ORIGINAL

Factors associated with changes over time in medication-taking behavior up to 12 months after initial mild cerebral infarction onset

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Abstract : Purpose : The aim of this study was to clarify the changes in medication-taking behavior and related factors over time in patients with initial mild cerebral infarction up to 12 months after onset. Methods : Thirty-one patients with initial mild cerebral infarction were surveyed a total of four times : on admission to hospital, 3 months after onset, 6 months after onset, and 12 months after onset. Patients were surveyed regarding medication compliance, awareness of taking medication, perceived behavioral control, lifestyle risk factors, and subjective norms. Results : Medication compliance improved over time from the time of admission, but no changes were seen in awareness of taking medication. A cluster analysis based on changes in medication compliance over time revealed a "Persistently high compliance group" and a "Persistently low compliance group" for medication compliance. The health locus of control in the "Persistently high compliance group" was perceived as the result of chance and fate. Conclusions : Assessing the current state of medication compliance and the health locus of control during hospitalization permitted an understanding of patient characteristics, and indicated a need for recurrence prevention education and medication guidance tailored to each patient's cognitive and behavioral characteristics. J. Med. Invest. 64 : 85-95, February, 2017

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INTRODUCTION

The recurrence rate for cerebral infarction is high at 10% within the first year, 30% within 5 years, and 50% in 10 years (1), with patients experiencing a marked decline in quality of life after each relapse. The Japanese Guidelines for the Management of Stroke (2) therefore recommend the management of risk factors and the use of anti-thrombotic agents.

Major factors responsible for cerebral infarction relapse include dehydration, smoking, and discontinuing medication (3). In particular, failure to adhere to anti-thrombotic medication, which requires continuous strict supervision while monitoring coagulation function, ranges from 12% to 40% (4, 5). Reasons for non-adherence include a lack of understanding of the medication's beneficial effects as well as side effects in the form of increased bleeding tendency, financial burden imposed by high drug prices, and inadequate access to medical care (5). Moreover, 18% of post-cerebral infarction patients are reportedly unable to undergo regular medical examinations (5). Meanwhile, issues among health care personnel include inadequate explanation and guidance on the importance of strictly managing both the underlying disease and prescribed medication in order to prevent cerebral infarction recurrence (6). The prevention of cerebral infarction recurrence can therefore be described as an issue of adherence on the part of both the patient and medical personnel.

In terms of patient education by nurses, approximately 70% of hospitals and clinics in Japan provide such education to cerebral infarction patients at discharge but only 10% have a systematic education program in place (7). A similar situation exists outside Japan, with one study highlighting the rigid and overly intensive nature of patient education to prevent stroke recurrence at the expense of a personalized approach (8). The impact of risk factors varies according to cerebral infarction type (9), and cerebral infarction patients often have multiple risk factors, making it difficult to ensure adequate management after their release from hospital (10).

All of these issues point to the need for practical education on prevention of cerebral infarction recurrence that takes into account how to manage individual risk factors and mental and physical condition while enabling patients to adhere to their regimen of anti-thrombotic medication after discharge.

The relationship between patients and health care professionals has changed considerably in recent years, with a move from the concept of compliance implying the patient's abidance with the health care provider's instructions towards a concept of adherence whereby the patient consents and agrees to a treatment plan proposed by the health care provider (11). Many of the studies on medication-taking behavior monitored by nurses over the past decade in Japan have targeted psychiatric patients. Meanwhile, studies are also beginning to emerge on medication-taking behavior among patients with hypertension (12) and those receiving home medical care (13). Moreover, some of the literature on cross-sectional studies on adherence awareness of medication-taking behavior with the objective of preventing recurrence has focused on patients with chronic heart failure (14) and those undergoing coronary stent surgery (15). A cross-sectional study on medication-taking behavior in stroke patients showed that their lifestyle habits, attitude toward medication, and whether or not their medication was explained

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to them were all associated factors (16), while a study on stroke outpatients qualitatively demonstrated medication-taking behavior patterns as well as the value and assessment of taking medication (17). All of these studies targeted chronic-stage stroke patients without clarifying how medication-taking behavior changes in acute-stage cerebral infarction patients.

