METHODOLOGY
CHAPTER II

2. METHODOLOGY

2.1 Study Design:

A single blinded, active controlled, outcome assessor blinded, and prospective randomized controlled trial with three months follow-up.

2.2 Source of data:

Data was obtained from the individuals with stroke recruited from inpatient department of Medicine and Neurology at the Justice K.S.Hegde Charitable Hospital, Deralakatte, Mangaluru, Karnataka, India.

2.3 Study duration:

Duration of the study was from March 2012 to September 2015 and followed up till December 2015.

2.4 Study Subjects:

Participants in the study consisted of acute stroke survivors.

2.5 Ethical Approval:

The current RCT was permitted by the Central Ethical Committee (CEC) of the Nitte University, Mangaluru in 2012 before the commencement of the study (Ref: NU/CEC/Ph.D-52/2012) (Annexure I).
2.6 Trial registration:

Study registered retrospectively with the Clinical Trial Registration of India, with CTRI number CTRI/2016/04/006795 (Annexure II).

2.7 Informed consent:

People with stroke were informed about the details of the study and written consent was attained from every individual, or from the representatives at the beginning of the study (Annexure V).

2.8 Sample Procedure:

The fixed allocation randomization procedure by using a computer generated random number sequence was performed.

2.9 Sample Size:

A pilot randomized controlled study was conducted among 30 subjects. Between groups mean difference (6) and pooled standard deviation (14.308) of Barthel Index were obtained at discharge-admission. The standardized difference obtained was 0.392.

The Sample Size calculation formula used: \[ n = \frac{2(1.96+0.842)^2 \times s^2}{d^2} \]

Where n=Sample size.

Significance (\(\alpha\)) = 1.96 (5% significance i.e. 0.05)

Power (\(\beta\)) = 0.842 (80%)

s= Pooled Standard deviation.
\( d = \text{Difference in mean between groups.} \)

Anticipating a dropout rate at 10%, using the following formula,

\[
\frac{n}{\alpha - d}
\]

Where, \( n = 89; d = 10\% = 0.1 \), a minimum of 98 subjects were needed in each group. A total number of 196 stroke survivors were needed for this study.

98 subjects were required for every one group with both sided significance of 0.05 (\(\alpha 5\%\)) and a power \((1-\beta)\) of 0.8 (80%).

208 subjects were recruited for this study, including both females and males with age groups above 18 years. The subjects were allocated to any of the two groups randomly.

2.10 Randomization:

208 Individuals with the acute stroke, including both females and males with age group 30 to 90 years were randomly allocated (1:1) to one of two groups (Group 1, Group 2), both the groups received the Routine care, Group 1 received the additional Very early mobilisation.

2.11 Sequence Generation:

The fixed allocation randomization procedure performed by using a computer generated the sequence of random numbers (www.random.org) to make sure an equal number of subjects allocated in both groups.
2.12 Allocation Concealment:

An allocation concealment procedure was sequentially numbered, opaque and sealed envelope method. When a participant picked the envelope, before opening the envelope the name of the participant was written on the envelope.

2.13 Implementation:

A person, who was not related to the study generated sequence, enrolled the participants and allocated them to groups based on the number found in the envelope.

2.14 Blinding:

Assessors were blinded at three months follow-up (Single blinded randomized controlled trial).

2.15 Study sample:

330 individuals with the stroke were assessed for eligibility, among that 106 individuals did not meet the study criteria and 224 were eligible recruited in the study. After recruitment 16 were excluded due to refusal to participate and withdraw due to family reasons. 208 were randomly allocated to both the groups (103 in the intervention group and 105 in the routine care group). A total 11 individuals were lost to follow-up due to the family reasons and death (4 in the very early mobilisation group and 7 in the routine care group). Therefore, 99 remained in the early mobilisation group and 98 in the routine care group for data analysis.
2.16 Inclusion criteria:

Participants were enrolled into the study if they were,

- Subjects age above 18 years.
- Both sex (Male, Female).
- Acute cerebrovascular accident subjects admitted to the hospital within 24 hours of symptom onset.
- Able to respond to verbal instructions (Conscious, rouseable and orientation to time, place and person).
- Systolic blood pressure between 120 to 180 mm Hg.
- Saturation of oxygen> 92% (with or without supplementation).
- Pulse 40 to 100 beats per minute.
- Within normal range of temperature < 38.5°C.
- Physician was aware about the study protocol, and diagnosed first time stroke participants were referred participants to take part in this study furthermore allowed and clearance was provided to go ahead upright position out of bed activities inside 48 hours of cerebrovascular accident onset.

