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Original Article

The impact of lesion location on medication self-management ability in patients with cerebrovascular disease

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ABSTRACT

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Objective: To elucidate the impact of cerebrovascular lesion location on patients' ability to manage their own medications, we retrospectively investigated the differences in ability between the left hemisphere damage group (Group L) and the right hemisphere damage group (Group R).

Methods: In patients with cerebrovascular disease who were discharged from the Kaifukuki rehabilitation ward of our hospital between October 2011 and March 2013 and between January 2016 and December 2017, Group L and Group R were compared.

Results: The study subjects were 282 patients, and both Group L and Group R had 141 patients each. The length of time required for achieving medication self-management was longer in Group L than in Group R ($p = 0.02$), showing a significant difference.

Conclusion: The delay in achieving medication self-management in Group L was considered due to impairment of the dominant arm by right hemiplegia, which, unlike in Group R, hindered the dexterity required for taking medications. In order for patients with cerebrovascular disease to become capable of managing their own medications, it is considered essential to assist in developing medication support plans according to lesion location.

Key words: medication self-management, cerebrovascular disease, cerebrovascular lesion location, Kaifukuki rehabilitation ward

Introduction

The cerebrum is broadly divided into the right and left hemispheres, and cerebral vascular territories are separated between the hemispheres. Cerebrovascular disease damages each hemisphere individually. Depending on the location of the lesion in the brain, patients exhibit various symptoms involving visual perception[1], body[2], and cognitive function[3], as well as movement disorders[4], and they also experience different outcomes of subsequent rehabilitation. Patients with right hemisphere damage have been reported to have poor rehabilitation outcomes[5, 6], and psychiatric symptoms such as attention impairment and affective flattening are presumed to be one of the causes. Problems associated with rehabilitation in patients with right hemisphere damage are considered not due to clinical symptoms of the damage, but rather to characteristic behavioral reactions caused by the clinical symptoms, such as inattention, lowered insight, disorders of emotion/motivation, and communication disorders. While differences in symptoms and roles between the hemispheres are becoming clear, there is no report on the impact of lesion location in the brain on patients' medication-taking behaviors. Such behaviors include adherence, obtainment of medication knowledge, and self-management ability. In this study, we aimed to elucidate the length of time required from the onset of cerebrovascular damage to the introduction of

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medication self-management for each lesion location and factors influencing the patients' ability to manage their own medications by retrospectively investigating differences in the ability between the left hemisphere damage group (Group L) and the right hemisphere damage group (Group R). Using the length of time required for medication self-management presumably resulting from differences between Group L and Group R as clinical indicators, we also analyzed factors influencing the time period from the onset date of cerebrovascular damage to the introduction of medication self-management.

Methods

1. Study patients

In the Kaifukuki rehabilitation ward of Showa University Fujigaoka Rehabilitation Hospital (hereafter "our hospital"), we retrospectively investigated those patients with cerebrovascular disease (cerebral infarction, cerebral hemorrhage) who were discharged between October 2011 and March 2013 and between January 2016 and December 2017. Among the patients who had achieved medication self-management, those who subsequently had medication errors, such as incorrect medication dosage and usage, during hospitalization were excluded from the study.

This study was conducted after review and approval by the Institutional Review Board of Showa University Fujigaoka Hospital (Approval No: F2017C74).

2. Investigation items

We investigated the following data from the patients' medical records: patient demographics (sex, age on admission), medication-related factors (the number of medications taken on admission, number of medications taken per day, number of as-needed medications taken on admission, number of topical medications used on admission, use/nonuse of single-dose packaging, achievement/non-achievement of medication self-management at discharge, time period from the onset date of cerebrovascular damage to the introduction of medication self-management), and disease-related factors (the disease, time period from the onset date of cerebrovascular damage to admission to our hospital and presence/absence of dementia, aphasia, dysphagia, dyslalia, or hemiplegia). Additionally, using the functional independence measure (FIM) for the evaluation of activities of daily living (ADL), the patients' scores on each FIM item on admission were investigated. The patients' admission FIM scores were given by nurses or physical therapists who worked in the Kaifukuki rehabilitation ward. During the investigation period, data were collected from paper medical records from October 2011 to March 2013 and from electronic medical records from January 2016 to December 2017, but there were no differences in the patients' characteristics or rehabilitation program.

