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The Effectiveness of Early Mobilization Time on Balance and Functional Ability after Ischemic Stroke

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Abstract

BACKGROUND: Early mobilisation (EM) after-ischemic stroke is a motor learning intervention aimed to restore nerve cells and to improve balance and functional ability. Unfortunately, the study of when this intervention began has not been widely studied.

AIM: On this study was compared the effect of EM started at 24 hours and 48 hours after an ischemic stroke on balance and functional ability.

MATERIAL AND METHODS: Randomized controlled trial involving 40 patients on 2 groups meeting predefined inclusion criteria. The levels of balance were measured using the Berg Balance Scale, and the functional ability was measured using the Barthel Index, at 5th and 7th day.

RESULTS: A significant difference was observed in both balance ($p = 0.038$) and functional ability ($p = 0.021$) obtained on the 7th day of assessment between both groups. A significant difference on the 5th day was observed only in the functional ability ($p = 0.002$) and not in the balance ($p = 0.147$), between the groups.

CONCLUSION: EM started at 24 hours after the ischemic stroke has been found to have a better impact on balance and functional ability compared to that at 48 hours.

Introduction

Early mobilisation (EM) is the following step in few days after stroke manifestation. In general, some physiotherapists apply mobilisation after 48 hours or even afterwards due to hospital bureaucracy. EM started at 24 hours after ischemic stroke which has been recommended by the AVERT Trial Collaboration Group [1], is part of neurorestoration to help restore nerve lesions. The recovery is probably mediated through basic mechanisms of nervous system restoration improving its function [2]. The reason for EM started 24 hours after stroke is related to the increase of certain proteins at the molecular level that plays a role in neuroplasticity, i.e. decreased caspase-3, increased expression of Bcl-2, MidKine (MK), Brain-derived Neurotropic Factor (BDNF), anti-platelet endothelial cell (PECAM-1) which will inhibit the apoptosis of nerve cells and increase the strength of nerve synaptic transmission, and subsequently enhance its motion and functional ability [3], [4], [5], [6]. However, most studies on EM gave 24 hours after a stroke are still tested in experimental animals (rats).

The expression of several proteins that act as a nerve growth factor (NGF) will be released several hours after ischemia. So, it is hypothesised that EM started at 24 hours after stroke will give better results than those that started at 48 after stroke.

The application of the EM started 24 hours after stroke in this study was included in The TIDIeR (Template for Intervention Description and Replication) guides based on content validity testing of earlier research [7]. The TIDIeR guides have been claimed as a good model for reporting an intervention [8]. EM can be expected to impact on the balance and functional ability in patients with ischemic stroke [9], [10]. The balance could be measured using the Berg Balance Scale (BBS) [9], [11], while the functional ability could be measured using the Barthel Index (BI) and has been reported as a good tool for measuring functional ability up to 3 months after stroke [10].

The aim of this study was compared to the effect of EM started at 24 hours and 48 hours after an ischemic stroke on balance and functional ability.

Material and Methods

Forty (40) patients were recruited based on a predefined inclusion criterion, admitted from three hospitals in Indonesia (Dr Moewardi Hospital, Dr Oen Surakarta Hospital, Government Surakarta Hospital) and had signed informed consent by the requirements of the local ethics committee. The study was conducted from April until October 2018. The inclusion criteria included, (1) patients diagnosed as ischemic stroke with decreased motor control, (2) patients having sensory and proprioceptive deficits with a muscle strength score of at least 2+, (3) patients with first-stage stroke scan, one side of the first attacked stroke and second stroke hemiparesis which had been confirmed without any deterioration of neurological complications (e.g. decreased awareness, sepsis, shock due to embolism), (4) patients without aphasia, (5) patients without severe cognitive impairment (MMSE score greater than 19).

Patients meeting inclusion criteria were randomly divided into 2 groups, i.e. treatment group was 20 subjects received EM at 24 hours and control group was 20 subjects received EM at 48 hours after diagnosis of ischemic stroke with CTScan. The EM of learning stages is a cognitive stage, associative stage and autonomous stage. The cognitive stage is sensory, visual, verbal, proprioceptive stimuli to the upper and lower limb, starting from the proximal part with clear commands. The associative stage: active assisted and free active exercise stimuli in the upper limbs and lower limbs. The associative stage to the autonomous stage using functional training.

The group receiving mobilisation at 24 hours groups underwent an assessment using the validated TIDIeR Guidelines (CVI and CVR) [7] and the group receiving mobilisation at 48 hours underwent routine hospital procedures (Table 1).

