Opinion

Thrombolytic therapy versus primary percutaneous coronary intervention: role of clinical pharmacist

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Cardiovascular drugs constitute one of the largest and most widely used among other diseases and cardiovascular drug market has largely been exploded [1]. Although these drugs have the potential to significantly improve the treatment of various cardiac diseases. They are potent agents with potential for serious adverse effects, toxicity and drug interactions. Newer agents are considerably costly than older drugs and, therefore, cost-effective strategies must be developed [2]. Thrombolytics are pharmacological agents come from bacterial origin as streptokinase and staphylokinase or from human origin as urokinase or t-PA. Thrombolytics are used to restore blood flow to infracted artery quickly. Only streptokinase, alteplase, reteplase and tenecteplase are approved by US-FDA for treatment of ST-elevation myocardial infraction (ST-EMI) [3]. This reopens blood vessels after their occlusion and prevents tissue necrosis. Although, the safe and effective use of each of these drugs requires a thorough understanding of appropriate patient selection, drug timing, dosing regimens and monitoring parameters. The greatest benefit to risk ratio for specific drugs is seen in certain subsets of patients the complexities of cardiovascular drug therapy illustrate the need for an in depth current knowledge of clinical trial evidence. In response to these new findings, the role of older agents was redefined and newer therapies have emerged as recommended therapies. Although thrombolytic therapy is well established in elderly patient but its use remains controversial in elderly patient over 75 years of age, in part due to increased bleeding tendency in this group, but showed safe, effective benefit with low incidence of adverse events if the elderly patients have carefully been selected [3]. Thrombolysis in pediatric patient is based on adult guidelines, where it should be individualized. Further studies in this population are required in order to provide safe and effective thrombolytic use. Choice of therapy for ST-EMI is controversial. But first one should answer: What is the thrombolytic agent of choice among those available in our drug market? The prototype streptokinase when given early has the following advantages: reducing mortality rate and lowering the incidence of re-infarction and intracerebral hemorrhage (ICH). But common side effects including allergic reactions, hypotension and increased bleeding tendency limits its use streptokinase is the drug of choice in countries with poor health resources, its use in Europe is limited day after day. Alteplase (fibrin-specific agent) has shorter half-life and is free from antigenicity and hypotension risks [3]. Although re-occlusion that accompanies its use can be overcome by concomitant administration of heparin but it is more expensive than streptokinase and carries risk of ICH. Out of our belief that physicians, pharmacists and other healthcare providers can collaborate in providing optimized patient care to cardiology patients with ST-EMI. Thus, thrombolytic therapy versus primary PCI has been investigated reviewed [3, 4]. In view of the evidence-based treatment recommendations for patients with ST-

EMI and the demographic, political and financial implications inherent in the establishment of systems of care to increase the number of patients with timely access to primary percutaneous coronary intervention (PCI), the acute myocardial infarction advisory working group developed principles to guide this initiative, a system of care for ST-EMI patients must have the following components:

Patient-centered care as number one priority, high-quality care that is safe, effective and timely, stakeholder consensus on systems infrastructure, increased operational efficiencies, appropriate incentives for quality, such as pay for performance, pay for value or pay for quality, measurable patient outcomes, evaluation mechanism to ensure quality-of-care measures reflects changes in evidence-based research, including consensus-based treatment guidelines (**Figure 1**), role for local community hospitals so as to avoid negative impact that could eliminate critical access to local health care and finally, reduction in disparities of healthcare delivery, such as those across economic, education, racial/ethnic or geographic lines.

