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Intra arterial heparin flushing increases Manual Muscle Test – Medical Research Councils (MMT-MRC) score in chronic ischemic stroke patient

Terawan Agus Putranto,[1,2*] Irawan Yusuf,[1] Bachtiar Murtala,[1] Andi Wijaya[1]

ABSTRACT

Background: Muscle strength impairment in stroke patient affect the patient daily life, especially when it occurs on the extremities muscles. Manual Muscle Testing (MMT) is an examination method to measure muscle strength using standardized scoring.

Objective: To find possible improvement of Manual Muscle Test (MMT) Score after administration of Intra Arterial Heparin Flushing in chronic ischemic stroke patient.

Method: This is an experimental study using pretest-posttest group design, with randomized controlled clinical trial, conducted among patients in Cerebrovascular Center Unit in Army Central Hospital Gatot Soebroto starting from February 2014. With 75 patients included in this study. The examination of muscle strength was done by trained physicians. The MMT score were taken before and after the IAHF procedure is conducted.

Results: This study found higher score of MMT-MRC scoring system on chronic stroke patient with IAHF procedure (mean MMT-MRC Score = 6,05 point. With p<0,05). Indicating that IAHF procedure is associated with better muscle strength improvement shown with higher MMT-MRC score on stroke patient, which will have better prognostic outcome in their recovery.

Conclusions: Intra Arterial Heparin Flushing have significant effect on chronic stroke patient with decreased muscle strength, which shows a significant increase of MMT-MRC score.

Keywords: Intra Arterial Heparin Flushing, Manual Muscle Test, Chronic Ischemic Stroke

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[1]Faculty of Medicine, Hasanuddin University, Makassar-Indonesia
[2]Gatot Soebroto, Army Central Hospital, Jakarta-Indonesia
Jl. Abdul Rahman Saleh No.24, Jakarta-Indonesia

INTRODUCTION

Updated Definition of Stroke for the 21st Century is that stroke should be broadly used in all of the following: CNS infarction, ischemic stroke, silent CNS infarction, intracerebral hemorrhage, stroke caused by intracerebral hemorrhage, silent cerebral hemorrhage, subarachnoid hemorrhage, stroke caused by subarachnoid hemorrhage, stroke caused by cerebral venous thrombosis, not specified - stroke. Stroke itself characterized as a neurologic deficit attributed to an acute focal injury of the central nervous system by a vascular cause.[1]

The word "stroke" first introduced by William Cole in 1689 in an essay called "A Physico-medical essay concerning the late frequencies of apoplexies".

Before Cole a very acute non-traumatic brain injuries were described as "apoplexy', a term introduced by Hippocrates in circa 400 BC. In 1950s, the physicians need another term to describe a temporary vascular related episodes of brain dysfunction that would not qualify as strokes, and then the term "Transient Ischemic Attack" came into use. Even then the World Health Organization have its own term of strokes, which is a "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting for more than 24 hours or leading to death, with no apparent cause other than that of vascular origin." This term was used since 1970 until present. Even though we all know that the brain injury can occurred for less than 24 hours, so this definition of stroke by WHO is actually obsolete. Ischemic stroke defined as an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction.[1] The most common neurological deficits found in stroke patient were paresis, speech, and sensory deficits. Clinical characteristics of stroke may be varied for different population groups, but male subjects most likely experiencing the gait disturbances.[2] The most common impairments found were limb weakness especially the upper limb, urinary incontinence, dysphagia, impaired consciousness, and cognitive impairment.[3] Dobkin in his study found that acute stroke patients that suffers upper limbs impairment, showed a significant (about 95%) recovery in 9 weeks, and 11 weeks for severe cases.[4] In this research we investigated the effect of Intra Arterial Heparin Flushing on muscle strength improvement in chronic ischemic stroke patient which measured with MMT-MRC scoring system. It was impossible

*Corresponding to: Terawan Agus Putranto Jl, Abdul Rahman Saleh, No.24, Jakarta-Indonesia.
terawan@rspadgs.net

to obtain a full muscle strength recovery in such short periods, but a mild muscle strength improvement after IAHF treatment will provide a good prognostic outcome in motor recovery for patients with chronic ischemic stroke.

The most common conservative therapy for patients diagnosed with stroke were antiplatelet drugs such as clopidrogel and aspirin, but this therapy have major systemic bleeding side effect. Despite the risk, this line of therapy is still being used as conservative therapy, and it seems the combination of antiplatelet such as aspirin and clopidrogel proved more effective than a single aspirin therapy itself.[5]

To measure muscle strength, there are some quantitative methods such as dynamometers and qualitative methods which is Manual Muscle Strength (MMT). The usage of dynamometer is not suitable for weak muscles and movement measurements with resistance.