Accordingly, there is a need for a longitudinal study identifying the factors that determine how attitudes and behaviors regarding taking medication change over time from immediately after cerebral infarction onset in order to obtain insights into education on prevention of cerebral infarction recurrence.

OBJECTIVE

The objective of the present study was to identify the changes over time in medication-taking behavior from initial mild cerebral infarction onset until 12 months later, and the factors associated with these changes.

CONCEPTUAL FRAMEWORK OF THE STUDY

The conceptual framework of this study shown in Figure 1 is based on the theory of planned behavior (18). According to this theory, human behavior typically involves an intention to act which affects the individual's attitude, subjective norms, and level of behavioral control towards that action (19). Attitude is determined by a person's expectations, value, and assessment of the action's outcome. Subjective norms are decided by the person's awareness of the expectations of those close to them, and their motivation to meet those expectations. Furthermore, the level of behavioral control is determined by a person's awareness of factors that encourage and inhibit actions, and awareness of one's own ability to control those factors using the necessary resources and opportunities at their disposal.

Managing patient risk factors and maintaining adherence to anti-thrombotic medication are essential in the prevention of cerebral infarction recurrence. The present study investigated medication-taking behavior as a way to prevent cerebral infarction recurrence based on the theory of planned behavior. Medication-taking behavior was defined as the intention to take and attitude toward taking anti-thrombotic medication or, in other words, both the patient's awareness and the actual behavior of taking medication. The level of behavioral control towards continued adherence as well as subjective norms in the form of education on preventing cerebral infarction recurrence by health care professionals and the patient's post-discharge care facility were deemed to be related to ensuring continued adherence. To identify the changes over time in medication-taking behavior from cerebral infarction onset and the factors associated with these changes, our conceptual framework also considered the time elapsed since cerebral infarction onset and the patient's basic attributes and condition.

METHODS

A. Study design

Longitudinal, prospective observational study

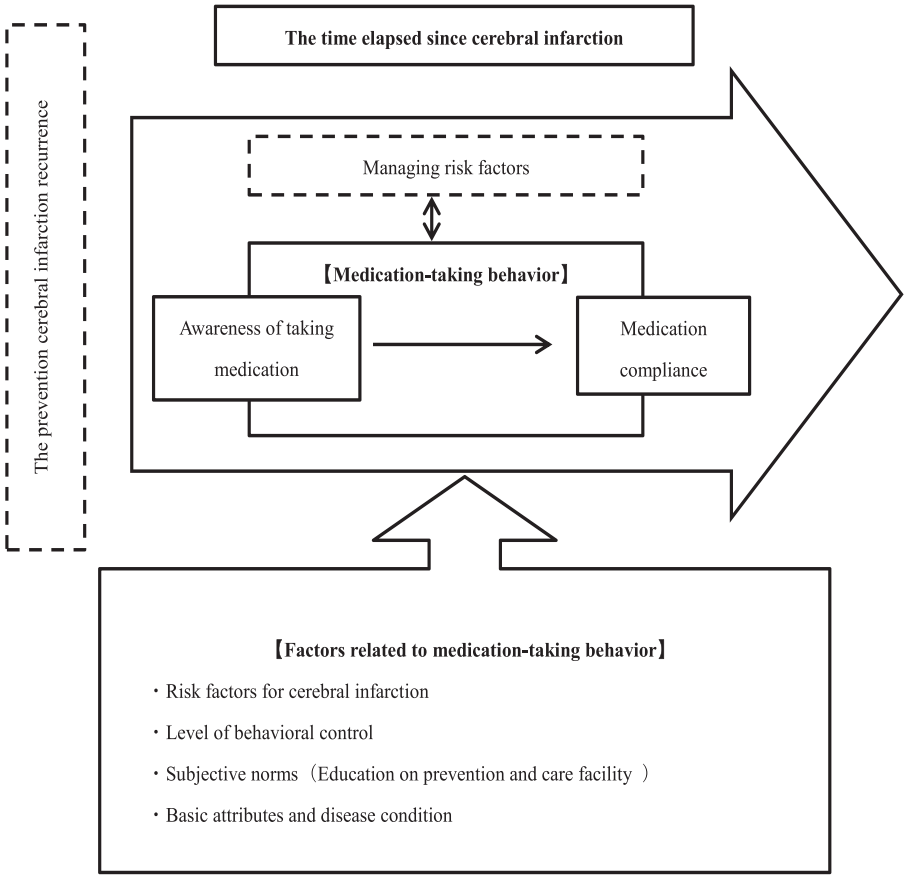

Figure 1 : The conceptual framework of this study
Figure 1 shows that correlation among important terms of this study.

