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Original Research Article

Effects of Very Early Mobilisation on Disability and Adverse Events in the First 3 Months Post Stroke: A Single-Blind, Randomized Controlled Trial

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ABSTRACT

Background: Very early mobilisation is believed to reduce disability and minimize the adverse events of the stroke victim.
Objective: To determine the effect of very early mobilisation in addition to the standard care on the level of disability and the number of potential adverse events in the first 3 months post stroke.
Design: Single blind, Randomized controlled trial.
Setting: University teaching hospital.
Methods: The intervention group (n=24) received early and frequent out of bed activities such as sitting, standing, walking. The mobilisation activities were initiated within 24 hours of the stroke onset for 5 to 30 minutes for at least twice a day, for seven days.
Outcome Measures: The level of disability was measured with modified Rankin Scale (mRS), Barthel Index and the number of potential adverse events.
Results: Fifty-four subjects (mean age = 63.30 years, SD = 10.58) were randomized equally into two groups. The most common adverse events were depression, shoulder pain, pneumonia, UTI, constipation, and falls among the subjects. The Intervention group reported comparatively less number of (59/126) adverse events than the Standard care (67/126). There were no statistical significant differences in the level of disability as well as potential adverse events at the 3 months follow-up ($p<.005$) among groups.
Conclusions: Very early mobilisation along with the Standard care may be beneficial in improving the level of disability and reduce the number of adverse events in the first 3 months post stroke.

Key words: Disability, Adverse events, Acute stroke, Very early mobilisation (VEM), Standard care (SC).

INTRODUCTION

Stroke is the second most common cause of death and the major cause of serious, long term disability worldwide. [1-3] Nearly all of the patients hospitalized with stroke suffer one more medical or neurological adverse events. [4-10] 51% of deaths occurred in the first month after stroke may be due to immobility related adverse events. [11]

Bed rest after stroke is believed to have a harmful effect on the heart, lung, and gastrointestinal, musculoskeletal, nervous systems. Bed rest is also said to be linked

with immobility related adverse events such as deep vein thrombosis, bed sores, falls, fractures, urinary tract infection, mood and dependency in daily living activities. [12]

The systematic review conducted by Allen et al in 2010 [13] stated that research till date gives very little support for the use of bed rest in the treatment of a wide range of conditions and suggests that bed rest may delay recovery and even result in harm.

P. Langhorne and colleagues [8] performed a prospective cohort, study in 311 stroke patients to determine the frequency of medical, immobility, and stroke related complications up to 30 months after stroke. The results of this study confirmed that, infections and fall are common. Further, they have also identified pressure sores, shoulder pain, and depression.

Mobilisation of acute stroke patients in bed and out of bed as early as possible is currently recommended to prevent medical and neurological complications. [14,15] 'Very Early Mobilisation' (VEM) is defined as an intensive out of bed activities of daily living (ADL) within the first 24 hours of symptom onset. [16] Very early mobilisation is a safe, feasible, affordable and easy to deliver intervention, which requires little or no equipment. Exposure to very early mobilisation may reduce disability, medical and immobility related adverse events. [17-24]

The purpose of the study: There is insufficient evidence regarding the effect of very early mobilisation on the level of disability and possible adverse events reported at three months after stroke to make any recommendations on the practice. Despite the limitation of high level evidence, a number of clinical guide lines in Australia, Europe and the United States of America currently recommend the use of early mobilisation after acute stroke. However, when to mobilize, dosage of the mobilisation (the duration, frequency, intensity) and physical activity associated with these concepts are not further described.

Objectives: The primary objective of this study was to determine the effect of very early mobilisation along with the standard care on the level of disability in the first 3 months post stroke.

The secondary objective of this study was to determine the effect of very early mobilisation along with the standard care on the number of possible adverse events in the first 3 months post stroke.

MATERIALS AND METHODS

The study was a single blinded, parallel grouped, randomized controlled trial with a blinded assessment at the end of follow up. This study was conducted at the stroke unit of the Department of Medicine of the University Teaching Hospital in Mangalore, Karnataka, India.

The subjects included were above 18 years. Stroke victims were admitted within 24 hours of the symptom onset in the stroke unit. They were able to react to verbal commands, both the sex, systolic blood pressure between 120 and 180 mm Hg, an oxygen saturation >92% (with or without supplementation), a heart rate between 40 and 100 beats per minute, with the temperature <38.5°C. The patients were recruited after obtaining physician permission to mobilize within 24 hours of stroke.