2.17 Exclusion criteria:

- Deterioration within the first hour of admittance to the hospital.
- Co-existing progressive neurological disorder.
- Unstable cardiac condition (e.g., acute myocardial infarction, severe cardiac failure).
- Lower limb bone fracture preventing mobilisation.
- Those who required palliative care.
2.18 Materials used in the study (Figure 2 and 3):

- Sphygmomanometer
- Stethoscope
- Pulse Oxymeter (Mind Ray PM-60- Shenzhen Mindray, Bio-medical Electronics Co., Ltd, China).
- Thermometer
- Adjustable Couch
- Assistive devices (Standing frame, tilt table, functional knee brace, Foot drop splint, gait belt, parallel bars, walker, stick, wheel chair, and stair case).
- Data collection sheets
- Barthel Index form
- The modified Rankin Scale form
- Self-reported questionnaires such as the Quality of Life (QoL) by SF -36 and Hospital Anxiety Depression Scale (HADS).
Figure 2: Material used in the study. A. Sphygmomanometer and Stethoscope, B. Pulse Oxymeter, C. Foot drop splint, D. Functional knee brace, E. Gait belt.

Figure 3: Material used in the study. A. Tilt table, B. Standing frame, C. Parallel bars, D. Stick, E. Walker, F. Stair case.
2.19 Methods:

The participants were randomly allocated to the following two groups, Very Early Mobilisation plus the Routine Care and the Routine Care alone.

Group 1-Very Early Mobilisation (VEM) plus Routine Care / Intervention Group:

Participants in the intervention group (n=103) received routine care and in addition, mobilisation was started (early and repetitive out of bed activities not less than two times a day) as earlier as possible after recruitment, mobilisation initiated inside 48 hours of the cerebrovascular accident onset. Time spent on mobilisation was decided by the subject’s capacity (five to thirty minutes per session), early upright out of bed activities were provided no less than 2 times per day, for 7 days or until the discharge from the hospital (whichever was earlier).\textsuperscript{53, 97}

The study protocol was functional oriented and activity specific and can be summarized as follows:\textsuperscript{53, 97}

- Mobilisation was initiated as early as possible.
- Subjects were encouraged to avoid bed rest if at all possible.
- Subjects were educated to be out of bed, upright sitting and moving out of couch no less than 2 times per day.
- Support was provided, for any weak hemiplegic shoulder while sitting, shifting and walking.
Very Early Mobilisation Group received following activities:

Early and frequent mobilisation or out of bed activities, including roll and sit up, sit at the edge of the couch, supported sitting in the bed, sit unsupported out of bed in the chair and sit to stand transfer with or without assistance, transfer feet on the floor, stand upright with or without support, stand to sit, and walking with or without support based on task oriented or goal oriented programme along with the rest in between. \[53, 97\]

Roll and sit up (Figure 4):

Roll and sit up is a useful functional activity for individuals with acute stroke and also useful for minimizing problems of shoulder joint.

Procedure:

Instruct the subjects to roll from supine position to the affected side lying position by weight bearing on the affected elbow. The hips and knees were bent and legs were moved away from the plinth.

Progression:

At the beginning the physiotherapist assisted the subject while rolling supine position to side lying position, kept the legs away from bed or lifting off the upper trunk and then progressed to the transition from supine to side lying on elbow to sitting and supine to long sitting.
Sitting position:

Sit at the edge of the couch with hand support (Figure 5):

Subjects were asked to sit at the edge of the couch at least 3-5 minutes according to their tolerance. In sitting position subjects were asked to perform weight bearings and weight shifting activities on the affected hand support.

Sit supported in bed:

Subjects were instructed and assisted to sit in the bed at least 3-5 minutes according to their tolerance. In the supported sitting position subjects were asked to perform weight bearings and weight shifting activities on the affected hand support.

Sit unsupported out of bed (Figure 6):

In this position individuals with the stroke were instructed to perform reach outs in all directions and functional activities such as feeding, personal hygiene with non-affected upper limb. Furthermore sit to stand transfer with assistance performed.