Table 1. Early mobilisation an application for groups

Provisions	Treatment group activity	Control group activity
Time	30 – 60 minutes	30 – 60 minutes
Focus of mobilisation	Exercise gradation: cognitive stage – associative stage – automatic stage	Nothing
Day 1	Stimulation on the skin, visual, verbal and join by active assisted exercise on extremities (focusing on patients cognitive)	-
Day 2	Stimulation on the skin, visual, verbal and join by active assisted exercise on extremities (Based Bobath and PNF Method)	Passive exercise and assisted exercise on extremities
Day 3	Active assisted and active exercise on extremities to functional pattern (focusing on patients' association) (Based Bobath and PNF Method)	Passive exercise and assisted exercise on extremities (Based Bobath and PNF Method)
Day 4	Control posture exercise Preparing to roll and sitting process	Rolling and sitting exercise
Day 5	Sitting stabilisation and posture control on sitting (focusing on doing association to get automatic movement)	Sitting stabilisation exercise
Day 6	Sitting and standing stabilisation Standing Functional ability exercise (like as feeding and dressing) (based CIMT Method)	Standing stabilisation exercise
Day 7	Functional ability exercise (like as feeding and dressing) (based CIMT Method) Gait exercise	Gait exercise

The balance was measured using BBS which has a maximum score of 56 [9], while the functional ability measured using BI with a score of 100 in 5 rating points [6]. Measurements BBS and BI conducted on the 1st, 5th, and 7th days with the reason, (1) consideration by the protocol that the time of observation during a hospital stay is 7 days, (2) to see the initial improvement that occurred.

The BBS score can predict the ability to activities because it determines the value to functional ability. BBS can be used to support hospitalised stroke patients who have a BBS score of 20 indicate the availability of speed [9]. It's a bit different from the other balance measurement like a Romberg test, Single-leg stance test, Step test; they are functional performance test. In terms of reliability and validity that BBS is one of the most popular and recognised balance measurement.

The evaluate tool of functional ability post-stroke was commonly done using the National Institute of Health Stroke Scale (NIHSS) and IB. The NIHSS is a method for assessing the severity of a stroke while IB is a better parameter for functional ability post-stroke. The reliability and consistency of internal IB for stroke patients is excellent, as well as of the contents are also excellent. The average change in IB score reaches 1.85 points which are considered very important by the time [12].

The differences in balance and functional ability scores respectively obtained at day 5th and day 7th against the baseline scores at 1st day with a reason to observe improvement from day to day at the beginning of the hospital treatment were statistically compared using Mann Whitney Test. Statistical significance was set at 5 %. Statistical analysis was performed using SPSS software version 20.

Results

Forty (40) patients with ischemic stroke consisting of 20 patients receiving early mobilisation at 24 hours and another 20 patients receiving mobilisation at 48 hours, were included in the study. There were no differences in the ages and sex between the two groups (Table 2).

Table 2. Demographic characteristic of the patients

The characteristic	Treatment group		Control group		p-value
	N = 20	%	N = 20	%	
Age					0.645
< 60 years	14	70%	12	60%	
> 60 years	6	30%	8	40%	
Mean (minimum: maximum)	57.95 (47:80)		58.75 (44:86)		
Median	56.5		58		
Sex					0.739
Male	14	70%	13	65%	
Female	6	30%	7	35%	
Location of lesion					0.209
Right	9	45%	13	65%	
Left	11	55%	7	35%	
Severity of Stroke					
ASPECTS > 7	20	100%	20	100%	-
Complicating factors					0.08
None/1 complicating factor	12	60%	8	40%	
Two (2)/more complicating factors	8	40%	12	60%	
None	1	5%	-	0%	
Hypertension	11	55%	7	35%	
Cor disease	-	0%	1	5%	
DM and Dyslipidemia	1	5%	9	45%	
DM and Cor disease	-	0%	1	5%	
Hypertension and DM	6	30%	1	5%	
Hypertension, DM, and Cor disease	1	5%	1	5%	

Most ischemic stroke patients were at the ages of less than 60 years and predominantly male gender. Patients receiving EM at 24 hours mostly had a left lesion the patients receiving EM at 48 hours mostly had right-side lesion was in the control group. Almost all patients have complication factors such as hypertension, diabetes mellitus and dyslipidemia. There were no significant differences between the 24 hours EM and 48 hours EM in the complication profiles. Meanwhile, the level of severity of stroke for subjects using CTScan by ASPECTS score was higher than 7.

The balance and functional ability showed significant differences between 24 hours EM and 48 hours EM on the 7th day, and in functional abilities on the 5th day (Table 3).

