ISSUES IN MEDICINE

Initiation of pre-hospital thrombolysis in South Africa

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The administration of thrombolytic therapy is a time-critical intervention that in South Africa was until recently limited to administration in coronary care units and some casualty departments. This approach can lead to significant treatment delay, particularly for rural/urban-rural patients, where inter-hospital transfers can be prolonged.

HPCSA decision on thrombolysis

The Health Professions Council of South Africa (HPCSA) Professional Board for Emergency Care Practitioners recently introduced thrombolysis as a new skill for use by emergency medical care graduates as part of a structured research programme supervised by the Durban Institute of Technology. The aim of this research project will be to inform and guide the roll-out of pre-hospital thrombolysis to all South African paramedics.

The introduction of pre-hospital thrombolysis will see a significant improvement in the management of ST elevation myocardial infarction (STEMI), and the associated additional education/decision-making process will impact on the remaining cardiac patients who are not suitable for thrombolysis.

Thrombolysis, or more correctly fibrinolysis, is a process that speeds up the body's own ability to remove coronary artery clots, thereby improving myocardial blood flow. The single biggest hurdle in the provision of reperfusion therapy is prolonged time to treatment. Each minute of delay in treatment results in a loss of 11 days of life for the patient.[1] Prompt provision of thrombolysis has therefore been compared to the urgency required for successful defibrillation.

Although patients[2] are responsible for the greatest overall delay in obtaining treatment, the impact of system delays can also be significant as transfer to hospital can be prolonged and not all casualty departments offer thrombolytic therapy. This is not the case internationally, where it has become part of pre-hospital treatment.[3]

Internationally pre-hospital thrombolysis by non-physicians is recommended in all systems that cannot ensure that patients will be in hospital within 60 minutes of contacting the emergency services.[3] A similar time target set in South Africa would place the administration of thrombolytic therapy firmly in the domain of the paramedic. The shift towards earlier administration of thrombolytic therapy is based on strong clinical evidence of patient benefit.[1,4-5]

The time saved with the introduction of pre-hospital thrombolysis can range from < 33 minutes[4] to > 130 minutes[1] depending on local emergency medical service (EMS) systems, hospital setup and transfer times. It is arguable that within the context of South African EMS we should be able to emulate and surpass the benefits demonstrated by the GREAT study,[1] which is currently the benchmark study for improving patient outcomes.

Research project on the initiation of thrombolysis

Paramedics in South African EMS can obtain registration with the HPCSA as advanced life support (ALS) practitioners on successful completion of either a short in-service course or a 3-year/4-year degree programme.[6] Currently practice of thrombolytic therapy is limited to paramedics who have completed additional study to obtain a 4-year degree in emergency medical care. A key aspect of the 4-year qualification is decision making, and this is reflected in the lack of strict protocol for delivery of thrombolytic therapy. The rationale for the lack of strict protocol is to develop evidence-based medicine and autonomous paramedic practitioners. This is currently not the case in other countries that have introduced pre-hospital thrombolysis within a strict framework.[7]

The key purpose of the research project is to determine how to implement pre-hospital thrombolysis fully within South African emergency EMS. Numerous avenues exist, but a tiered system with autonomous paramedic practitioners at one end supported by protocol-driven thrombolysis by other ALS providers may be the first step in the wider introduction of pre-hospital thrombolysis.

To ensure autonomous practice at a higher degree of clinical decision making is essential, as thrombolysis is not appropriate

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in all cases of myocardial infarction, and despite its mortality benefits thrombolysis is not a benign therapy.

Thrombolysis is associated with a number of significant side-effects, including a 1% risk of fatal intracranial haemorrhage[8,9] and an accelerated risk of cardiac rupture among certain patient subgroups.[10] However, with the exception of cardiac rupture all potential side-effects remain static with time, but clinical benefit is greatly affected by treatment delay.[1,10]

The safe autonomous administration of thrombolytic therapy therefore requires the paramedic to 'risk stratify' patients while developing additional assessment skills such as interpretation of the 12-lead electrocardiogram (ECG) and use of additional ECG lead placement to diagnose isolated posterior or right ventricular infarcts.