Transfer feet on the Floor (Figure 7):

Subjects were instructed to practice reaching forward and upward in sitting in the chair or at the edge of the couch. Subject should work within the range he/she can control, gradually increasing it.
Figure 4: Supine roll and sit up with support.

Figure 5: Sit at the edge of the couch with hand and therapist support.
Figure 6: Out of bed activities- Sit unsupported and reach outs.

Figure 7: Sitting at edge of the chair and couch, practicing forward and upward.
Figure 8: A&B, Sit to stand with therapist support. C&D, Sit to stand with wall bar support.
Sit to stand/Standing up (Figure 8 A&B, C&D):

Subjects were asked to perform sit to stand activities in front of the wall bar, using arm supported wooden chair or with the support of gait belt. The physiotherapist provided support while performing sit to stand.

Procedure:

In sitting position, subjects were instructed to scoots to the front of the chair, keep feet under the hips, then to bend the trunk forward and push up into standing using upper limb support.

Progression:

Subjects were instructed to practice sit to stand without support and therapist supervision.

Standing activities (Figure 9: A&B, C&D):

Standing activities are very helpful for weight bearing and weight shifting on the affected lower limb. Improves trunk control and balance, improves or maintain range of motion, prevents or decrease muscle contractures, managing pressure sores, improves bowel function, improves circulation, osteoporosis, muscle wasting, spasticity and also subjects feels high in motivation.

Procedure:

Supported standing was done with the help of supportive devices like tilt table, standing frame, functional knee brace and walker. The subjects were given 3-5 minutes of supported standing (based on the tolerance of the individual) with rest periods in between.
Progression:
Subjects were instructed to stand with minimal support with the help of functional knee brace and wall bar/parallel bar/walker/stick support and practiced wide base and narrow base standing, symmetrical weight bearings on both lower extremities and weight shifting and reach outs on the affected leg, a single leg standing, walk standing, and step standing, then progressed to unsupported standing with physiotherapist supervision. Finally standing was practiced without therapist supervision.

Walking/gait (Figure 10: A&B, C&D):

Early gait activities:

Individuals with the stroke were asked to practice walking forward, backward and sideways and cross stepping with support using parallel bar or walking aid and then practiced without support. Then practiced weight shifting from one foot to the other, stepping over different heights stools. Further stepping up and down using the stepper or small stool.

Advanced gait activities:

Walking unsupported on level surface, an irregular surface, the figure of eight walking, walking in a busy corridor, ramp up and ramp down, stair climbing up and down activities.
Figure 9: A&B. Supported standing with tilt table and standing frame, C&D. Supported standing with parallel bars and functional knee brace.
Figure 10: A&B. Supported walking with parallel bars, C&D. Supported stair climbing up and down.
Dosage:

Duration of Intervention:

- Single session duration: 5-30 minutes as tolerated by the individual.
- The total duration of Intervention: Seven days or till the discharge.
- Total duration of follow-up: Three months.

Frequency of intervention:

Minimum two sessions per day.

Intensity:

Mild and Moderate level intensity activities were included.

Safety: [53]

The protocol included monitoring of vital parameters such as pulse rate, Blood pressure, saturation of the oxygen and body temperature prior to each mobilisation inside the initial three days of cerebrovascular accident. The protocol was assisted by the nursing staff with supervision of the trained Neuro-physiotherapist.

In the presence of any deviations like blood pressure drop of >30 mm Hg during mobilisation, interventions were discontinued. The amount of duration of each out of bed activity was decided by the patient level of tolerance.
Group 2: Routine Care

Individuals in the routine care group (n=105) received usual stroke care activities such as appropriate positioning of the subject in the bed, passive and active range of motion exercises of the affected limb, activities in the couch, balance activities in sitting position, and education of subjects and family started inside 48 hours after cerebrovascular accident, for 45 minutes a day, for 7 days or until the discharge. [111-116]

Correct positioning in bed (Figure 11):

Subjects were advised and educated about correct positioning in bed and position in chair, see the table 4.

Mobilisation in bed:

Subjects were instructed to move sideways, rolling over on to the affected side and rolling over on to the unaffected side and moving forwards and backwards while sitting in the bed.
Table 4: Correct positioning methods for individuals with stroke.

