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Early Intensive Multi-faceted Rehabilitation in Stroke Patients: What is the Best Effective Rehabilitation Time?

İnmeli Hastalarda Erken Yoğun Çok-Yönlü Rehabilitasyon: En Etkili Rehabilitasyon Süresi Nedir?

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ABSTRACT Objective: We aimed to evaluate the effects of the intensive and multi-faceted rehabilitation program in patients during the first 3 weeks after stroke, and to determine the most effective time to initiate treatment. **Material and Methods:** Forty two patients who were treated in our clinic were included in the study. The demographic characteristics of the patients, the level of stroke severity assessed by the National Stroke Institute Severity Scale (NIHSS), the functional stages assessed by the Brunstrom and Chedocke McMaster Stroke Assesment (CMSA) Scale and the disability levels assessed by the Functional Independence Measure scale were recorded. All patients received a multi-faceted and intensive rehabilitation program 20 sessions in total. The patients were divided into 3 groups according to the times of initiation of rehabilitation i.e during the first 9 days (Group 1), between days 10 and 14 (Group 2) and between days 15 and 21 (Group 3). The evaluation parameters assessed before the treatment, 4th weeks and 3th months were compared within and between the groups. **Results:** According to the treatment start times; the change in CMMS hand, arm, legand postural control scores, Brunstroom upper, lower limbs and hand levels and the NIHSS score was found to be higher in the first 9 days compared to the other 2 groups in the beginning of treatment. **Conclusion:** Early intensive and multi-faceted rehabilitation program is effective for motor and functional recovery in ischemic stroke patients. Moreover, the start of treatment within the first 9 days provides the most improvement.

Keywords: Ischemic stroke; rehabilitation; early rehabilitation

ÖZET Amaç: Bu çalışma ile inme sonrası ilk 3 hafta içinde uygulanan yoğun ve çok yönlü rehabilitasyon programının hastalardaki etkilerini değerlendirmeyi ve tedaviye başlamak için en etkili zamanı belirlemeyi amaçladık. **Gereç ve Yöntemler:** Kliniğimizde tedavi gören 42 hasta çalışmaya dâhil edildi. Hastaların demografik özellikleri, Ulusal İnme Enstitüsü Şiddet Ölçeği [National Stroke Institute Severity Scale (NIHSS)] ile değerlendirilen inme şiddeti seviyesi, Brunstrom ve Chedocke McMaster Ölçeği (CMMÖ) ile değerlendirilen fonksiyonel evreler ve Fonksiyonel Bağımsızlık Ölçümü skoru kaydedildi. Tüm hastalara toplamda 20 seans çok yönlü ve yoğun rehabilitasyon programı uygulandı. Hastalar rehabilitasyona başlama zamanlarına göre ilk 9 gün (Grup 1), 10-14 gün (Grup 2) ve 15-21 gün (Grup 3) olarak 3 gruba ayrıldı. Tedavi öncesi, 4. hafta ve 3. ay değerlendirme parametreleri gruplar içi ve gruplar arası karşılaştırıldı. **Bulgular:** Tedaviye başlama süresine göre; CMMÖ el, kol, bacak ve postüral kontrol skorları, Brunstroom üst, alt ekstremite ve el ve NIHSS skorundaki değişim ilk 9 günde tedaviye alınan grupta diğer 2 gruba göre daha yüksek bulundu. **Sonuç:** Erken yoğun ve çok yönlü rehabilitasyon programı, iskemik inmeli hastalarda motor ve fonksiyonel iyileşme için etkilidir. Üstelik tedaviye ilk 9 gün içinde başlanması en fazla iyileşmeyi sağlar.

Anahtar Kelimeler: İskemik inme; rehabilitasyon; erken rehabilitasyon

Stroke is a major health problem that affects a large part of the community with high incidence and mortality rates, and causes disability in survivors. Post-stroke disability impairs the quality of life of patients, affects the life of patients' relatives, and leads to both socioeconomic and social problems. The target in stroke rehabilitation is to enable the highest functional independence level possible for the indi-

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vidual and to improve the quality of life despite the current limitations.[1]

Rehabilitation of patients after stroke is very important in reduction of mortality, disability and in the long term, the need for institutional care. Data including animal experiments indicate that early mobilization and rehabilitation after stroke is important to accelerate recovery and increase brain after stroke develop more frequently and earlier, physical activities such as sitting on the bed, standing and walking are recommended from the early period, and believed to accelerate recovery.[2]

Despite this information, little is known about the effect of exercise on penumbra, and some authors suggest that motor activity may increase the lesion size by reducing the blood supply.[3]

In conclusion, the questions of how the frequency and duration of out-of-bed mobilization should be and when and at which dose rehabilitation should be initiated after stroke are still unanswered.[4]

This study aimed to evaluate the effects of the intensive and multi-faceted rehabilitation program in patients admitted to our clinic during the first 3 weeks after stroke and to determine the most effective start time to initiate treatment.