3. Criteria for the introduction of medication self-management

The introduction of medication self-management for inpatients in our hospital was indicated for patients who had achieved all the eight items necessary for medication-taking behaviors shown in Figure 1 and were deemed capable of safely self-administering medications after discussion with physicians, pharmacists, nurses, and occupational therapists. Medication self-management in this study was defined as: "being able to take the correct medications as prescribed by the physician, at the right dose and at the right time, in the absence of the caregiver." Patients failing to do so were defined as noncompliant.

4. Comparison between Group L and Group R

Univariate analysis was performed to compare the patient demographic factors, medication-related factors, disease-related factors, and scores on each FIM item between Group L and Group R.

☐ Do you know the purpose of the drugs?	YES / NO
☐ Can you count the number of drugs?	YES / NO
☐ Do you know when to take the drugs?	YES / NO
☐ Can you remember when you took the drugs?	YES / NO
☐ Can you bring the drugs to your mouth?	YES / NO
☐ Can you swallow the drugs?	YES / NO
☐ Could you manage your daily medication by yourself?	YES / NO
☐ Could you continue taking drugs?	YES / NO

Figure 1. Eight items that are necessary to introduce medication self-management.

5. Analysis of factors influencing medication self-management in Group L and Group R

In Group L and Group R, subjects were divided into self-management and non-self-management within each group, and univariate analysis was performed. In consideration of multicollinearity, the FIM item was defined as the total score of the admission FIM motor items and the admission FIM cognitive items, and each FIM item was not used as a factor. Subsequently, logistic regression analysis was performed using achievement/non-achievement of medication self-management as an objective variable and factors with significant differences noted by univariate analysis as explanatory variables. Stepwise backward selection was used for the selection of explanatory variables. The validity of the regression model was evaluated by the lack-of-fit (LOF) test and the area under the receiver operating characteristic (ROC) curve, which is an indicator of the relationship between estimated sensitivity and specificity.

6. Analysis of factors influencing the time period from the onset date of cerebrovascular damage to the introduction of medication self-management

Multiple regression analysis was performed using the time period from the onset date of cerebrovascular damage to the introduction of medication self-management as an objective variable and patient demographic factors, medication-related factors, disease-related factors, and FIM item scores as explanatory variables. In consideration of multicollinearity, aphasia and left/right hemiplegia were excluded from the factors, and the FIM item was defined as the total score of admission FIM motor items and admission FIM cognitive items. Stepwise backward selection was used for the selection of explanatory variables. In addition, the variance inflation factor (VIF) was calculated to evaluate the multicollinearity between the factors.

7. Statistical analysis

For comparisons between the two groups, the Shapiro-Wilk W test was performed for continuous variables. If data followed a normal distribution, the *t*-test was used; otherwise, the Wilcoxon rank-sum test was used. Among categorical variables, the chi-squared test was used for the presence/absence of hemiplegia, Fisher's exact test for other factors, and the Wilcoxon rank-sum test for the comparison of FIM item scores. The significance level was $p < 0.05$ for all tests.

The statistical software used was JMP® Pro 14 (SAS Institute Inc., Cary, NC, USA).

Results

1. Patient background

The study subjects were 282 patients with a mean age of 69.9 ± 12.0 years, consisting of 186 men and 96 women. Of these, both Group L and Group R had 141 subjects each (Table 1).

Table 1. Characteristics of the patients: host-related factors ($n = 282$).

Variable	*n* (%) or Mean ± SD
Age (years)	69.9 ± 12.0
Sex	
Male	186 (66.0)
Female	96 (34.0)
Diagnosis	
Cerebral infarction	189 (67.0)
Cerebral hemorrhage	93 (33.0)

2. Comparison between Group L and Group R

As a result of the Shapiro-Wilk W test, it was confirmed that the data did not follow a normal distribution for any of the investigation items. In the comparison of patient background on admission between the self-management and the non-self-management groups, significant differences were observed in age, time period from the onset date of cerebrovascular damage to the introduction of medication self-management, presence/absence of aphasia, and presence/absence of left/right hemiplegia. Medication self-management was introduced to 50 patients in Group L and 56 patients in Group R (Table 2).