The MMT measurements method first developed by Lovett and described by Wright in 1912 and had been revised, advanced and promoted to be a wide range of methods. One of the revised method which was most widely accepted and used in this study, was proposed by Medical Research Council (MRC). The original MRC scales were described as follows: 0 = no muscle contraction detected; 1 = flicker or trace contraction were detected; 2 = active movement detected but the ability against gravity were eliminated; 3 = active movement and the ability against gravity were detected; 4 = active movement with ability against gravity and resistance were detected; 5 = normal muscle strength detected.[6]

Motor disability can be caused by an ischemic lesion in motor cortex, premotor cortex, motor tract, or any associated pathway in cerebral or cerebellum organ.[7] The motor cortex coordinate movement through corticospinal neuron directly or through projection against different nucleus in brain stem that elongated through spine.[8,9] Thrombosis play an important role in ischemic stroke pathogenesis.[7] Various thrombolytic therapy regimen is used to obtain higher cerebral perfusion after ischemia. So far only serine protease tissue-type plasminogen activator (tPA) was approved by FDA as a thrombolytic for treating stroke.

Randomized controlled trials (RCTs) data from European Cooperative Acute Stroke Study (ECASS) III and the Safe Implementation of Thrombolysis in Stroke - International Stroke Treatment Registry (SITS-ISTR) showed that intravenous rtPA is an effective therapy to improve the outcome of patients with ischemic stroke if given within 3 until 4,5 hours after stroke onset.[10-14]

Unfortunately, not many patients could have the thrombolytic treatment after stroke attack. In Gatot Soebroto Army Central Hospital, 57,33% stroke patients came in at chronic phase (> 30 days). Thus, new therapeutic strategies with a wider window time will be very useful to reduce ischemic morbidity in chronic phase.[13-16]

Intra Arterial Heparin Flushing (IAHF) modified Digital Subtraction Angiography (DSA) in Gatot Soebroto Army Central Hospital showed a clinical improvement in chronic stroke patients empirically. Heparin usually used as flushing solution for catheterization.[11] Heparin have a role not only as an anticoagulant but also as a fibrinolytic. Heparin increases plasminogen conversion into plasmin by stimulating tissue plasminogen activator.[17-20] Heparin also has potential in increasing thrombolysis by inhibit TAFI (thrombin activatable fibrinolysis inhibitor) formation.[21-24] Thus, heparin commonly used to treat both arterial and vein thrombosis because of its safety proven reason.[7,8,12] Intravascular studies showed that heparin therapy can reduce the clot size, suggested its potency in brain reperfusion after ischemic.[18]

MATERIALS AND METHODS

Design and Samples

This is an experimental study using pretest-posttest group design, with randomized controlled clinical trial that was approved by Hasanuddin University Ethical Committee with register number UH14110582, with 75 chronic ischemic stroke patients in Cerebrovascular Center Gatot Soebroto Indonesian Army Central Hospital started from February 2015.

Inclusion

The inclusion criteria including:

a Patient diagnosed with chronic ischemic stroke (by radiology and neurology examination)
b Age 30 – 70 years old, and
c Agreed to follow the IAHF procedure and signed the informed consent form.

Exclusion

The exclusion criteria including:

a Any allergic to contrast and heparin,
b Blood clotting abnormality.
c Subjects with high risk or contraindication according to cardiology, pulmonology, internal medicine, and anesthesiology procedures.
d Not able to undergo MRI examination.
e Cannot understand or not able to follow study instructions.
f Motoric dysfunction caused by another disease.

g Subjects diagnosed with brain stem stroke for more than 6 hours or less than 2 weeks (involution state).

Manual Muscle Test Measurement

The Manual Muscle Test (MMT) – Medical Research Council (MRC) scale method measurements used in this study with 6 scales, including: 0 = stands for no movement detected; 1 = only a weak contraction that can visualized or sensed at muscle; 2 = the muscle can be moved horizontally but unable to move against gravity; 3 = muscle strength declined and muscle contraction can moved the joints against gravity if there is no resistance added; 4 = muscle strength declined but muscle contraction can move joints against resistance; 5 = normal muscle contraction against full resistance. This measurement will be performed by a trained physicians and neurologist.

IAHF Procedure

After the patients and instruments preparation, 5000 IU heparin diluted with 500 cc NS Otsu. Topical anesthesia EMLA was applied on femoral artery area, continued with povidone iodine 7,5% and alcohol 70%. Local anesthesia *lidocain* was injected intracutaneous and subcutaneous. Femoral artery was punctured with *abocath* 18 G, and short guidewire was inserted. Fluoroscopy was performed to see the anatomical imaging. Diluted heparin was flushed intra-arterial in both right and left carotid arteries and vertebral arteries. After completing the flushing process, femoral artery bleeding was stopped using either conventional technique or angio-seal.