The subjects were excluded, if the condition deteriorated within the first hour of admission to the hospital {National Institutes of Health Stroke Scale [25] (NIHSS)}. Pre morbid modified Rankin Scale [26] (mRS) Score >3, transient ischemic attacks, concurrent progressive neurological disorder, unstable coronary condition (e.g. acute myocardial infarction) or other medical condition that would impose hazard to the patient, or if their physiological variables (blood pressure,

oxygen, heart rate, temperature) go beyond set safety limits, severe heart failure, lower limb fracture preventing mobilisation, as well as those patients having terminal cancer.

The stroke victims were randomly allocated equally to either the Intervention group or the Standard care group by the computer generated; randomization procedures using a concealed opaque envelop method.

The Intervention group received very early mobilisation in addition to the standard care treatment. Performed early and frequent out of bed activities including sitting, standing, walking. The duration of mobilisation was determined by the patient's tolerance (5-30 minutes) and the frequency of minimum two times per day for seven days or until the discharge whichever was sooner. [24]

Both the groups received standard care treatment including routine stroke unit care, for 45 minutes a day, for seven days or until discharge. [24]

Outcome Measures: The modified Rankin Scale (mRS): Reliable and valid scale to measure the level of disability of the stroke victims. The scale ranges from 0-6, zero score indicates perfect health without symptoms and six on mRS indicates death. We defined good out come as modified Rankin Scale score of 0-2, the poor outcome as modified Rankin Scale score of 3-6. [26]

The Barthel Index: BI is one of the most widely used tool measure the functional disability, we categorized BI as dependency in activities of daily living (BI score<80), independency in activities of daily living (BI score>80). [27]

The Number Of Potential Adverse Events Reported In The First 3 Months Post Stroke: Medical complications (cardiac, pulmonary, deep vein thrombosis (DVT) and infections), Immobility related complications (pressure sores, falls, constipation, joint contractures, shoulder pain, depression), Stroke related complications (another stroke, coma) were recorded.

The level of disability and the number of possible adverse events were recorded by the blinded assessor and diagnosed by Physician / Neurologist at the three months follow up.

Ethics: The study was approved by Central Ethical Committee of the Nitte University (Ref: NU/CEC/Ph.D-52/2012). Signed informed consent was obtained from all subjects, or their representatives at the beginning of the study.

Statistical Analysis: Descriptive statistics were used to provide information of the subjects baseline and clinical characteristics and to assess disability (mRS score), number of potential adverse events in the first 3 months post stroke. Continuous data were presented as mean (standard deviation) and categorical data were presented as number and percentage. Differences of these characteristics among the group was analysed by using the Student't' test, the Chi square test, and the Fisher exact test.

To study the difference in outcome measure among the group was analysed by using the Chi square, Odds ratio, 95% CI for odds ratio was obtained. All analyses were performed using the Statistical Package for Social Science (SPSS), version 16.0 (SPSS Inc., Chicago, IL, USA). Significance level was set at $P < 0.05$.

RESULTS

A total of Seventy-five stroke subjects were screened for eligibility during the period of September 2014 to June 2015. Recruitment and participant flow chart is represented in figure 1.

Fifty-four subjects (mean age = 63.30 years, SD = 10.58, range = 40-90 years) were randomized into two groups with equal number (27) in each group. There

were six dropouts (three in the Intervention group two in the Standard care group) due to personal reasons at the three months follow up. Thus twenty-four in Intervention group and twenty-five in the Standard care group were completed follow-up (Figure 1).

The distribution of demographic and clinical characteristics of subjects were given in the table 1, there was a difference in sex, type of stroke, hypertension, smoking, alcoholics, pre morbid mRS score among the groups.