B. Subjects

To observe medication-taking behavior as a way to prevent cerebral infarction recurrence, the study targeted first-cerebral infarction patients, specifically those who had experienced a mild cerebral infarction, which accounts for approximately half of all cerebral infarction (20). The patients were admitted to three facilities that provide acute stroke care as part of the stroke care network of Prefecture A. The first-cerebral infarction patients had a National Institutes of Health Stroke Scale (NIHSS) score of 5 or lower on admission, no cognitive impairment, and were able to verbally communicate. The NIHSS evaluates stroke symptoms and is composed of 11 items including level of consciousness, palsy, sensory impairment, and language ability. Total scores range from 0 to 31, with a higher score indicating greater stroke severity (21).

C. Survey Method and Details

1. Survey Method

Study data was collected between October 2012 and September 2014. The study survey was conducted a total of four times, namely at admission and at 3, 6, and 12 months after cerebral infarction onset. During admission, patients were interviewed or completed a self-administered questionnaire. At 3, 6, and 12 months post-cerebral infarction, patients were interviewed over the telephone or completed and sent by mail a self-administered questionnaire.

2. Survey Details

a. Medication-taking behavior

In terms of medication-taking behavior, the level of compliance with medication instructions was assessed using the "Drug Compliance Scale" (22), and awareness of taking medication was evaluated using a self-administered questionnaire consisting of the "Medication Assessment Index" (23). Because the subjects were elderly individuals with potential motor dysfunction and because this was a longitudinal study involving four self-administered questionnaires in 1 year, two questionnaires were selected to keep the questions to a minimum and to facilitate continuous assessment. These four questionnaires were conducted during admission and at 3, 6, and 12 months post-cerebral infarction.

1) Medication compliance : The Drug Compliance Scale comprises four items on whether patients were taking their medication as instructed and three inverse items (indicated below by a dagger in this text) and has been found to correlate with actual self-monitoring pill count methods (24). Patients were asked to grade how the item applied to them in four grades ("Always," "Often," "Sometimes," or "Never") and the individual and total scores were evaluated. Total scores ranged from 4 to 16 points, with a higher score indicating better drug adherence.

2) Awareness of taking medication : The Medication Assessment Index comprises 11 items about patient awareness of motivation, understanding, acceptance, and cost burden of taking medication and five inverse items (indicated below by an asterisk) and has been tested for reliability and validity. Patients were asked to grade each item according to four grades ("Strongly agree," "Somewhat agree," "Somewhat disagree," or "Strongly disagree") and the individual and total scores were evaluated. Total scores ranged from 11 to 44 points, with a higher score indicating better awareness of taking medication.

b. Factors related to medication-taking behavior

Based on previous studies (12, 16, 25), lifestyle habits, physical condition, number of medications, and whether education was received were included in the surveyed items as variables associated with medication-taking behavior in stroke and hypertension patients.

1) Lifestyle habits constituting risk factors : Patients were asked about smoking, excessive alcohol consumption (≥ 1 unit of alcohol per day), exercise (≥ 30 minutes per day), and obesity (body mass index ≥ 25) before the onset.

2) Level of behavioral control : This variable was evaluated using a self-administered questionnaire containing the "Health Locus of Control Scale" (HLC) (26). The HLC scale measures where patients seek their locus of control for health behaviors, and consists of five subscales (Supernatural HLC, Internal HLC, Chance HLC, Family HLC, and Professional HLC) each with five items for a total of 25 items and has been tested for reliability and validity. Responses are based on six grades, with a higher subscale score indicating a stronger tendency towards that particular locus of control. Patients were surveyed once during admission and once more at 12 months post-cerebral infarction.