Statistical analysis

Statistical analysis was performed with SPSS 15.0 for Windows Evaluation Version. Kolmogorov – Smirnoff test was performed to find the data distribution model. The differences in MMT-MRC score before and after treatment were tested using paired T Test or Wilcoxon test alternatively with P value of 0.001 were considered significant.

RESULT

75 chronic ischemic stroke patients were participated in our study. MMT values before and after IAHF treatment were analyzed using paired T-Test, as shown in Table 1.

Table 1 The Difference of MMT Pre and Post IAHF treatment

IAHF	Mean ± SD	Median (Min-Max)	p
Pre	30,21 ± 10,47	30(4-50)	0,000
Post	36,27 ± 11,59	37(11-55)	

Table 2 MMT Score mean difference before and after IAHF treatment

Variable	Mean ± SD	Median	p
AMMT	6,05 ±3,49	6(0-15)	0,000

We found that MMT score mean value increased 30,21 (CI 95% SD 10,47) before IAHF treatment become 36,27 (CI 95% SD 11,59) after IAHF treatment. There is a significant difference between pre and post IAHF treatment in Chronic Ischemic Patient (p<0,05). To find the efficacy of the IAHF procedure on chronic ischemic stroke patients, we counted the Delta value between MMT score before and after IAHF treatment as shown in table 2.

DISCUSSIONS

Motoric function assessments were used as one of diagnostic methods for diagnosing a prognostic outcome in Multiple Sclerosis, Stroke, or patients in Intensive Care Unit (ICU).[25-27] As a prognostic assessment method for stroke patients, MMT with lower score show a bad prognostic outcome.[28] Another method to assess muscle strength is a quantitative methods using instrument such as Dynamometry.[29] In this study we measured the subject's motoric strength using MMT-MRC scoring system. This method has been proved to be effective to determine muscle strength degree in stroke patients.[30] This method was also the only method to asses' muscle strength and the level of paresis in patients with peripheral nerve lesion.[6]

The motoric function of our body is managed by motor cortex in our brain. In stroke patients with paresis, the neuron output impulse was decreased because of the decrease of motor neurons pool ability to move targeted motoric unit. In anatomical perspective, there are two main components in motor cortex that play important roles for motoric function, including primary motor cortex (M1) and secondary motor cortex which was divided into Posterior Parietal Cortex (PPC), Premotor Cortex, and Supplementary Motor Area (SMA). M1 triggers the neural impulses that control the final execution of motoric unit, then the PPC change the incoming visual information into a motoric command, and the Premotor Cortex roles as a sensory guidance of a movement which coordinates the body orientation against the movement itself, and the last one is SMA, responsible to coordinate and plan the complex motor movements and coordinate our both hands movements. The pathway of neuron impulse itself to stimulate a muscle contraction starts from primary motor cortex then conducted through corticospinal tract out from the spinal nerve through the cervical column cavity then the peripheral motor neuron

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relays the signals into the arms region to activate the myofibrils group located in biceps until a muscle contraction happened in that location.[31]

Muscle weakness in chronic stroke patients might be associated with the decline of descending impulse input from motor area in brain hemisphere affected by stroke, disturbance of muscle activation, and muscle atrophy. The EMG examination shows that patients with chronic hemiparesis has a different muscle activation pattern that differs according to the muscle contraction. The motor contraction abnormality itself caused by troubled descending motor tract, this might explain the imbalance of muscle activities on post stroke patients. Thus, extremities muscle weakness in patients with chronic hemiparesis caused by neuromuscular performance changes.[32]

Lesion in motor cortex especially in M1 region in stroke accident and brain trauma will ended up as necrosis in focal area that finally will cause the loss of M1 output to spinal cord and in the end will cause functional disability.[33] The normal function of muscle needs an intact connection along the motor pathway (which a connection between nerve cells that elongated from brain into spinal cord and ended in muscle unit), damage in any point will decrease the brain ability to control muscle movement. The decline of this ability will cause weakness which also called paresis. MMT is a reliable diagnostic tool to measure muscle weakness on stroke patients.[34]

In this study the MMT score was found significantly increased after IAHF treatment. This treatment could induce a better motor cortex function especially within the area where stroke induced lesion disturbing the motor pathway. When the motor pathway was fixed, the neuronal output impulse will be recovered, thus the muscle strength will be increased, showed by increased MMT scores.

CONCLUSIONS

Our study showed that IAHF treatment can significantly improve muscle strength, represented by MMT score in chronic ischemic stroke patients with onset more than 30 days. So far IAHF was suggested to be a new potential stroke therapy with good prognostic outcome and wider time window. Serial MMT score measurement in three months might be done to observed as further studies.

CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest.

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