<table>
<thead>
<tr>
<th>Position</th>
<th>Supine position, Lying on affected side and Lying on un affected side</th>
<th>Sitting position in chair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and Neck</td>
<td>Neutral and Symmetrical</td>
<td>Straight position</td>
</tr>
<tr>
<td>Trunk</td>
<td>Aligned to midline</td>
<td>Trunk extended</td>
</tr>
<tr>
<td>Affected Upper Limb</td>
<td>A pillow was placed under the affected limb, so that scapula protracted (A pillow wasn’t used under affected limb, lying on affected side), shoulder forwarded and elbow extended, forearm supination, wrist in neutral, fingers were extended and thumb kept in abduction position A cone or cylinder was kept in the hand.</td>
<td>Arm board or a pillow was used for affected upper limb.</td>
</tr>
<tr>
<td>Affected Lower Limb</td>
<td>Supine position: A pillow was not placed. Affected side lying: A pillow was placed under the affected leg. Un affected side lying: A pillow was kept under the affected leg. Knee slightly flexed and ankle and foot kept in neutral position.</td>
<td>Both hip and knee were kept at 90° and foot was fixed on the floor.</td>
</tr>
</tbody>
</table>
Figure 11: A. Supine position, B. Affected side lying, C. Unaffected side lying, and D. positioning in the chair.
**Bridging (Figure 12 A&B):**

Bridging or pelvic elevation is a basic skill required for facilitation of movement within bed, bed pan activities, scooting, sit to stand, stand to sit transfer, ambulation and stair climbing up and down.

**Procedure:**

Subjects were assumed hook lying position with hip joint and knee joint were bent and feet flat on the couch. Subjects were taught to lift the pelvis and hold for 6-8 seconds, and lower pelvis down to the plinth slowly. The therapist assists pelvic elevation by placing the hands on the subject’s lower thigh and tapping over the gluteus maximus.

**Progression:**

Subjects were instructed to progress, bridge and a single straight leg lift, bridge and scoot to either side.

**Precaution:**

While performing bridging activity, breath holding and lifting the pelvis more than the head height was avoided in subjects with hypertension.

**Range of motion exercises (Figure 13 A&B):**

Physiotherapist educates and demonstrated initially bilateral upper limb activities, passive movements for affected lower limb, if individual had hemiplegia. If the subject is having hemi-paresis, they were instructed to do the active assisted movements, such as, heel dragging, pelvic bridging, straight leg raise of affected limb, alternate straight leg raise, bridge with straight leg raise, keeping legs out of the couch and putting back on the bed, side leg straight leg raise, and prone straight leg raise in the bed.
Figure 12 A&B: Assisted pelvic bridging and Independent pelvic bridging.

Figure 13: A. Therapist guided limb range of motion activity, B. Independent bilateral upper limb activity.
Sitting balance activities:

Subjects were asked to sit comfortably at the edge of the couch and asked to perform symmetrical weight bearing on the buttocks, weight shifting with extended arm support, reach outs in all directions, manual perturbations were provided by the therapist and performed functional activities in sitting position.

Education of the subjects and family:

Education of the subject and caregiver related to the positioning, activities in the bed, balance sitting and sit to stand was provided.

Dosage:

Duration of Intervention:

- Single session duration: 45 minutes.
- The total duration of Intervention: Seven days or till the discharge.
- Total duration of follow-up: Three months.

Frequency of intervention:

One session per day.

Intensity:

Low to moderate level intensity activities was included.

Both group 1 and group 2 received treatments within 48 hours after stroke. Intervention was provided by an experienced neuro physiotherapist/principle investigator face to face to the subject and intervention was delivered within Inpatient department of Medicine and Neurology at the Justice K.S.Hegde Charitable Hospital, Deralakatte, Mangaluru, Karnataka, India.
2.20 Data collection:

Outcome measures were taken for all recruited individuals, at a baseline (within 48 hours of the onset of cerebrovascular accident); at 7 days or at discharge from the hospital (whichever was sooner), and at 3 months follow-up after cerebrovascular accident.