3) Subjective norms : Patients were asked whether they received education on prevention of cerebral infarction recurrence and about the care facility they attended after release at 3 months post- cerebral infarction.

c. Basic attributes and disease condition : The following variables were investigated by examining patient medical records or in an interview during admission : age, sex, household family members (Y/N), employment (Y/N), cerebral infarction type, infarct site, NIHSS, treatment details, duration of hospitalization, symptoms, past medical history, previous medication history, and type and number of medications.

D. Analytical method

Descriptive statistics were determined for each surveyed item. To investigate changes over time in medication-taking behavior, individual and total item scores for medication compliance and awareness of taking medication during admission and at 3, 6, and 12 months post- cerebral infarction were examined using the Friedman test and with Wilcoxon's signed-rank test after applying the Bonferroni correction to data with a significant difference at two time points. Cluster analysis was performed to classify subjects according to similarity of changes in medicating-taking behavior and to identify the characteristics of these changes. Cluster analysis is a technique for grouping numerous objects characterized by multiple variables into clusters according to similarity based on an index of inter-object similarity (27).

First, hierarchical cluster analysis based on Ward's method was performed using the total scores for medication compliance and awareness of taking medication at each of the four time points. Next, Friedman's test was performed to determine the characteristics of changes over time in the medication-taking behavior of each group. After that, intergroup comparisons were performed to identify the characteristics of each group, and the factors associated with medication compliance in each group were investigated.

Differences in quantitative variables were tested using the Mann-Whitney U test and Kruskal-Wallis test, while categorical variables were tested using the Fisher's exact test, and correlations were analyzed using Spearman's rank correlation coefficient.

SPSS Windows 23.0 J software was used to perform the statistical analyses using a 5% significance level.

E. Ethical considerations

This study was conducted with the approval of our organization's ethical review board and the ethical review board of each study site. When a patient meeting the study's participation criteria was admitted, a nurse at the study site asked the patient whether he/she would be willing to participate in the study. The patient then signed an informed consent form after receiving a full explanation about the study objective, content, and methods, that the patient's decision on whether or not to participate would be respected, that the patient could withdraw from the study at any time, that the patient's personal information would be anonymized and his/her privacy protected, and that the patient's decision not to participate or to withdraw from the study would not result in any penalty in terms of

treatment. Permission to use the self-administered questionnaires was obtained from the parties who developed them.

RESULTS

Initial data was collected from 51 cerebral infarction inpatients, and analyses were performed on 31 of these patients (60.8%) for whom data was obtained at all four time points up to 12 months post-cerebral infarction. Continuous data collection could not be performed on two patients who withdrew from the study, eight patients who did not return their questionnaire, and 10 patients whose questionnaire responses were incomplete.

A. Subject characteristics (Table 1)

In the analysis set of 31 patients, there were 22 men (71.0%), the mean age was 66.0±8.4 years [mean±standard deviation (SD)], and 15 were employed (48.4%). Lacunar infarct was the most common stroke type occurring in 19 patients (61.3%), 30 patients (96.8%) were receiving acute-stage cerebral infarction therapy with anti-platelets and anti-coagulants, and mean hospitalization period was 16.2±5.8 days. There were 14 patients with one or more cerebral infarction risk factors (45.2%), 13 patients with hypertension (41.9%), four patients with diabetes mellitus (12.9%), and two patients with dyslipidemia (6.5%). Seventeen patients were taking medication taken prior to admission (54.8%), with nine types