Table 3. An overview of the balance and functional abilities of patients after ischemic stroke after early mobilisation

Balance	Treatment Group, n = 20			Control Group, n = 20			p-value
	Median	Mean	SD	Median	Mean	SD	
1st day	0	0.50		0	0.50		
5th day	12.50	23.18	12.70	8.00	17.83	7.31	0.147
7th day	38.50	33.75	16.55	20.50	22.1	13.75	0.038
Functional Ability							
1st day	20.00	22.90		22.00	23.40		
5th day	56.50	55.05	11.15	34.00	38.94	13.47	0.002
7th day	75.50	70.90	17.93	51.00	56.45	20.79	0.021

The balance between the control and treatment groups showed no significant difference ($p > 0.05$) at the 5th day but showed a significant difference on the 7th day ($p < 0.05$). On average the increase in the balance values of treatment and control groups on the 7th day were 33.75 (60.26%) and 22.50 (40.17%) respectively that difference in the value of balance by 11.65 points (20.80%). While the functional ability description between control and treatment group showed a significant difference in both the 5th and 7th day ($p < 0.05$). The average increase in the functional ability of the treatment and control group on the 5th day were 55.05 (55.05%) and 38.94 points (38.94%) and the 7th day were 70.90 (70.90%) and 56.45 (56.46%) respectively. The difference in the value of functional ability on the 5th and 7th day was 16.61 points (16.61%) and 14.95 points (14.95%) respectively.

Discussions

The demographic characteristic of the subjects in this study showed no significant difference between the two groups, the mean age of subjects was 58.35 years, over 67.5% were male, and 55% had right lesions. Similarly, complicating factors statistically showed no significant differences between the two groups despite various complication factors. The highest complication factor was hypertension that has been occurred 55% in the group given EM started at 24 hours and 35% in the group given EM started at 48 hours after ischemic stroke. The second sequence of complication factors was DM and dyslipidemia that has been occurred 5% in the group given EM started at 24 hours and 45% in the group given EM started at 48 hours after ischemic stroke. Meanwhile, the level of stroke severity of both groups is the same, i.e. ASPECTS score was greater than 7. Demographic characteristics showed that all characteristics, including the stroke severity, had no significant differences.

The EM given to the subjects was done as a stimulation to improve neuroplasticity, so that the nerve cells in the brain respond to injury by adapting through structural or functional reorganization to restore function [13] because of the synaptic circuits can be changed by synaptic transmission through change synaptic proteins that can last up to a few minutes [14], [15].

The statistic results showed that the EM between both groups is significantly different in affecting the balance on the 7th day ($p = 0.038$). The level of BBS showed an average increase of balance score of 33.25 for EM at 24 hours and 22.05 for EM at 48 hours with the difference of balance increase was 11.65 points or 20.80%. Meanwhile, the 5th day showed no significant difference between both groups ($p = 0.147$), but it can be seen that there was an increase of balance score in both groups was 22.68 points (40.5%) for EM at 24 hours and 17.33 points

(30.94%) for The EM at 48 hours. This suggests that the 24 hours EM after an ischemic stroke had an impact on the after-stroke healing process.

Furthermore, the functional ability features between the two groups also showed that EM between 24 hours and 48 hours after ischemic stroke gave significant difference on the 7th day (p = 0.021) and the 5th day (p = 0.002). The level of BI measured on the 7th showed an average increase in the functional ability of 48.00 for the EM at 24 hours and 33.05 for EM at 48 hours. The difference in improvement in functional ability was 14.95 points or 14.95%. While on the 5th day that the level of BI showed an increase of 32.15 points (32.15%) for EM at 24 hours and 15.54 points (15.54%) for EM at 48 hours. That showed an average difference in the increase of functional ability score between both groups was 16.61 points (16.61%). The improvement of functional ability was in line with the improvement in balance. It indicates that the balance both dynamic and static given affect the functional ability. EM provided with clear stage, and appropriate dosages were related to optimising outcomes especially after 3 months post-stroke [1]. Another study [16] that very early mobilisation is not associated with beneficial effect when carried out in patients 24 or 48 hours after the onset of a stroke. There were no significant differences IB score at 3 months, but the length of the hospital stay in the early mobilisation group (24 hours after the attack) was shorter than that in the late mobilisation (48 hours post-attack). There was a possibility of developing improvements from day to day at the beginning of the hospital treatment.