3. Analysis of factors influencing medication self-management in Group L and Group R

Factors significantly different between the self-management and non-self-management groups in Group L were age, number of medications taken per day, number of as-needed medications taken on admission, number of topical medications used on admission, presence/absence of dysphagia, FIM motor items, and FIM cognitive items, whereas those in Group R were age, time period from the onset date of cerebrovascular damage to admission to our hospital, number of as-needed medications taken on admission, number of topical medications used on admission, presence/absence of dementia and dysphagia, FIM motor items, and FIM cognitive items (Table 3). Results of the logistic regression analysis showed that factors associated with the introduction of medication self-management in patients with cerebrovascular disease were age and FIM cognitive items in Group L and age, FIM motor items, and FIM cognitive items in Group R (Table 4).

Evaluation of the validity of the regression model showed that the *p*-value by LOF was 0.78 in Group L and 0.99 in Group R; as both were greater than 0.05, the estimated model was confirmed to be appropriate. The values of the area under the ROC curve were 0.84 in Group L and 0.91 in Group R; as both were close to 1, the model was confirmed to be highly accurate.

Table 2. Comparison of variables between Group L and Group R.

Variable		Group L (n=141)	Group R (n=141)	p Value
		n, Mean ± SD	n, Mean ± SD	
Characteristics of the patients	Age (years)	68.3±12.1	71.5±11.6	0.02*
	Sex: Male/Female	98/43	88/53	0.26
Medication-related items	Number of drugs	5.9±3.4	5.7±3.5	0.43
	Number of doses per day	3.5±2.0	3.5±1.9	0.93
	Number of doses of medicine to be taken only once	0.6±0.9	0.7±0.9	0.42
	Number of external medicines	0.7±1.2	0.8±1.3	0.42
	One-dose packages	94	91	0.80
	SM at discharge	50	56	0.54
	Post-onset introduction of medication self-management day (days)	80.8±44.1	65.6±45.9	0.02*
Disease-related items	Post-onset rehabilitation hospital day (days)	28.1±17.2	27.9±16.0	0.87
	Dementia	7	15	0.12
	Aphasia	65	12	<0.01*
	Dysphagia	39	44	0.60
	Dysarthria	59	58	1.00
	Hemiplegia: left/right	6/110	114/8	<0.01*
FIM items	Eating	4.9±2.1	5.2±1.9	0.43
	Grooming	4.4±2.3	4.5±2.0	0.98
	Bathing	3.6±2.1	3.5±2.1	0.75
	Dressing upper body	3.8±2.1	3.7±2.0	0.79
	Dressing lower body	3.6±2.1	3.5±2.1	0.68
	Toileting	4.0±2.3	4.1±2.3	0.55
	Bladder	4.8±2.6	4.7±2.5	0.84
	Bowel	4.6±2.5	4.5±2.4	0.52
	Bed chair transfer	4.2±2.1	4.1±1.9	0.84
	Toilet transfer	4.1±2.1	4.0±2.0	0.77
	Tub shower transfer	3.6±1.9	3.4±1.9	0.37
	Walking/wheelchair mobility	3.5±2.3	3.3±2.3	0.71
	Stairs	1.8±1.7	1.9±1.8	0.62
	Comprehension	5.2±2.1	5.4±1.9	0.61
	Expression	5.1±2.1	5.5±1.9	0.19
	Social interaction	5.4±2.3	5.7±2.0	0.49
	Problem-solving	4.7±2.3	5.0±2.1	0.47
	Memory	4.9±2.2	5.0±2.1	0.75
	Motor	50.9±24.4	50.5±23.7	0.89
	Cognitive	25.2±10.3	26.5±9.1	0.47
	Total	75.8±32.6	77.0±31.0	0.86

SM, medication self-management group.
Significant difference, *p Value < 0.05.