MATERIAL AND METHODS

STUDY DESIGN

The prospective and single-center study was conducted at 47 stroke inpatients who were admitted to acute stroke unit or neurology clinic at Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital between December 2017 and December 2018. The study was approved by the ethics committee of Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital (date: 3/11/2016, decision no: 17/08) according to the principles of the Declaration of Helsinki.

PARTICIPANTS

Patients aged between 18 and 80 years who had first-ever ischemic stroke, who had medical stability and stroke duration between 1 and 21 days as well as were those who agree to participate included in the study.

Patients who had stroke duration >21 days and with hypoxic anoxic brain damage after cardiac arrest, with traumatic-non-traumatic intracranial hemorrhage, with known pre-existing dementia/ Alzheimer's disease and severely impaired cognitive function, with known progressive neurological disease or peripheral nerve involvements such as polyneuropathy and/or history of psychiatric disease or malignancy, with history of trauma, fracture, fixed joint contracture, amputation or phlebitis at the affected side, with severe hepatic or renal failure, decompensated heart disease and/or severe bleeding diathesis were exclude.

Five of 47 patients were excluded from the study because of they did not come to the control and study was completed with 42 patients.

The patients and their relatives (at least one of their family members/relatives) were informed about the study and their written consents were obtained. Approval was obtained before the study from the hospital's local ethics committee, and the study was conducted in accordance with the Declaration of Helsinki criteria.

DEMOGRAPHIC AND DISEASE CHARACTERISTICS

Data regarding the age, gender, educational status, hand dominance, body mass index, comorbidities, stroke type and location of lesion for the patients were recorded.

ASSESSMENT OF FUNCTIONAL IMPAIRMENT AND DISABILITY

The motor functions of the patients were assessed by the Brunnstrom motor staging method. The Brunnstrom motor staging assessed on three areas i.e upper limbs, lower limbs and hands was scored between 1 and 6 for each area.[5]

The National Institutes of Health Stroke Scale (NIHSS) was used to examine the neurological functions of the patients. In this scale, the total score ranges from 0 to 42.[6]

The functional impairment and disability state assessment was made using the Functional Independence Measeure (FIM) Scale and Chedoke McMaster Stroke Assessment (CMSA) Scale physical impairment inventory. While the FIM tool

analyses motor and cognitive functions of disability, and contains sections consisting of self-cade, sphincter control, transfers, locomotion, communication and social cognition with 18 questions in total which are scored between 1 and 7, the CMSA scale physical impairment inventory consists of six items that contain shoulder pain, postural control, arm movements, hand movements, leg movements and foot movements each of which are assessed between 1 and 7 points.[5] The maximum total score is 42.[7]

INTERVENTION

All patients received a multi-faceted and intensive rehabilitation program in 20 sessions in total, 5 days a week for 4 weeks; 1 session per day (in at least 2 divided phases for each session that lasted 90-120 minutes in total). This program was applied 45-60 minutes per day, 5 days a week using methods that lasted 45-60 minutes per day and contained rehabilitation of occupational, deglutition, speech, neglect and cognitive functions according to the mobilization, mobility and treatment requirements of the patients. During the program, an in-bed/out-bed exercise program was applied with respect to functional independence such as daily life activities, occupational and transfers that were participated by active caregivers and observed by physiotherapists.

During this program;

- A pillow was placed under the arm so as to maintain the shoulder abduction and slight outer rotation to prevent contractures that may develop in the upper limbs. For lower limbs; maintenance of legs in neutral position and the ankles in 90-degrees dorsiflexion.

- Exercises to improve joint range of motion (ROM), flexibility, extension, strengthening, walking, balance and daily life activities, constraint-induced movement therapy, and electrical stimulation to the required muscles were given. Transfer and ambulation training was provided to prevent falls. Several neurophysiological theraphy approaches i.e. Bobath, Brunnstrom, Rood and Proprioceptive Neuromuscular Facilitation (PNF) were selected and applied according to the patient's condition.