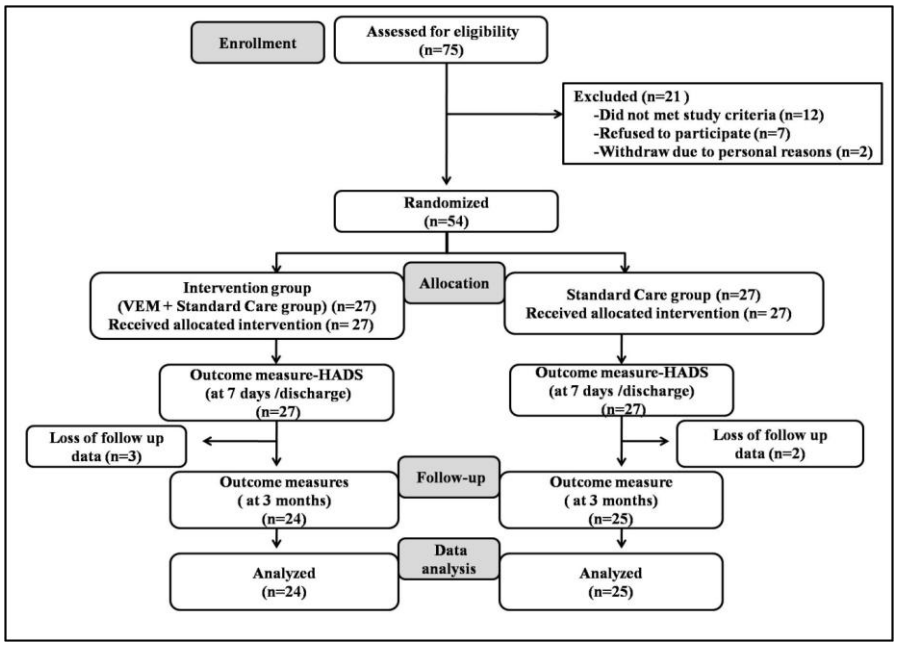

Figure 1: Participants flow chart

Table1: Demographic and clinical characteristics of acute stroke subjects.

Characteristics	Intervention (N= 24) Number (%)	Standard Care (N= 25) Number (%)	P-value
Age(Years) Mean (SD)	61.16 (8.07)	65.36 (11.65)	0.151[a]
Sex			0.007[b]
Male	13 (54.2)	15 (60)	
Female	11 (45.8)	10 (40)	
Side affected			0.116[b]
Right	15 (62.5)	15 (60)	
Left	9 (37.5)	10 40)	
Type of Stroke			< 0.001[b]
Thrombotic	17 (70.8)	17 (68)	
Embolic	2 (8.3)	2 (8)	
Haemorrhage	5 (20.8)	6 (24)	
Stroke risk factors			
Hypertension	17 (70.8)	19 (76)	< 0.001[b]
Diabetes mellitus	14 (58.3)	13 (52)	0.475[b]
Cardiovascular disease	8 (33.3)	11 (44)	0.116[b]
Smoking	6 (25)	8 (32)	0.003[b]
Alcoholics	7 (29.2)	4 (16)	<0.001[b]
Severity (NIHSS)			0.475[b]
Mild (0-7)	13 (54.2)	14 (56)	
Moderate(8-16)	11 (45.8)	10 (40)	
Premorbid mRS Score			0.002[b]
0	11 (45.8)	9 (36)	
1	10 (41.7)	14 (56)	
2	3 (12.5)	2 (8)	

SD= Standard deviation, NIHSS=National institutes of health stroke scale
[a] Analysed by Student independent t-test. [b]Analysed by Chi-square test.

Table 2: Comparison of modified Rankin Scale scores (mRS 0-2 as good outcome, 3-6 as poor out come), Dependency in ADL (Barthel Index score <80) in the first 3 months post stroke.

Outcome measure	Intervention N=24 n (%)	Standard Care N=25 n (%)	Chi square P-value	Odds ratio	95% Confidence Interval
mRS (0-2) Good outcome at 3 months	16 (66.7)	13 (52)	0.296[a]	1.846	0.581- 5.864
mRS (3-6) Poor outcome at 3 months	8 (33.3)	12(48)			
Dependency (BI score < 80) at 3 months	9 (37.5)	18 (72)	0.015[a]	0.233	0.70 - 0.776
Independency (BI score > 80) at 3 months	15 (62.5)	7 (28)			

mRS = modified Rankin Scale, BI score=Barthel Index score. [a] Analysed by Chi square test.

Table 3: Potential adverse events in the first 3 months post stroke

Adverse Events	Intervention n %	Standard Care n %	Total	P -value
Pneumonia	5 (20.8)	6 (24)	11 (22.4)	0.341
Deep vein thrombosis	5 (20.8)	4 (16)	9 (18.4)	0.900
Fractures	2 (8.3)	3 (12)	5 (10.2)	0.275
Falls	5 (20.8)	5 (20)	10 (20.4)	0.303
Pressure sores	3 (12.5)	5 (20)	8 (16.3)	0.737
Constipation	8 (33.3)	8 (32)	16 (32.7)	0.516
Painful shoulder	8 (33.3)	10 (40)	18(36.7)	0.666
Urinary Tract Infection	5 (20.8)	6 (24)	11(22.4)	0.122
Contractures	4 (16.7)	5 (20)	9 (18.4)	0.181
Seizures	2 (8.3)	1 (4)	3 (6.1)	0.879
Intra cerebral bleeding	2 (8.3)	3 (12)	5 (10.2)	0.606
Another Stroke	2 (8.3)	2 (8)	4 (8.2)	0.122
Depression	8 (33.3)	9 (36)	17(34.7)	0.507

Table 2 shows modified Rankin Scale scores at three months follow up, 66.7% (16 of 24) patients of the Intervention group had good outcome (mRS score 0-2) compared to 52% (13 of 25) patients in the Standard care group. The odds ratio of 1.846 and 95% Confidence Interval for odds ratio was 0.581-5.864. There were no statistical significant differences in the level of disability among the groups (p=0.296).