Examples of the degree of decision-making skill required would be deciding whether an elderly hypertensive woman (< 50 kg in weight) with an inferior infarct, who is between 10 and 12 hours post infarct, will benefit from thrombolysis,[10] or deciphering whether left bundle-branch block is a new or chronic ECG change. It is clear that thrombolysis in the South African context cannot rely on simple ECG pattern-recognition protocols used elsewhere.

In addition to the administration of thrombolytic therapy the practitioner needs to learn to challenge previously held beliefs, particularly regarding the prophylactic treatment of cardiac arrhythmias such as R-on-T phenomena and frequent ventricular ectopics, especially after thrombolysis. The routine treatment of these arrhythmias provides no mortality benefits and can result in potentially drug-induced side-effects such as hypotension, AV node block and drug toxicity.[11,12]

Thrombolysis is only appropriate for a relatively small number of patients with an acute coronary syndrome, but all paramedics need to consider the vital importance of treating pain and the appropriate management of arrhythmias.[3,13] Paramedics should also encourage their colleagues at basic and intermediate level to use Entonox as pain relief in cardiac patients and to summon ALS assistance as soon as possible.

Continued early use of aspirin is of vital importance. Some studies have shown significant mortality benefits with aspirin use, similar to the benefits with thrombolysis,[14,15] but internationally aspirin tends to be underadministered by ALS personnel.[16] The wider use of aspirin by all EMS personnel should be encouraged and supported, as aspirin use has few contraindications and is highly effective in reducing cardiac mortality in all patients, not just those with STEMI.

Primary coronary intervention (PCI) versus thrombolysis

There is great debate regarding thrombolysis versus PCI.[17,18] It has been argued that there is less time pressure when choosing PCI over thrombolysis;[18] this resulted in numerous trials in which thrombolysis was withheld and the patient transferred for PCI.[19,20] De Luca and colleagues[21] recently challenged this approach by demonstrating that total 'ischaemic time' affects mortality and that for every 30-minute delay before performing PCI mortality increases by 7.5%.

In their study Widimsky *et al*.[19] recommended thrombolysis if patients present within 3 hours of symptom commencement. The evidence from Steg *et al*.,[20] based on prehospital thrombolysis, clearly demonstrated a mortality benefit for thrombolytic therapy if administered less than 2 hours from the onset of symptoms when directly compared with PCI.

It is appropriate to highlight that clinical trials comparing thrombolysis with PCI have a number of issues that need to be considered. Brophy and Bogaty[17] highlighted a number of these, such as inclusion bias, prolonged in-hospital delays before initiating thrombolysis, comparison of PCI with streptokinase and not with fibrin-specific agents, and exceptional door-to-balloon times during clinical trials.

The USA's National Registry of Myocardial Infarction (NRMI) project recently demonstrated that the benefits of PCI over fibrin-specific agents disappear if PCI takes longer than 69 minutes.[22] This potentially represents the time taken to reperfuse an occluded artery using thrombolytic therapy.[23] When we consider the evidence presented by Pinto[22] and by Nallamothu *et al*.,[24] who highlighted that less than 5% of patients (entered into the NRMI) experiencing a STEMI achieved a door-to-balloon-time of 90 minutes, we perhaps need to consider again the role of prompt thrombolysis.

So what's the role for PCI?

Increasingly the specific role of PCI will be as a 'rescue' therapy for failed reperfusion,[20,25,26] treatment of high-risk patients in cardiogenic shock,[27] and treatment of patients with significant contraindications to thrombolysis.[17] However, an increasingly important role of early PCI could be within the field of facilitated PCI following thrombolysis.[26,28]

Facilitated PCI

Facilitated PCI involves the use of early thrombolysis supported by early PCI, typically within the first 24 hours. The GRACIA-1 and GRACIA-2 trials[26,28] using glycoprotein IIa/IIIb inhibitors and stent have demonstrated this approach to be safe and clinically effective. GRACIA-2[28] recently demonstrated that 61% of patients receiving thrombolysis (tenecteplase) supported by facilitated PCI had total resolution of ST elevation at 6 hours compared with 41% of patients receiving PCI only.

Conclusion

South African paramedics are entering an exciting time and need to grasp the mantle of evidence-based pre-hospital

cardiac care. The introduction of pre-hospital thrombolysis plus the supporting education that underpins this extension of patient management should have a far-reaching clinical impact. Of equal importance are the clinical benefits that earlier pre-hospital thrombolysis will offer patients, particularly if supported by early angiographic intervention.

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