Table 1 : Subject characteristics

Characteristics		n(%)
<Basic attributes>		
Age(years)	Mean±SD [Range]	66.0±8.4 [49~83]
Sex	Male/Female	22 (71.0)/9 (29.0)
Household family members	Y/N	28 (90.3)/ 3 (9.7)
Employment	Y/N	15 (48.4)/16 (51.6)
<Disease condition>		
Subtype of cerebral infarction	Lacunar	19 (61.3)
	Atherothrombotic	6 (19.4)
	Cardioemolic	2 (6.5)
	Others	4 (12.9)
Infarct site	Cerebrum	27 (87.1)
	Brainstem	3 (9.7)
	Cerebellum	1 (3.2)
	Multiple	2 (6.5)
NIHSS at admission	0	8 (25.8)
	1	8 (25.8)
	2	9 (29.0)
	3	2 (6.5)
	4	3 (9.7)
	5	1 (3.2)
Treatment details	Antitrombotic therapy	30(96.8)
	Trobolysis with alteplase	1 (3.2)
Hospitalization period	Mean±SD [Range]	16.2±5.8 [8~39]
<Risk factors for cerebral infarction>		
Disease	Yes	14 (45.2)
	hypertension	*13 (41.9)*
	diabetes mellitus	*4 (12.9)*
	dyslipidemia	*2 (6.5)*
	atrial fibrillation	*0 (0)*
	ischemic heart disease	*1 (3.2)*
	No	17 (54.8)
Lifestyle habits	Yes	25 (80.6)
	smoking	*8 (25.8)*
	no exercise	*19 (61.3)*
	alcohol consumption	*7 (22.6)*
	obesity	*13 (41.9)*
	No	6 (19.4)
<Number of drugs>		
Prior to admission	0/1~2/3~9	14 (45.2)/7 (22.6)/10 (32.2)
After admission	1/2~3/4~11	10 (32.2)/11 (35.5)/10 (32.2)

Table 1 shows that basic attributes and disease characteristics of 31 subjects during admission.

of drugs being the highest number of medication taken. The number of newly-prescribed anti-thrombotic and other drugs up to discharge was zero in two patients (6.5%), one-two drugs in 24 patients (77.4%), and three-four drugs in five patients (16.1%). More than 20% of patients had lifestyle habits constituting cerebral infarction risk factors.

B. Responses to items on medication-taking behavior during admission (Table 2)

In terms of medication compliance, 26 patients (83.9%) responded that they were taking their medication as instructed. Meanwhile, 15 patients (48.3%) selected "Sometimes," "Often," or "Always" in response to the item "I forget to take my medication†," with the mean score for this item being the lowest of all four survey items at 3.42±0.72 (mean±SD). Eight patients (25.8%) selected either "Sometimes" or "Often" in response to the question "I stop taking medication based solely on my own decision†," thus providing the second lowest mean score at 3.68±0.60.

Scores for awareness of taking medication were high at 3.35±0.76 for the item "Taking medication is bothersome" and 3.35±0.66 for the item "My medication regimen easy to understand." The items with the lowest mean score were "It is not good to rely on medication†," at 2.55±0.81, "I perceive the benefits of my medication" at 2.87±0.72, and "The cost of medication is a burden†" at 2.90±0.94.

C. Changes in medication-taking behavior at 12 months post-cerebral infarction (Table 3)

1. Changes in medication compliance

At all three study sites, the individual and total item scores for medication compliance at 12 months after cerebral infarction onset had increased compared to during admission. Items that had changed significantly at the four time points from admission to 12 months post- cerebral infarction were "I stop taking medication based solely on my own decision†" (during admission and 12 months post- cerebral infarction) and "I forget to take my medication†" (during admission and 3 months and 12 months post- cerebral infarction), with a significant increase occurring over time and a tendency towards not discontinuing medication based solely on one's own decision.

2. Changes in awareness of taking medication

In terms of awareness of taking medication at 12 months post-cerebral infarction, there were high scores for the item "Taking medication is bothersome†" (3.45±0.72) and "I understand the need for medication" (3.39±0.67). Conversely, the lowest scores were seen for "The cost of medication is a burden†" at 2.48±0.89, and "It is not good to rely on medication†" at 2.61±1.09. Changes over time in item scores at 12 months post- cerebral infarction compared to during admission had increased for six items and decreased for five items. There were no significant changes over time in individual or total item scores.

D. Classification of characteristics of changes over time in medication compliance (Table 4)

There was no significant change over time in awareness of taking medication so only the characteristics of changes over time in medication compliance were investigated. Specifically, characteristics were categorized using cluster analysis of total medication compliance scores for the four time points from admission to 12 months post- cerebral infarction and were then classified into two groups using a dendrogram.

