New Horizon in Treatment of Acute Ischemic Stroke

Essay
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List of Abbreviations

AAASPS	African American Antiplatelet Stroke Prevention Study
ACA	Anterior cerebral artery
ACAS	Asymptomatic Carotid Atherosclerosis Study
ADP	Adenosine diphosphate
AHA	American Heart Association
ASA	American Stroke Association
ATLANTIS	Alteplase Thrombolysis for Acute Non interventional Therapy in Ischemic Stroke
ATP	Adenosine triphosphate
CASANOVA	Carotid Artery Surgery Asymptomatic Narrowing Operation Versus Aspirin
CAST	Chinese Acute Stroke Trial
CBF	Cerebral blood flow
CLOTBUST	Combined Lysis Of Thrombus in Brain ischemia using transcranial Ultrasound and Systemic TPA
CT	Computed tomography
DIAS	Desmoteplase In Acute Stroke
DWI	Diffusion weighted imaging
ECASS	European-Australian Cooperative Acute Stroke Study
ECASS III	European Cooperative Acute Stroke Study
ECST	European Carotid Surgery Trial
EMS	Emergency Management of Stroke
ESO	European Stroke Organization
ESPS-2	The second European Stroke Prevention Study

List of Abbreviations (Cont.)

ESPRIT	European and Australian Stroke Prevention Reversible Ischemia Trial
FDA	Food and drug administration
Fr	French
g	Gram
GP	Glycoprotein
i.e.	That is
IA	Intra-arterial
IAS	Intracranial arterial stenosis
ICA	Internal carotid artery
ICAM	Intracellular adhesion molecule
ICH	Intracranial hemorrhage
IMS	Interventional Management of Stroke
INR	International normalized ratio
IST	International Stroke Trial
IV	Intravenous
Kg	Kilogram
KHz	Kilohertz
LMW	Low molecular weight
M1	Proximal segment of middle cerebral artery
MACE	Mayo Asymptomatic Carotid Endarterectomy
MB	Microbubbles
MCA	Middle cerebral artery
MERCI	Mechanical Embolus Removal in Cerebral Ischemia

List of Abbreviations (Cont.)

Mg	Milligram
MHz	Megahertz
Ml	Milliliter
Mm	Millimeter
MRA	Magnetic resonance angiogram
MRI	Magnetic resonance imaging
MR RESCUE	Magnetic Resonance and Recanalization of Stroke Clots Using Embolectomy
MRS	Modified rankin scale
NASCET	North American Symptomatic Carotid End arterectomy Trial
NIHSS	National Institute of Health Stroke Scale
NINDs	National Institute of Neurological Disorders & stroke
NMDA	N-methyl-D-aspartate
PROACT	Prolyse in Acute Cerebral Thromboembolism
PRoFESS	Prevention Regimen for Effectively Avoiding Second Strokes
PTA	Percutaneous transluminal angioplasty
PTAS	Percutaneous transluminal angioplasty and stenting
RE-LY	Randomized Evaluation of Long term anticoagulation therapy

List of Abbreviations (Cont.)

ROCKET AF	Rivaroxaban Once daily oral factor Xa inhibition Compared with vitamin K antagonist for the prevention of stroke and Embolism Trial in Atrial Fibrillation
rtPA	Recombinant tissue plasminogen activator
SAINT	Stroke Acute Ischemic NXY Treatment
SAMMPRIS	Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis
SPECT	Single proton emission computed tomography
SPORTIF	Stroke Prevention using Oral Thrombin Inhibitor in Atrial Fibrillation
TASS	Ticlopidine Aspirin Stroke Study
TCCS	Transcranial Color Coded Sonography
TCD	Transcranial Doppler
TIA	Transient ischemic attack
TOAST	Trial of Org 10172 in Acute Stroke Treatment
TOSS	Trial Of cilostazol in Symptomatic intracranial arterial Stenosis
TRUMBI	Transcranial low frequency Ultrasound Mediated thrombolysis in Brain Ischemia
TUCSON	Transcranial Ultrasound in Clinical Sonothrombolysis
ug	Microgram
US	Ultrasound
Vs	Versus
WASID	Warfarin-Aspirin Symptomatic Intracranial Disease

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Introduction

Stroke is the third most common cause of death and it is the most commonly disabling disease. In ischemic stroke, the restoration of blood flow has to occur within a limited time window that is accomplished by fibrinolytic therapy ***(Frendl and Csiba, 2011).***

The size of the ischemic lesion is proportional to the caliber of the occluded artery, and to the duration of the occlusion, and will only be reduced by the blood flow available through the collaterals. A general rule (with many exceptions) is that distal occlusions e.g., middle cerebral artery (MCA) or anterior cerebral artery (ACA) have a higher risk for cerebral infarction than proximal ones e.g., internal carotid artery (ICA) because the latter has more collateral blood flow available to compensate. A sudden arterial occlusion triggers the development of the ischemic cascade **(*Kuroiwa et al, 2007).***

Antithrombotic therapy plays a key role in early ischemic stroke prevention. A multitude of antithrombotic agents exist with varying pharmacological, efficacy, and safety profiles. The benefit of antithrombotic therapy is delicately balanced against the risk of hemorrhagic events ***(Marc et al, 2010).***

Given the narrow therapeutic window for treatment of acute ischemic stroke, timely evaluation and diagnosis of ischemic stroke is paramount ***(Marler et al, 2000).***

In 1995, the National Institute of Neurological disorders and stroke (NINDS) trial produced a real breakthrough in

fibrinolytic therapy. It proved the efficacy of recombinant tissue plasminogen activator (rtPA) therapy in all subtypes of ischemic stroke. It also proved that the benefits of thrombolysis (rtPA) extend beyond 1 year after the treatment ***(Kwiatkowski et al, 1999).***

NINDS Trial 1 and NINDS Trial 2 tested intravenous (IV) rtPA with the dose of 0.9 mg (milligram)/kg (kilogram) of, maximum 90mg , 10% of the total dose is given as an IV bolus over 1 minute and the remaining 90% is administered as a constant IV infusion over 60 minutes, or placebo and found that patients treated with rtPA within 3 hours of onset showed significant improvement ***(Saver, 2004).***

In May 2009, the American Heart Association/American Stroke Association (AHA/ASA) guidelines for the administration of rtPA following acute stroke were revised to expand the window of treatment from 3 hours to 4.5 hours to provide more patients with an opportunity to receive benefit from this effective therapy ***(Del Zoppo et al, 2009).***

Despite the fact that the Intra-arterial (IA) thrombolysis with rtPA can be an option for revascularization according to the European Stroke Organization (ESO), AHA and ASA guidelines **(*Adams et al, 2007)***, further investigations are recommend to define the appropriate role for this intervention. This is because the recent studies included relatively small number of patients (compared with IV trials) and the optimal dose of IA therapy has not been determined yet (most common dose is IA 20-30 mg in 2 hours). Therefore further trials