Dependency in ADL (Barthel Index Score <80): The Intervention group reported 37.5 % (9/24) were dependent in ADL than the Standard care group 72% (18/25). There were statistical significant differences in the dependency in activities of daily living (p=0.015).

The Length of the Hospital Stay (Days): The median length of hospital stay was 8 and IQR 8-10 days in the Intervention group. It was higher in the Standard care group (median=10, IQR =9.5-14 days). It indicates the length of hospital stay is more (p<0.001) in the Standard care group than the Intervention group.

Mortality: The Standard care group reported one death, where the subject was above seventy-five years old, female, had adverse events of urinary tract infection, serious fall and fracture.

From the above table (Table 3) it is clear that the p values are <0.05.There was no differences in the occurrence of adverse events among the groups at 5% level of significance.

The Intervention group reported modest number of potential adverse events, most commonly were painful shoulder 8 (33.3%), depression, constipation 8 (33.3%), and urinary tract infection and falls 5 (20.8%). Whereas the Standard care group reported little more number of adverse events, including most commonly reported were, painful shoulder 10 (40%), depression 9 (36%), constipation 8 (32), pneumonia, urinary tract infection 6 (24%), Falls,

pressure sores, contractures, constipation 5 (20%).

DISCUSSION

The current randomized control trial result shows that, 66.7% (16 of 24) patients of the Intervention group had good outcome (mRS score 0-2) compared to 52% (13 of 25) patients in the Standard care group (P=0.199). Furthermore the Intervention group reported comparatively less number of (59/126) adverse events than the Standard care group (67/126) in the first 3 months post stroke. However, there was no statistical significant differences in the level of disability as well as potential adverse events at 3 months follow-up ($p<0.005$) among groups.

The results of the current study go along with D Sorbello et al, [28] who performed a secondary analysis from phase II, randomized control trial to explore whether the very early and frequent mobilisation (VEM) affected type of complication (immobility/stroke related), number and severity in the first 3 months after stroke. The result showed as there was no significant group differences in the number, type or severity of complications by 3 months, common complications were falls, while depression was absent. Older the age, longer length of stay was associated with an immobility related complication.

The present study supports the findings of the most recent the multi centre, large randomized control trial published by the AVERT Trial collaboration group. [29] The trial was aimed to compare the efficacy of frequent, high dose, very early mobilisation with standard care after stroke. 2104 patients were randomly assigned to either very early mobilisation (n= 1054) or usual care (n=1050). The results of this trial showed that the higher dose, very early mobilisation protocol was associated with a reduction in the odds ratio of favorable out come at 3 months.

The current randomized controlled study results not in line with Sundseth et al, [30] who conducted a prospective, randomized, controlled trial on the outcome after mobilization within 24 hours of acute stroke. Study results identified that patients who were mobilized within 24 hours after stroke onset had an increased poor outcome, death rate, and dependency among patients. However the patients who were mobilized between 24 and 48 hours showed improvement in neurological functioning.

Non-significant difference in the level of disability as well as potential adverse events at 3 months follow-up among the groups could be attributable to difference in type of stroke, hypertension, smoking, alcoholics, pre morbid mRS score (pre-stroke disability) or due to chance. It is also possible that the stroke related adverse events (seizures, another stroke, intracerebral bleeding) in the Intervention group represents harm associated with early mobilisation. Further more four patients who were randomized into the standard care group received recombinant tissue plasminogen activator drug from the medical section which instantly improved hemiplegic side limb function. This study did not exclude those patients.

Non-significant difference among the groups could be due to the Interventions were delivered for short period of time (seven days/or until the discharge which ever was sooner). Furthermore there was a long gap of eleven weeks after discharge from hospital. During this period the Standard care group subjects might be involved in the active mobilisation.

The limitations of this study are small sample size, the patients recruited were not representatives of the whole stroke population (patients with severe aphasia

were excluded). Low power and longer follow up were not undertaken. Future studies may also benefit from larger sample sizes with homogenous groups and longer intervention period, which would increase the generalizability of the results.

CONCLUSIONS

The results of the current randomized controlled trial show that the very early mobilisation along with the standard care may be beneficial in improving the level of disability and reduce the number of potential adverse events. However, there was no statistical significant differences in the level of disability as well as potential adverse events at 3 months follow-up ($p<0.005$) among the groups.

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