Additionally, in accordance with the multi-faceted and intensive rehabilitation protocol, a computer-aided cognitive rehabilitation program was applied by our clinical psychologist 3 times a week in sessions that lasted 60 minutes.

A structured training program that contained patient care, problems that may be encountered and solution recommendations was provided by the same social services specialist once a week in 60-minute sessions to patients and their companions.

According to all these methods, an intensive rehabilitation program was applied to the patients in minimum 90 and maximum 180 minutes per day.

STUDY PROTOCOL

All assessment parameters used for the patients were repeated immediately before the treatment (the 1st day), at the end of the rehabilitation program (4th weeks-discharge) and 3th month (control).

The patients were divided into 3 groups according to the times of initiation of rehabilitation i.e during the first 9 days (Group 1), between days 10 and 14 (Group 2) and between days 15 and 21 (Group 3). The evaluation parameters assessed before the treatment, 4th weeks and 3th months were compared within and between the groups.

STATISTICAL ANALYSIS

The data were analyzed on the SPSS for Windows 22.0 software package. Descriptive statistics were indicated as mean±standard deviation or median (minimum-maximum) for continuous variables and number of observations and (%) for nominal variables. Concordance of continuous variables with normal distribution was assessed using the Kolmorov-Smirnov test. Significance of the difference between the repeated measures within groups was assessed using the Wilcoxon signed ranks test, and values below $p<0.017$ were considered significant. Significance of the difference between the groups in terms of variables were investigated using the Anova test because of the presence of normal distribution, and using Pearson's Chi-square test for nominal variables. A Tukey post-hoc analysis was performed for the relationship of subgroups. Results were considered statistically significant for $p<0.05$.

Post-hoc power analysis was performed with G*Power software (3.1.9.2). Post-hoc power analysis for the CMSA posture subscale (an alpha value equal to 0.05, Cohen's d of 0.20 (small effect), and two-tailed hypothesis) demonstrated an observed power of 91.9%.

RESULTS

The mean age of 42 patients included in the study was 68.0 (66.3±11.4) years, and 21 (50%) were female and 21 (50%) were male. Demographic and characteristics of patients are shown in Table 1.

The patients were divided into 3 groups according to the times of initiation of rehabilitation i.e during the first 9 days [Group 1, 13 patients (31%)], between days 10 and 14 [Group 2, 12 patients (29%)] and between days 15 and 21 [Group 3, 17 patients (40%)]. No significant difference was found between the groups in terms of demographic (age p=0.978, gender p=0.107), presence of comorbidity (p=0.542) and disease characteristics (hemiplegic extremity p=0.275, Banford classification p=0.070).

With the treatment applied, the changes in the scores for NIHSS (p=0.001, p=0.001, p=0.004), Brunstroom hand (p=0.001, p=0.001, p=0.001), upper limb (p=0.001, p=0.001, p=0.001) and lower limb (p=0.001, p=0.001, p=0.001) levels, FIM total (p=0.001, p=0.001, p=0.001) and motor (p=0.001, p=0.001, p=0.004) scores, CMSA posture (p=0.001, p=0.001, p=0.001), arm (p=0.001, p=0.001, p=0.001), hand (p=0.001, p=0.001, p=0.001), leg (p=0.001, p=0.001, p=0.001) and foot (p=0.001, p=0.001, p=0.001) between the pre-treatment and, 4th weeks and 3th months, and between 4th weeks and 3th months assessments.

While a significant improvement was seen in FIM cognitive scores between the pre-treatment values and, 4th weeks and 3th months follow-up values (p=0.001, p=0.004 and p=0.038, respectively), the change between 4th weeks and 3th months was not significant (p>0.05).

When the pre-treatment values were compared between the groups, a significant difference was found in no parameter (p values were NIHSS:0.087, Brunstroom hand: 0.055, upper limb: 0.052, lower limb: 0.141, FIM total: 0.052, FIM motor: 0.085, FIM cognitive: 0.129, CMSA posture: 0.283, arm: 0.072, hand: 0.067, leg: 0.120, foot: 0.144, respectively)

In the subgroup analysis of the results that were considered significant in terms of treatment change;

TABLE 1: Demographic and disease characteristics and comorbidities of the patients.