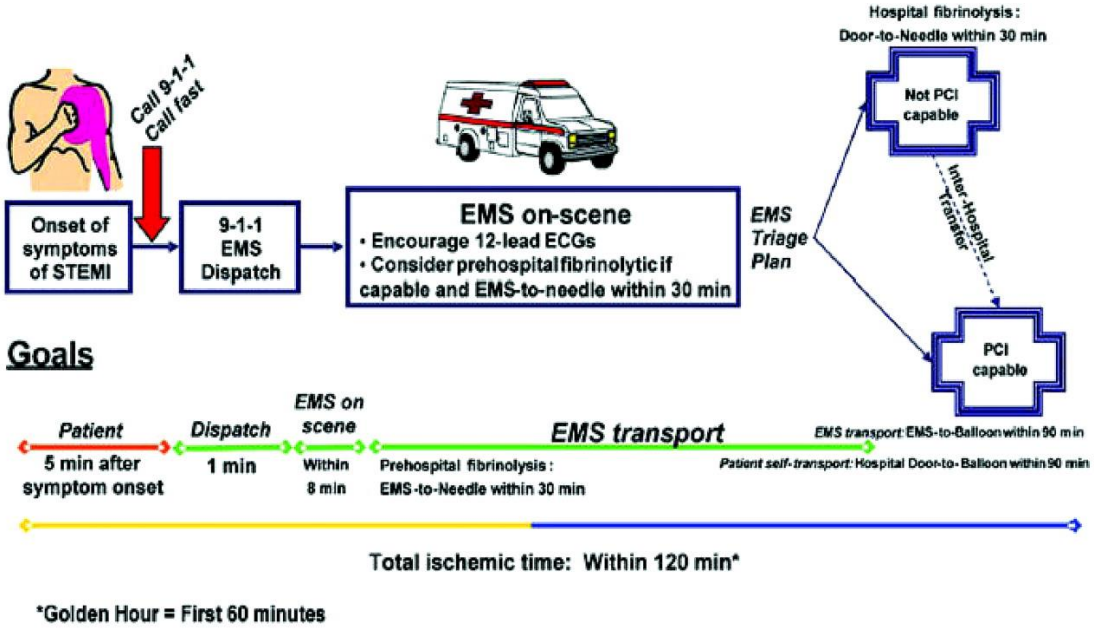

Figure 1: Options for transportation of patients with ST-EMI and initial reperfusion treatment

Alternative, sirolimus analogue under investigation is biolimus A9 which evaluated in two biodegradable (PLA) polymer-coated stainless steel where about 70% of the drug is eluted over 30 days followed by sustained release with polymer degradation. biolimus-eluting stent has proved effective when compared to BMS and paclitaxel eluting stent (PES). Tacrolimus is macrolide immunosuppressant drug licensed for recipients of organ transplantation. The cellular mechanisms of tacrolimus differ from sirolimus: tacrolimus acts by binding FK506-binding protein 12 (FKBP12) and subsequently inhibiting calcineurin and suppressing T cell proliferation. The cellular effect is to hold cells in the G0 phase, where they are able to function but unable to replicate. Tacrolimus has preferential effect on smooth muscle cells (SMCs) as opposed to endothelial cells and unlike the mammalian target of rapamycin (mTOR) inhibitors and paclitaxel, does not increase expression of tissue factor [5]. A stainless-steel stent loaded with tacrolimus in abluminal reservoirs performed no better than BMS. A Cobalt Chromium (CoCr) stent coated with PLGA and tacrolimus is under investigation. Pimecrolimus, tacrolimus analogue was investigated on its own but in combination with paclitaxel. It exerts multiple anti-inflammatory effects including inhibition of IL-2 synthesis via calcineurin inhibition. The Synchronnium stent consists of a stainless steel stent coated with biodegradable polymer incorporating heparin and sirolimus. The addition of heparin aims to decrease the thrombogenicity of the stent. Genistein, natural isoflavanoid phytoestrogen is currently under investigation in combination with sirolimus. Flavanoids have some potentially beneficial characteristics as anti-platelet aggregation, anti-inflammatory and anti-oxidant properties. An alternative approach, concentrating on healing as opposed to SMC inhibition, is used in genous endothelial progenitor cell (EPC) capture stent. This is stainless steel stent coated with murine monoclonal

antihuman CD34 antibodies which attract circulating EPCs thereby encouraging rapid endothelialisation and reducing the risk of thrombosis. The EPC capture stent appears effective in stable patients and in the setting of acute myocardial infarction [6].

