of acute vessel thrombosis. Following rupture of the thin fibrous cap of an atherosclerotic plaque, there is sudden platelet activation and aggregation. This platelet plug is interwoven with thrombus and fibrin.[3]

Immediate medical therapy to re-establish flow in the vessel is achieved by fibrinolysis as well as a heparin type compound and an antiplatelet agent (aspirin and clopidogrel traditionally). Superimposed on this, passivation of the plaque has been achieved by using high doses of statins.

MANAGEMENT

Primary percutaneous coronary intervention (PCI) is the current buzzword worldwide regarding STEMI management. The reality is that with about 180 practicing cardiologists in the country (most not in public practice)4 and with eight public centres catering for over 80% of the 55 million population, most South Africans who sustain a STEMI will probably never receive an angiogram, let alone primary PCI. Data also shows that even in a tertiary institution, diagnosis is often delayed and fibrinolytic initiation can take up to six hours.[5] It therefore makes more sense to drive the advantages of early diagnosis and intense appropriate fibrinolysis and medical management.

FIBRINOLYTICS VERSUS PRIMARY PCI

In SA, fibrinolytic usage still needs to form the mainstay of STEMI therapy. The agent of choice in 2016 would be tenecteplase, due to the ease of administration, rapidity of action and the lower incidence of bleeding. It is also more effective in infarcts older than hour hours.[6]

Streptokinase or actilyse (rTPA), which are often more readily available, are also acceptable fibrinolytic therapies. Data now suggests as well that one year mortality from primary PCI and from a pharmacoinvasive strategy (fibrinolytic followed by routine angiography) is similar.[7]

ADVANCES IN ANTIPLATELETS AND ANTICOAGULATION

The standard of therapy until recently included aspirin and clopidogrel. Two newer P2Y12 receptor antagonists are now available: Ticagrelor and prasugrel. They both have a much shorter onset of action and half-life, as compared to clopidogrel. There are also no known issues with regards to resistance.

Both landmark trials (PLATO and Triton) show decreased morbidity and mortality at the expense of a slightly higher bleeding rate. Unfortunately their use has only been studied in the setting of primary PCI and their use in combination with fibrinolysis is yet to be studied.[8,9]

Cangrelor is an intravenous P2Y12 receptor antagonist which has received US Food and Drug Administration approval in 2015. Its major advantage is its rapid onset of action of one to two minutes.[10] Further data will be needed to determine exactly where this agent will fit into the current armamentarium of drugs.

In terms of anticoagulation, low molecular weight heparin (enoxaparin) has superseded the use of unfractionated heparin due to the ease of subcutaneous administration and their predictable pharmacokinetics. Enoxaparin works well in conjunction with fibrinolysis and receives a Class I indication in this setting.[11]

The HEAT PPCI trial caused major waves amongst interventionalists as it demonstrated unfractionated heparin having better outcomes than bivalirudin (thrombin inhibitor) at 1/400th the price.[12]

Unfortunately, no subsequent large trial has managed to reproduce these results, and as a result, there has been no change in guidelines, with bivaluridin remaining the anticoagulant of choice in primary PCI.[13,11]

Some excitement ensued From the Atlas TIMI 51 trial which showed the novel oral anticoagulant (NOAC), rivaroxaban, when added to dual antiplatelet therapy (DAPT) in patients with acute coronary syndromes managed to decrease mortality and cardiac events at a slightly increased risk of bleeding. The results from this trial have now been clouded in doubt due to large amounts of missing data. Thus far, no clear role for the use of the NOACS in the setting of acute coronary syndromes has been elucidated.[14]

NEWER CONCEPTS

An interesting comeback has been the use of the GIK regimen - an infusion of glucose, insulin and potassium - which had been proposed many decades ago by Sodi Pallares. This has been retested now in the Immediate trial with suggestions that it does manage to reduce infarct size.

We eagerly await a larger, more powerful trial in this regard. The glucagon like peptide, exanetide has also been shown in a small trial to be effective in reducing infarct size. Other studies have considered using agents to try and reduce infarct size and improve mortality.

Cyclosporin A, which has been shown to mimic the physiology of ischemic preconditioning, has been tested but has not shown any benefits. Similarly, adenosine and nitric oxide have been used to try and reduce infarct size with no convincing benefits thus far.[15]

Overall, there has been fulfilling advances in the management of STEMI. However, issues that remain core to achieving good outcomes are that the diagnosis has to be accurate and the initiation of centre appropriate therapy (fibrinolytic or primary PCI) needs to be regarded as an emergency.

The biggest challenge to treating STEMI in SA remains a fragmented public/private healthcare system and it needs to always be remembered that time is muscle and the sooner reperfusion is achieved, the better patient outcomes will be.

References available on request. SF