Evaluated parameters	n=42 n (%), mean±SD
Gender	21 (50)
Female	21 (50)
Male	
Age (years)	66.3±11.4
Dominant hand	
Right	42 (100)
Left	0
Education	
Iliterate	15 (35.7)
5 years	12 (28.6)
8 years	6 (14.3)
11 years	4 (9.5)
More than 11 years	5 (11.9)
BMI (kg/m^2)	27.2±4.2
Comorbidities	
HT	33 (78.6)
DM	18 (42.9)
HPL	26 (61.9)
Heart disease (CAD, AF, valvular disease)	18 (42.9)
COPD	4 (9.6)
Hypothyroidism	2 (4.8)
Pituitary failure	1 (2.4)
Venous insufficiency	1 (2.4)
Stroke type	
Ischemic	42 (100)
Hemorrhagic	0
Hemiplegic extremity	
Right	25 (60)
Left	17 (40)
Bamford classification	
Total anterior	7 (16.7)
Partial anterior	10 (23.8)
Lacunar	5 (11.9)
Posterior	15 (35.7)

mean±SD: mean±standard deviation; BMI: Body mass index; HT: Hypertension; DM: Diabetes mellitus; HPL: Hyperlipidemia; CAD: Coronary artery disease; AF: Atrial fibrillation; COPD: Chronic obstructive pulmonary disease.

The **NIHSS change** was significant in group 1 patients compared to the other two groups (Group 2 and 3, respectively) in terms of the changes between pre-treatment and 4th weeks (p=0.043 and p=0.009, respectively), between pre-treatment and 3th months (p=0.023 and p=0.004), and between 4th weeks and 3th months (p=0.011 and p=0.009).

The **Brunstroom change** was significant in Group 1 patients compared to the other two groups for hand in terms of the changes between pre-treatment and 4th weeks (p=0.022 and p=0.013, respectively), between pre-treatment and 3th months (p=0.027 and p=0.009), and between 4th weeks and 3th months (p=0.024 and p=0.018). For upper limb, the changes between pre-treatment- 4th weeks (p=0.003 and p=0.001, respectively), between pre-treatment and 3th months (p=0.037, p=0.003), and between 4th weeks and 3th months (p=0.021 and p=0.003) were significant. For lower limb, only the change between pre-treatment-3th months was significant (Group 1-2 p=0.046, Group 1-3: p=0.013).

With respect to the **CMSA, posture score,** the changes were significant in Group 1 patients compared to the other two groups (Group 2 and 3, respectively) in terms of the changes between pre-treatment and 4th weeks (p=0.032 and p=0.017, respectively), pre-treatment and 3th months (p=0.013 and p=0.011) and between 4th weeks and 3th months (p=0.042 and p=0.044). Significant improvement was found in Group 1 compared to Group 3 in the changes between pre-treatment and 4th weeks (p=0.047 and p=0.045, respectively), between pre-treatment and 3th months (p=0.012 and p=0.009), and between 4th weeks and 3th months (p=0.024 and p=0.001) with respect to the **arm score**, between pre-treatment and 4th weeks (p=0.043 and p=0.039, respectively), between pre-treatment and 3th months (p=0.015, p=0.008), and between 4th weeks and 3th months (p=0.034 and p=0.029) with respect to the **hand score**, but significant improvement was seen only in terms of changes between pre-treatment and 4th weeks (p= 0.024 and p=0.036, respectively), and between pre-treatment and 3th months (p=0.015, p=0.035) with respect to the **leg and foot scores** in Group 1 compared to Group 3 (Table 2A, Table 2B).

TABLE 2A: Comparison results of the change among the pre-treatment, 4th weeks and 3th months controls.