Role of clinical pharmacist in management of ST-EMI

ST-EMI is a very serious condition. Patients should be admitted to a coronary care or intensive care unit capable for extensive monitoring. Management of ST-EMI requires complex early and long-term post-reperfusion pharmacotherapy. Cardiology clinical pharmacists can play a crucial role in care of ST-EMI patients, independently and as a multidisciplinary team to ensure that safe early reperfusion is achieved and maintained.

Clinical pharmacist can play a vital role in optimization of drug therapy through sharing the medical team in daily patient-care rounds, reviewing prescribed medications to cardiac patients, counseling and offering advice on optimal drug use and providing valid pharmaceutical information. Evaluation of the patient's response to drug therapy by reviewing patient's medical records to examine all progress notes, orders and laboratory results thus assessing the prescribed dose, dosage form, route of administration and monitoring of each drug individually. Applying safe drug use by monitoring and checking blood count for patients on antiplatelet therapy and maintaining therapeutic concentration of heparin especially in children by regular checks of the activated partial thromboplastin time (APTT) or antiXa concentrations. Provide patient education and discharge counseling on patient medication-taking. To maximize adherence to evidence-based post-STEMI treatments with emphasis about avoidance of OTC medications, aiming at prevention of potential drug interactions, regular OPD-drug therapy follow-up, demonstrating importance of regular medication intake and feasibility of lifestyle modification, and their impact on the health state improvement. Thrombolytic and antithrombotic agents that are quite expensive have a narrow therapeutic window and bear risks of bleeding, hypotension and allergic reactions for cardiac patients.

The clinical pharmacist could develop a cost-effective treatment regimen strategy by selecting patients in whom non-fibrin specific agent may offer better outcomes over t-PA; elderly patient over 75 years are more susceptible to intracerebral hemorrhage to whom catheterization (primary PCI) rather than thrombolytic therapy is superior. With the rising number of patients arriving to hospital with ST-EMI, and poor availability of primary PCI capabilities, thrombolytic therapy is beneficial in carefully selected elderly patients with ST-EMI if the risk of major adverse events is acceptably low [3, 4].

Accurate medication and allergy history taking. Suggesting initiation therapy: pharmacological (thrombolytic therapy) or mechanical (primary PCI) according to patient's presentation time and PCI capability. Proper preparation of the thrombolytic medications, detecting incompatibilities and counseling the nursing staff about proper handling and administration of intravenous therapy.

Providing valid drug information to the medical team as well as to the patients. Providing pharmacokinetic consultations as required for dosage adjustment particularly of debilitating elderly patients. Identifying and implementing drug therapy where positive pharmacoeconomic impact could be achieved for the society, health facility, and the patients. Intervening for safe shifting to available pharmacological alternative on effective drug therapy basis. Intervening to discontinue the drug therapy on occasion as severe bleeding, allergic reactions. Prevent, detect, monitor, document and report drug-drug, drug-disease, drug-lab, drug-food interactions, adverse reactions and medications errors. Ensure the drug(s) is given and used for an appropriate indication according to updated guidelines. Monitor the use of expensive medications to assure their use is consistent with approved criteria. Participation in clinical trials and conducting scientific research in field of acute coronary syndrome and particularly in safe use of thrombolytic in elderly and mostly elderly females.

Participation in patient care clinical rounds in cardiology department and in coronary care unit and effective discussion of medication order clarifications with the prescriber, documenting any changes in patient and pharmacy records. Monitoring and evaluating drug therapy and using own experience to improve therapy efficacy, safety and quality of health service.

Ethical issues

Including plagiarism, Informed Consent, data fabrication or falsification and double publication or submission have completely been observed by the authors.

Author's contribution

All the authors contributed equally and approved final form of the manuscript.

Conflict of interest

No influence of financial gain or personal rivalry declared.

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