2.21 Outcome measures:

2.21.1 Primary Outcome measures:

1. The number of serious complications/adverse events reported at three months follow-up.

2. An activity of daily living (ADL) was measured with Barthel Index Scale.

3. Disability was measured with the modified Rankin Scale (mRS).

1. The number of potential adverse events /complications reported at three months follow-up:

Serious and life threatening complications like infections, DVT, fall, fractures, pressure ulcers, were classified as a life threatening adverse event. The numbers of serious adverse events reported at three months follow-up were taken up for data analysis.

2. Barthel Index:

An activity of daily living was measured with Barthel index. It is a most widely used measure of basic activities of daily living (ADL) in individuals with the stroke. It is a ten item rating scale includes self-care, bladder and bowel, and
mobility items. Maximum score in the Barthel Index is 100, which indicates complete freedom in activities of daily living; minimum score is ‘0’ which indicates total dependency in ADL. The BI has established psychometric properties and has high association with established tools used for measuring independence in daily living activities. \[124-127\]

**Strength:**

Barthel Index has high validity, outstanding intra-rater and inter-rater reliability and responsive measure of performance of ADL in stroke population. It is a simple, easy and quick to administer (5-10 minutes) and interpretation of the score.

**Weakness:**

It has definite ceiling effect in the mild stroke individuals and floor effect in a severely disabled acute stroke individual.

Initially, licensed Barthel Index (version 1.0) was procured from author, Mapi research trust, Lyon, France.

3. **The modified Rankin Scale (mRS):**

Level of disability was measured with modified rankin scale (mRS) in this study. mRS is a 7 points Likert scale, score ranges from 0-6, where zero indicates no disability, five indicates severe disability and six indicates death. It is a simple and easy to administer and, time efficient i.e., not more than 5 minutes. Further it requires limited training. mRS has good inter-rater reliability, good validity and responsive, sensible, feasible tool, it has limited floor and ceiling effect. \[127-131\]
Interpretation of modified rankin scale: Poor outcome can be defined as >3 mRS, favourable outcome can be defined as <3 mRS.

2.21.2 Secondary Outcome measures:

1. Quality of life (QoL) was measured by using the medical outcome short form SF-36 v2.

2. Psychological well-being was measured with the Hospital Anxiety Depression rating Scale (HAD Scale).

1. Medical outcomes short form (SF-36 v2):

Quality of life (QoL) was measured with SF-36 v2. Kannada, Malayalam and Indian English versions of SF-36 V2 were used in this study. In this study we summarized 8 major domains calculated scores into two major headings, physical composite score (PCS) and mental composite score (PCS). Highest score on each major heading indicates having good quality of life. The SF-36 has been commonly used in individuals with cerebrovascular accident. It has high intra rater and inter reliability (Pearson’s r scores ranging from 0.89 to 0.99) and high validity. [132-134]

Initially, licensed SF-36V2 questionnaire was procured from Quality Metric Incorporated, USA in the regional language (Kannada and Malayalam) and in Indian English.

2. Hospital Anxiety and Depression rating Scale (HADS):

The most widely recommended self-administered outcome tool to measure the psychological wellbeing (anxiety and depression) is Hospital Anxiety and
Depression Scale. It is a reliable, valid screening tool measures anxiety and depression in stroke individuals as well as in general hospital subjects. Administration time ranges from 2-5 minutes. \[^{135, 136}\]

It has total 14 items that assess the subject to reflect on their psychological status in the past week. Seven items assess depression, of which two items assess the lack of interest, and two items evaluate appearance and feelings of lingering down. Seven items evaluate anxiety, of which two items evaluate autonomic anxiety (fear and butterflies in the abdomen), and the five items evaluate nervousness as well as agitation. \[^{137, 138}\]

This scale has two subscales, 14 items related to the anxiety are summed to generate an anxiety score (HADS-A) and another 14 items related to the feeling of depression are summed to make depression score (HADS-D). Every item in this scale is rated on a four point Likert scale, minimum score is zero, which indicates no symptoms, whereas maximum score three, is given for definite case of anxiety or depression. Maximum score in each subscale is ‘21’ which indicates maximum distress and minimum score is ‘0’ which indicates no psychological distress. \[^{137, 138}\]

Initially, licensed HADS questionnaire in the regional language (Kannada and Malayalam) and in Indian English was procured from GL Assessment, Mapi foundation, UK.