4. Analysis of factors influencing the time period from the onset date of cerebrovascular damage to the introduction of medication self-management

As a result of the multiple regression analysis, the time period from the onset date of cerebrovascular damage to admission to our hospital, use/nonuse of single-dose packaging, and FIM motor item scores were extracted. The standard regression coefficients were 56.62, 11.18, and −49.12, respectively, showing that the time period from the onset date of cerebrovascular damage to admission to our hospital had the greatest influence. VIF was calculated to be ≤ 2 for each factor, confirming no influence of multicollinearity (Table 5).

Table 3. Comparison of variables between medication self-management and non-medication self-management groups.

Variable		Group L			Group R		
		SM (n=50)	non-SM (n=91)	p Value	SM (n=56)	non-SM (n=85)	p Value
		n, Mean ± SD	n, Mean ± SD		n, Mean ± SD	n, Mean ± SD	
Characteristics of the patients	Age (years)	63.2±12.2	71.1±11.1	<0.01*	66.2±11.6	74.9±10.3	<0.01*
	Sex: Male/Female	39/11	59/32	0.13	37/19	51/34	0.48
Medication-related items	Number of drugs	5.4±3.3	6.3±3.4	0.11	5.4±3.4	6.0±3.6	0.25
	Number of doses per day	2.9±2.1	3.9±1.9	<0.01*	3.1±1.6	3.7±2.1	0.07
	Number of doses of medicine to be taken only once	0.5±0.9	0.7±0.8	0.04*	0.5±0.7	0.9±1.0	0.04*
	Number of external medicines	0.4±0.9	0.9±1.3	<0.01*	0.5±1.0	1.0±1.4	0.02*
	One-dose packages	36	58	0.36	36	55	1.00
Disease-related items	Post-onset rehabilitation hospital day (days)	24.5±14.3	30.1±18.3	0.06	22.9±9.9	31.2±18.3	<0.01*
	Dementia	0	7	0.05	2	13	0.03*
	Aphasia	20	45	0.30	3	9	0.36
	Dysphagia	7	32	<0.01*	11	33	0.02*
	Dysarthria	20	39	0.86	28	30	0.12
	Hemiplegia: left/right	1	5	0.39	43	71	0.60
FIM items	Motor	63.6±17.1	43.8±25.1	<0.01*	69.4±15.7	38.1±19.4	<0.01*
	Cognitive	31.2±6.3	21.9±10.7	<0.01*	32.8±3.4	22.4±9.3	<0.01*

SM, medication self-management group.
Significant difference, *p Value < 0.05.

Table 4. Results of stepwise multiple regression analyses.

Group L (n＝141)

Variable	Regression coefficient	Odds ratio	95% confidence interval	p Value
Age (years)	−0.08	0.92	0.89–0.96	0.04
Cognitive FIM	0.15	1.16	1.09–1.24	<0.01
Intercept	0.50			0.05

LOF: 0.78.
Area under ROC curve: 0.84.

Group R (n＝141)

Variable	Regression coefficient	Odds ratio	95% confidence interval	p Value
Age (years)	−0.05	0.95	0.91–1.00	0.03
Motor FIM	0.07	1.07	1.04–1.11	<0.01
Cognitive FIM	0.15	1.16	1.03–1.31	0.02
Intercept	−5.26			0.05

LOF: 0.99.
Area under ROC curve: 0.91.

Table 5. Multiple regression analysis for post-onset introduction of medication self-management day.

Variable	Parameter estimate	Standard error	t Value	p Value	VIF	Standardized estimate	95% confidence interval
Post-onset rehabilitation hospital day (days)	1.22	0.25	4.91	<0.01	1.03	56.62	33.76–79.47
One-dose packages	11.18	3.35	3.34	<0.01	1.13	11.18	4.54–17.81
Motor FIM	−1.42	0.19	−7.55	<0.01	1.12	−49.12	−62.02–−36.21
Intercept	134.87	14.91	9.05	<0.01	—	68.79	62.50–75.07

VIF, variance inflation factor.

Discussion

In this study, we used data on patients with cerebrovascular disease, including FIM items and medication-related information on admission, and examined differences in the medication self-management ability between Group L and Group R.