	Pre-treatment-4th weeks		Pre-treatment-3th months		4th weeks- 3th months	
Evaluated parameters	**Mean±SD**	**p value**	**Mean±SD**	**p value**	**Mean±SD**	**p value**
NIHSS (0-42)						
Group 1	3.90±3.55		4.81±2.08		1.36±1.62	
Group 2	2.45±1.91	**0.030**	3.10±2.68	**0.007**	0.20±0.42	**0.013**
Group 3	1.76±1.36		2.21±1.52		0.23±0.43	
Brunstroom (1-6)						
Hand						
Group 1	1.54±1.43		2.37±1.34		1.22±0.99	
Group 2	0.40±0.70	**0.042**	1.17±0.74	**0.029**	0.12±1.00	**0.023**
Group 3	0.56±1.09		0.83±1.33		0.08±0.28	
Upper limb						
Group 1	1.54±1.36		2.63±1.20		1.19±0.83	
Group 2	0.40±0.87	**0.047**	1.22±1.18	**0.001**	0.86±1.06	**0.015**
Group 3	0.36±0.77		0.66±1.07		0.16±0.38	
Lower limb						
Group 1	1.81±1.16		2.63±1.43		0.81±0.87	
Group 2	1.80±1.03	**0.089**	2.12±1.45	**0.039**	0.37±0.51	**0.073**
Group 3	1.00±0.81		1.16±1.11		0.25±0.45	

mean±SD: mean±standard deviation; NIHSS: National Institutes of Health Stroke Scale.

TABLE 2B: Comparison results of the change among the pre-treatment, 4th weeks and 3th months controls.

	Pre-treatment-4th weeks		Pre-treatment-3th months		4th weeks- 3th months	
Evaluated parameters	**Mean±SD**	**p value**	**Mean±SD**	**p value**	**Mean±SD**	**p value**
FIM(18-126)						
Total						
Group 1	18.36±10.44		35.54±18.16		17.18±11.72	
Group 2	20.10±13.64	0.286	36.75±15.67	0.291	17.12±8.54	0.154
Group 3	13.23±8.24		27.00±15.98		9.83±13.32	
Motor						
Group 1	26.36±7.63		41.63±16.13		16.27±12.2	
Group 2	17.60±12.58	0.487	33.00±15.25	0.052	16.12±9.77	0.298
Group 3	13.00±8.54		27.00±16.09		9.08±13.39	
Cognitive						
Group 1	3.00±4.09		3.00±4.09		1.00±0.0	
Group 2	2.50±4.92	0.188	3.15±4.92	0.279	1.00±2.13	0.263
Group 3	0.23±0.83		1.00±2.00		0.75±1.42	
CMSA(0-42)						
Posture						
Group 1	2.27±0.78		2.82±0.78		1.05±0.52	
Group 2	1.20±1.19	**0.016**	1.20±0.92	**0.024**	0.30±0.92	**0.038**
Group 3	1.13±0.92		1.08±1.08		0.23±0.57	
Arm						
Group 1	1.45±1.43		2.45±1.29		1.00±0.77	
Group 2	0.80±1.10	**0.046**	1.07±1.40	**0.009**	0.22±0.74	**0.001**
Group 3	0.74±0.80		0.83±0.82		0.0±0.0	
Hand						
Group 1	1.09±1.13		2.19±1.22		1.00±1.00	
Group 2	0.30±0.48	**0.034**	1.02±0.83	**0.047**	0.27±0.92	**0.007**
Group 3	0.29±0.75		1.00±1.04		0.23±0.49	
Leg						
Group 1	2.27±1.00		3.00±1.26		0.72±0.90	
Group 2	2.00±1.33	**0.024**	2.50±1.60	**0.015**	0.37±0.51	0.106
Group 3	1.07±0.86		1.41±0.90		0.25±0.45	
Foot						
Group 1	1.72±1.19		2.25±1.50		0.72±1.00	
Group 2	1.40±1.42	**0.036**	1.75±1.48	**0.035**	0.37±0.74	0.137
Group 3	0.69±0.94		1.08±0.90		0.33±0.49	

mean±SD: mean±standard deviation; FIM: Functional Independence Measeure; CMSA: Chedoke-McMaster Stroke Assessment.

DISCUSSION

Stroke is a major health problem that affects a large part of the community with high incidence and mortality rates, and causes disability in survivors.[8] Motor impairment is commonly seen after stroke, and the critical factor is inability of the patient to live independently. Improvement occurs through neurobiological mechanisms such as cell formation, functional plasticity, axonal sprouting and synaptogenesis from the first few days after stroke with the highest levels of improvement during the early period.[9]

Prolonged bed rest adversely affects many systems such as musculoskeletal system, cardiovascular system, respiratory system and immune system, leading to development of immobilization-associated

complications such as pneumonia, atelectasis, deep vein thrombosis, pulmonary embolism, immunosuppression, pressure sore and muscle atrophy more frequently and earlier. Therefore physical activities such as sitting on the bed, standing and walking are recommended from the early period after stroke, and believed to accelerate recovery.[3] The early period after stroke is also the most appropriate period for brain plasticity and remodeling.