The EM started 24 hours after stroke is associated with the induction of several molecular proteins, e.g. BDNF in the cerebral hemispheric, either lesioned or unlesioned to improve in the event of after ischemic stroke [17]. Increased levels of BDNF on the side of the lesion occur around the neuronal, ependymal, and microglial cells at 24 hours after stroke. Meanwhile, the increase on the side of the unlesioned occurs in the nerve and ependymal cells at 4 to 24 hours after stroke. Increased BDNF also occurs in the cerebral artery and astrocytes 8 days after stroke [18]. If EM is given 48 hours after stroke, it will slow to exploit the expression of several proteins in the brain including BDNF which has an important role as a modulator in the improvement of cell nerve after stroke [19]. BDNF expression will be released after the brain has ischemia, and is a member of the neurotrophin family directly involved in the neurite growth, synaptic transmission, and neurotransmitter synthesis. The EM can improve the ability of BDNF to bind to tropomyosin-receptor kinase B (TrkB) after the event of hypoxia/ischemia [20]. The TrkB is capable of enhancing nerve regeneration through the maturation, growth, and development of nerve cells in the brain, protecting nerves from metabolic disorders, inducing mRNA in the hippocampus, and plasticity of nerve cells that will modulate the survival of nerve cells. The binding between on the BDNF and TrkB may inhibit inflammation, neurotoxicity, and nerve cell apoptosis. EM was also clinically useful in related to the degree of disability which can be seen from the dependency in the daily activities. Exercise can influence nerve plasticity which correlates with intracortical network and motor circuits system that will improve its functional ability.

Although only a few studies discuss the positive effect of EM given 24 hours after a stroke on the experimental animals (rats), they show the neurorestoration process as it does in the results of this study. Some studies report similar results. Ischemic rats with middle cerebral artery occlusion given treadmill can increase expression levels of MK, NGF, PECAM-1, and decrease caspase-3 in the peri-infarct area [21]. The EM started 24 hours in the observed ischemic mice in which it indicated a decrease in the number of apoptosis, inhibition of caspase-3, cleaved caspase-3, an increase in Bcl-2 expression [3]. The rats also showed a decreased volume of infarction and increased motor function. Supported by study, the EM started 24 hours using passive movement in rats with cerebral infarction showed very low caspase-3 and escape latency, while very high Bcl-2 mRNA expression that improved mediation conditions were due to inhibition of apoptotic nerve cells [4]. It provides a change in post-synapse receptor composition, synaptic transmission strength due to synaptic remodelling associated with local cell regulation including mRNA translation, cytoskeleton remodelling, and the role of the receptors both inside and outside synapses [6]. A study [22] on the EM using conscious exercise with mild to moderate intensity at 24 hours after an ischemic stroke can provide neuroprotection in brain injury models. It is related to apoptosis as well as oxidative damage [23]. The EM using the practice of proprioceptive neuromuscular facilitation methods and cognitive exercises starting 6-24 hours after a stroke can improve significant functional ability compared to standard procedure time although the results bring out the same disability after three months [5].

This EM was based on a stroke recovery process that associated with an oedema resolution and return of blood circulation in the penumbra areas that have ischemic, supporting a spontaneous recovery that can be extended a period of resolution from the acute phase to 4 - 6 weeks after stroke which capable of generating adaptive plastic potential that can accelerate the rehabilitation of stroke, when the primary motor cortex (M1) and corticospinal are damaged that the ipsilesional premotor area (PMAs) can be used instead [22].

The EM begins with the provision of stimuli derived from sensory information such as visual, verbal, somatosensory, proprioceptive stimulation, facilitated movements, active participation and active movement targeted movements so that plasticity also occurs in muscle [15], provides neural improvement and allows for plasticity of neurons as well as motor circuits system due to a series of motion skills using neuro-rehabilitation exercise [24] and conscious physical experience was a great modulation of neural plasticity nervous system in the after stroke [25]. The stimulus that affects neuroplasticity is the basis for the reorganisation of nerve cells including parts of the brain both in the area of the cortex sensory, subcortical, or cerebellum that create the function of balance by the intercortical network [26]. In case that the provision of exercises for postural response was necessary for the balance function. Because the key of EM by exercise is to connect the mind and movement of the limb to inhibition of the inter-hemispheric rebalance, activate the hemisphere and increase motor control particularly on the side lesions [27]. Mobilisation with postural response using posture control exercises, rolling, sitting upright or standing upright to improve balance further enhances the functional ability of after ischemic stroke patients especially for EM at 24 hours after diagnosis of ischemic stroke based on CT Scan.

The concept of EM with progressive exercises that have been formulated by researchers into The TIDIeR as a guide, has been gradually designed starting from the cognitive stages (providing visual, verbal, tactile, proprioceptive stimulus) further upgraded to the associative stages until the movement automatic [28], [29], [30], repeatedly performed, giving feedback [31], with full awareness [32], using functional movements performed automatically resulting in permanent changes [28], [33] and providing functional change.

Some of the limitations of this study are the sample size that was at a minimum so that it is difficult to generalize the results of the study, the characteristics of the patients especially the varied complication factors and the health status of the subjects to control during follow-up and the observation of improving balance and functional ability which was only carried out for 7 days.

The implications of this study are EM with recommended motor learning after 24 hours post-ischemic stroke according to conditions in the criteria, especially for efforts to improve the balance and functional ability of patients with ischemic stroke. It is recommended to observe the expression of nervous growth factor, e.g. BDNF protein after EM started 24 hours after ischemic stroke.

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