In the comparison between Group L and Group R, significant differences were observed in the "presence/absence of aphasia," "presence/absence of hemiplegia," and "time period from the onset date of cerebrovascular damage to the introduction of medication self-management." It was confirmed that medication self-management was introduced to Group R more than 2 weeks earlier on average than to Group L. Previous studies have indicated that patients in Group R have poor adaptation in rehabilitation after cerebrovascular damage despite the advantages of being less likely to exhibit aphasia and having the dominant hand unaffected [5, 6]. However, in this study, medication self-management was achieved earlier in Group R than in Group L. This may be associated with the presence/absence of aphasia and hemiplegia. Regarding aphasia, there is a report on medication guidance for patients with the disorder. Horikawa et al. pointed out that because understanding medication guidance depends on the ability to understand language, it takes time for aphasia patients to learn its contents and establish a relationship with pharmacists, which consequently shortens the length of time spent on medication guidance for aphasia patients compared to other patients[7]. Medication guidance for aphasia patients requires collaboration with speech-language-hearing therapists, and pharmacists need to establish relationships with patients and provide appropriate medication guidance after understanding the patients' language disorder.

In addition, many patients in Group L have impaired right-hand performance due to right hemiplegia, which may hinder the dexterity required for taking medications, such as "removal of medications." In an investigation that conducted a handedness test in

Japanese subjects, 90.5% of the subjects were reported to be right-handed[8], indicating a high likelihood of impaired dominant hand function in Group L. Therefore, the length of time required for a switch in handedness in occupational therapy was considered to play a part in the delay in introducing medication self-management.

The common factors associated with the introduction of medication self-management in Group R and Group L were age and FIM cognitive score. The FIM motor score was also identified in Group R. In a preceding study on the introduction of medication self-management in stroke patients, age, FIM motor items (walk/wheelchair), and FIM cognitive items (memory) were reported to be factors influencing the introduction of medication self-management[9], which are similar to our findings. However, the present study confirmed that "FIM motor items" affect Group R but have little association with Group L. This is because, since patients in Group L suffer impairment in the right arm, which is dominant for most patients, the inability to maintain dexterity presumably led to greater dependence on cognitive skills than motor skills. On the other hand, patients in Group R retain their dominant hand function and thus, much of their motor function remains along with their cognitive function. This was suggested to be a factor leading to the introduction of medication self-management.

Factors influencing the length of time required for achieving medication self-management were "time period from the onset date of cerebrovascular damage to admission to our hospital," "single-dose packaging," and "FIM motor items." "Time period from the onset date of cerebrovascular damage to hospital admission" has been reported as a factor contributing to a decline in the rate of successful return to home and prolongation of hospital stay, and similar results were also obtained in this study. This may be because the severity of the disease requiring prolongation of acute treatment and delayed patient transfer to the Kaifukuki rehabilitation ward delay the initiation of intensive rehabilitation, consequently delaying an elevation in ADL.

"Single-dose packaging" was also a factor contributing to the delayed introduction of medication self-management. This may be due to the background leading to the use of single-dose packaging or the condition of the packaging itself. There is a report claiming that patients' awareness of what they are taking affects their medication-taking behaviors[10]. Patients may not be able to recognize the types of medications they are taking due to the single-dose packaging, which can be a factor hindering medication compliance. Single-dose packaging is a useful method for patients who have trouble removing medications from the packages due to paralysis and other conditions, but needlessly suggesting its use should be avoided. Instead, it would be worth identifying patients who truly need single-dose packaging and working with them to solve the problem while providing appropriate information.

One limitation of this study is that there was a significant difference in age in the patient background between Group L and Group R. Age has been reported to be a negative factor in the achievement of medication self-management in stroke patients[9]. In this study, the mean age was higher in Group R than in Group L, and thus data on the non-self-management in Group R unavoidably affected the analysis. Additionally, as this study was conducted retrospectively, patients' dominant hand could not be identified from their medical records. Since the discussion in this study was based on the report that "a large proportion of the population are right-handed," a prospective investigation encompassing patients' handedness is considered necessary. Although this study was a comparison between Group L and Group R, further investigations and analyses are needed taking into consideration the impact of disease and severity.

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