Despite all these potential benefits of early rehabilitation, there are suggestions that enlargement of the penumbra area during the early exercise and mobilization after stroke as a result of increased bleeding volume in patients with intracerebral hemorrhage and reduction of blood supply in the middle cerebral artery associated with mobilization in those with ischemic lesions. Early mobilization may also lead to falls and associated injuries in patients. Because of such concerns, use of rehabilitation during the very early period is usually uncommon in patients with stroke.[10,11] So the questions of how the frequency and duration of out-of-bed mobilization should be and when and at which dose rehabilitation should be initiated after stroke are still unanswered.[4]

There are different recommendations in the guidelines with respect to timing and intensity of mobilization after stroke, and indefinitive and inconclusive statements such as 'early mobilization is recommended for less affected patients', 'patients must be mobilized preferentially within 24 to 48 hours after stroke'. The effectiveness of such clinical guidelines depends upon the healthcare professionals who follow the recommended practices.[4]

We therefore included in our study patients who were admitted during the period between days 1 and 21 after stroke to find an answer to the question "early rehabilitation, how early?". In this study, the effect of the time of initiation of rehabilitation after ischemic stroke on prognosis was investigated. Forty two patients who had ischemic stroke were divided into 3 groups according to the times of initiation of rehabilitation after the ischemic stroke i.e during the first 9 days, between days 10 and 14 and between days 15 and 21, and their functionalities were assessed at baseline, 4th weeks and 3th months by NIHSS, Brunstroom, FIM and CMSA. The study demonstrated that the functional outcome in the group in which rehabilitation was initiated within the first 9 days after stroke was better in the follow-ups at 4th weeks and 3th months, and rehabilitation initiated within the first 9 days after stroke was more beneficial.

In the literature, the largest study on early rehabilitation after stroke is the AVERT (A Very Early Rehabilitation Trial). This study suggests that early mobilization from the first 24 hours after stroke is safe and beneficial.[10] The hypothesis of the AVERT study was that more intense and early out-of-bed activity after stroke will improve the functional outcome at 3. month, will reduce complications associated with immobility, will accelerate walking without increasing neurological complications, will result in improved quality of life at month 12, and is cost-effective.

The phase 2 AVERT study conducted by Bernhardt et al. compared very early treatment and standard care in 71 acute stroke patients, and it was found that early mobilization initiated within 24 hours after the onset of the symptoms is safe and feasible. No significant difference was found between the two groups i.e the first 24 hours and thereafter, in terms of death and early neurological deterioration.[12] There was no significant difference in terms of the number, type and severity of the complications seen at the 3-month follow-up. It was underlined that studies with longer follow-up are warranted to see the efficacy of early mobilization in reduction of long-term complications.[13]

On the other hand, the phase 3 AVERT study is a multi-center, international, randomized, controlled study conducted at 56 stroke units to resolve the controversies about early mobilization of stroke patients, in which 2104 subjects aged above 18 years who had had their first stroke and admitted to hospital within the 24 hours and the study group received earlier (within the 24 hours), more intensive and longer rehabilitation. When the results were examined, it was seen that while the case fatality rate at month 3 was higher in the very early mobilization group, there was no significant difference between the groups. No difference was found between the results of patients who received and did not receive recombinant tissue plas-

minogen activator therapy. Complications associated with immobility were low in both groups (i.e those mobilized within the first 24 hours and those mobilized after the first 24 hours). No difference was found between the 2 groups in terms of improvement of walking. These results were attributed to current highly advanced patient care in stroke units and to the fact that the patient mobilized at the latest time point even in the group that received the routine treatment was mobilized within the first 48 hours.[9]

In a randomized, controlled study conducted by Poletto et al. on 37 ischemic stroke patients (mean age: 65 years, mean NIHSS score: 11), the patients were divided into 2 groups as those who were early and frequently mobilized and those who were given the standard treatment and their functionality by the NIHSS scores, Modified Rankin Scale ve Barthel Index, complications developed, and fall and mortality rates during 3 months. The complication rates and mortality were similar between the two groups, and it was reported that rehabilitation containing frequent mobilization from the early period can be safely applied.[14]

The above study and the other studies in the literature show that initiation of treatment during the early period, e.g. day 20-30, has a significant effect on functional gain as in our study.[5,14-16] However, in our study, since we sought an answer to the question "early but how early", the patients were assessed in shorter periods (such as the first 9 days, 15 days and 21 days), and it was seen that the first 9-day period is the opportunity window, and a difference of even 5 days thereafter may have a negative effect on functionality.

