Sonothrombolysis in Acute Ischemic Stroke

Thesis

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List of Abbreviations

ACA	:	Anterior cerebral artery
AchA	:	Anterior choroidal artery
AF	:	Atrial fibrillation
AHA	:	American heart association
ASA	:	American stroke association
BHI	:	Breth holding index
BUN	:	Blood urea nitrogen
CBC	:	Complete blood count
CLOTBUST	:	Combined lysis of thrombus in brain ischemia using transcranial ultrasound and systemic TRA
CO_2	:	Cargon dioxide
CT	:	Computed pomography
CTA	:	Computed tomography angiography
C-US	:	Continuous ultrasound
DEFUSE	:	Diffusion weighted imaging for understanding stroke evolution
DIAS	:	Desmoteplase in acute stroke
DWI	:	Diffusion weighted imaging
ECASS	:	European cooperative acute stroke study
ECG	:	Electrocardiography
EMS	:	Emergency management of stroke
ESO	:	European stroke organization

List of Abbreviations (Cont.)

EXTEND	:	Extending the time for thrombolysus in neurological emergency deficit
FBS	:	Fasting blood sugar
FDA	:	Food and Drug administration
HITS	:	High intensity signals
i.e.	:	That is
IA	:	Intraarterial
ICA	:	Internal carotid artery
IMS	:	Interventional management of stroke
IQR	:	Interguartile range
LDL	:	Low density lipoprotein
LFUS	:	Low-frequency ultrasound
M1	:	Proximal segment of middle cerebral artery
M_2	:	Distal segment of middle cerebral artery
M_4	:	Terminal brances of middle cerebral artery
MB	:	Microbubbles
MCA	:	Middle cerebral artery
MES	:	Microenbolic signal
Mets	:	Metabolic syndrome
MFV	:	Mean flow velocity
MHZ	:	Megahertz

List of Abbreviations (Cont.)

MRCI	:	Mechanical embolus removal in cerebral ischemia
MRI	:	Magnetic resonance imaging
N	:	Number
NIHSS	:	NIH stroke scale
NINDs	:	National institute of neurological disorders & stroke
NS	:	Non significant
PCA	:	Posterior cerebral artery
PET	:	Position emission tomography
PFO	:	Patent foramen ovale
PI	:	Pulsatility index
PS	:	Power & sample size
RBS	:	Rabdom blood sugar
r-tPA	:	Recombinant tissue plasminogen activator
S	:	Significant
SBP	:	Systolic blood pressure
SD	:	Standard deviation
SICH	:	Symptomatic intracranial hemorrhage
SPSS	:	Statistical package for social science
Std	:	Standard

List of Abbreviations (Cont.)

TCCD	:	Transcranial color coded duplex
TCD	:	Transcranial Doppler
TIA	:	Transient ischemic attack
TIBI	:	Thrombolysis in brain ischemia
TIMI	:	Thrombolysis in myocardial infarction
TOE	:	Transoesophageal echo
tPA	:	Tissue plasminogen activator
TRUMBI	:	Transcranial low frequency ultrasound mediated thrombolysis in brain ischemia
TUCSON	:	Transcranial ultrasound in clinical sonothrombolysis
UET	:	Ultrasound-enhanced thrombolysis
US	:	Ultrasound

Introduction

Acute ischemic stroke is characterized by the sudden loss of blood circulation to an area of the brain, resulting in sudden onset of a focal neurologic deficit ***(Lopez et al., 2006)***.

Cerebrovascular disease was the second leading cause of death worldwide in 1990, killing more than 4.3 million people. It was also the fifth leading cause of lost productivity, as measured by disability-adjusted life years (DALYs) ***(Flynn et al., 2008).***

Transcranial Doppler (TCD) is a non-invasive, non-ionising, inexpensive, portable and safe technique that measures the velocity of blood flow through the brain's blood vessels ***(Sarkar et al., 2007)***. So, it is helpful in the diagnosis of acute ischemic stroke as it can provide rapid information about major arterial occlusion or stenosis (especially middle cerebral artery occlusion), and also the hemodynamic status of the cerebral circulation, as well as monitoring of reperfusion and recanalization ***(Alexandrov et al., 2009).***

TCD has emerged as a tool to treat ischemic stroke since the last few years. The potential advantage of ultrasound (US) is to decrease the risk of systemic bleeding complications due to its site-specific effect. Moreover, external application is

noninvasive and is readily available. A 2-MHz pulsed-wave diagnostic ultrasound beam provides real-time bedside monitoring of thrombolysis. It can augment residual flow and speed up thrombolysis, allowing patients to recover from stroke more rapidly and completely ***(Alexandrov and Mikulik, 2006).***

Some recent researchers studied the effect of combined use of intravenous tissue plasminogen activator (TPA) and TCD ultrasound on recanalization of the occluded intracranial arteries, it shows that thrombolysis with intravenous tissue plasminogen activator (TPA) can be enhanced with ultrasound. Ultrasound delivers mechanical pressure waves to the clot, thus exposing more thrombus surface to circulating drug ***(Alexandrov and Tsivgoulis, 2007).***

Low-frequency US with high power has been demonstrated to produce cavitations and fluid motion in the thrombus ***(Alexandrov and Molina, 2007).*** Some experimental studies use the administration of micro bubbles (MB) (e.g. galactose-based air-filled MB & sulphur hexafluoride-filled MB) as it may augment the effect of ultrasound-enhanced systemic thrombolysis in acute stroke. Bubble structural characteristics may influence the effect of MB on sonothrombolysis ***(Rubiera et al., 2008).*** Other recent studies suggest that acceleration of thrombolysis using pulsed wave US is effective & can enhance thromblysis even without rt-PA ***(Eggers et al., 2005).*** Although some experimental studies and

pilot clinical evidence show that TCD has role in the enhancement of thrombolysis with or even without rt-PA ***(Alexandrov and Tsivgoulis, 2007)***, yet more studies are needed to evaluate the potential of TCD ultrasound technology to enhance thrombolysis & to study the effect of vascular risk factors (e.g DM, hyperlipidemia) as predictors of recanalization.

Aim of the Work

Our aim is to study the effect of continuous insonation using 2-MHz transcranial Doppler US on the recanalization rate and the short-term outcome of subjects with acute ischemic stroke due to Middle Cerebral Artery (MCA) occlusion.