Another important aspect of our study is that a multi-faceted and intensive rehabilitation program that contained training of family members and a social services specialist was adopted as the early rehabilitation program rather than applying a treatment consisting of only conventionral methods only.

In the literature, PNF and cognitive therapeutic exercises as well as exercises for ROM, mobilization and strengthening have been reported as methods applied after stroke; however the efficacy and safety of these methods have not been demonstrated systematically. The guidelines state the rehabilitation program for stroke only as 'patients must be mobilized as frequently as possible'.[17]

The early period after stroke is the period during which the brain is most responsive to rehabilitation which decreases over time. Studies showed that compared to late rehabilitation, early rehabilitation increases neural plasticity and cortical reorganization and significantly reduces infarction volume.[18] However, there are also studies in the literature which reported that intensive rehabilitation especially during the early period may be dangerous since it increases bleeding risk in patients with intracerebral hemorrhage and blood supply in patients with ischemic stroke.[19-21]

There are limited studies that investigated the potential effect of the duration and frequency of treatment on outcomes in humans and animals. An investigation conducted by Bell et al. on mice affected by stroke demonstrated that training with high doses twice a day had a better effect on outcomes compared to low doses once a day.[5] In one or two animal studies, it was reported that moderate exercise initiated at the 24th-48th hour after stroke reduces the lesion volume and protects the perilesional tissue from oxidative damage and inflammation, and that there was a linear relationship between post-stroke vertical activity amount and good functional outcome.[16]

In AVERT study; the emphasis of very early mobilizitation was to assist the patient to be upright and out of bed (sitting or standing as able) at least twice per day; in addition to their usual care, 6 days per week.[13] Another multicenter randomized, controlled study, Active Mobility Very Early After Stroke, compared 20 min per day of "soft" physical therapy (PT) (passive range-of-motion exercises aimed at preventing immobility-related complications) with soft PT plus 45 min of active intensive exercises, both commencing within 72 h of stroke. This trial found no difference in motor impairment at 90 days, as measured by the Fugl-Meyer Motor Scale.[22] In a study, conducted by Chippala and Sharma exercise duration: 5-30 minutes, frequency: minimum 2 times per day, Bernhardt et al. approximately 31 minutes, frequency: at least twice per day,

6 days per week reported as.[9,23] In our study; all patients received a multi-faceted and intensive rehabilitation program 90-120 minutes/per day, 5 days a week.

The main limitation of this trial is the small sample, which reduces the statistical power needed to demonstrate the effect of the intervention. Due to a slow enrollment, fewer patients than anticipated were available for analysis. In addition, the duration and intensity of out-of-bed activities that patients had outside of the rehabilitation period may have also affected the results. Taking these limitations into account, our results may help guide the development of more effective acute stroke rehabilitation.

In the light of the information obtained from these studies, the information about what is meant with early mobilization and intensive rehabilitation after stroke, and about the optimal duration, dose and intensivity for this was obtained.

We believe that our study provides information to clarify this issue. While our rehabilitation program was intensive, it was applied in several divided phases with resting periods during the entire day without causing fatigue to the patient. No complications were seen in our patients, and significant improvements were observed in those who received this intensive program. This result suggests us that an early, multi-faceted and intensive rehabilitation program will be effective when applied in a controlled manner on patient basis.

CONCLUSION

In this study, better functional outcome was observed at week 4 and month 3 in the group in whom rehabilitation was initiated within the first 9 days after stroke, and it was found that rehabilitation initiated within the first 9 days after stroke was more beneficial. Although many studies recommend initiation of rehabilitation during the early period after stroke, the timing of initiation is not specified. In this study the patients were assessed in shorter periods (such as the first 9 days, 9-15 days and 15-21 days), and it was seen that the first 9-day period is the opportunity window, and a difference of even 5 days thereafter may have a negative effect on functionality. A multifaceted and intensive rehabilitation program applied during the early period after stroke, especially during the first 9 days, is effective and safe when applied in a controlled manner on patient basis.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

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