Type I was the "persistently high medication compliance group"

Table 2 : Responses to items on medication-taking behavior during admission

Medication compliance : The Drug Compliance Scale	Always	Often	Sometimes	Never	Mean±SD	【Median】
① I take my medication as instructed	26 (83.9)	5 (16.1)	0 (0)	0 (0)	3.84±0.37	【4.0】
② I tend to stop taking my medication at my own discretion†	0 (0)	2 (6.5)	6 (19.4)	23 (74.2)	3.68±0.60	【4.0】
③ I allow time to pass between consultations, resulting in days on which I do not take my medication†	0 (0)	0 (0)	5 (16.1)	26 (83.9)	3.84±0.37	【4.0】
④ I forget to take my medication†	1 (3.2)	1 (3.2)	13 (41.9)	16 (51.6)	3.42±0.72	【4.0】
Total item scores					14.77±1.56	【15.0】
Awareness of taking medication : The Medication Assessment Index	Strongly agree	Somewhat agree	Somewhat disagree	Strongly disagree	Mean±SD	【Median】
① Do you feel the effects of your medication?	6 (19.4)	15 (48.4)	10 (32.3)	0 (0)	2.87±0.72	【3.0】
② Is your medication helpful in preventing aggravation of your illness?	5 (16.1)	24 (77.4)	1 (3.2)	1 (3.2)	3.06±0.57	【3.0】
③ Is the description of your medication helpful in understanding the medication?	6 (19.4)	21 (67.7)	4 (12.9)	0 (0)	3.06±0.57	【3.0】
④ Overall, are you compliant with your medication?	8 (25.8)	20 (64.5)	3 (9.7)	0 (0)	3.16±0.58	【3.0】
⑤ Do you think it is not good to rely on medication?†	2 (6.5)	14 (45.2)	11 (35.5)	4 (12.9)	2.55±0.81	【2.0】
⑥ Do you think it would be okay to take less medication than you are currently taking?†	0 (0)	9 (29.0)	15 (48.4)	7 (22.6)	2.94±0.73	【3.0】
⑦ Are you worried about the side effects of your current medication?†	1 (3.2)	7 (22.6)	9 (29.0)	14 (45.2)	3.16±0.90	【3.0】
⑧ Is the act of taking your medication tiresome?†	0 (0)	5 (16.1)	10 (32.3)	16 (51.6)	3.35±0.76	【4.0】
⑨ Are the instructions on how to take your medication easy to understand?	13 (41.9)	17 (54.8)	0 (0)	1 (3.2)	3.35±0.66	【3.0】
⑩ Do you understand why your medication is necessary?	9 (29.0)	22 (71.0)	0 (0)	0 (0)	3.29±0.46	【3.0】
⑪ Is the cost of your medication a burden?†	1 (3.2)	12 (38.7)	7 (22.6)	11 (35.5)	2.90±0.94	【3.0】
Total item scores					33.71±3.52	【33.0】

Table 2 shows that frequency distribution and measure of central tendency in subjects' answer to questionnaires for medication-taking behavior during admission.
†(dagger) shows inverse item.
Data are number (%).

Table 3 : Change over time in medication- taking behavior at 12 months post cerebral infarction

	Item	During admission	Post-cerebral infarction			Wilcoxon's signed-rank test
			3 months	6 months	12 months	
Medication compliance	① I take my medication as instructed	3.84±0.37【4.0】	3.87±0.34【4.0】	3.87±0.43【4.0】	3.90±0.30【4.0】	ns
	② I tend to stop taking my medication at my own discretion†	3.68±0.60【4.0】	3.90±0.54【4.0】	3.87±0.56【4.0】	4.00±0.00【4.0】	admission< 12 months**
	③ I allow time to pass between consultations, resulting in days on which I do not take my medication†	3.84±0.37【4.0】	3.94±0.25【4.0】	3.97±0.18【4.0】	3.97±0.18【4.0】	ns
	④ I forget to take my medication†	3.42±0.72【4.0】	3.90±0.70【4.0】	3.77±0.62【4.0】	3.81±0.40【4.0】	admission< 3 months** admission< 12 months**
	Total item scores	14.77±1.56【15.0】	15.61±0.76【16.0】	15.48±1.31【16.0】	15.68±0.65【16.0】	admission< 12 months**
Awareness of taking medication	① Do you feel the effects of your medication?	2.87±0.72【3.0】	2.77±0.67【3.0】	2.77±0.81【3.0】	2.97±0.61【3.0】	ns
	② Is your medication helpful in preventing aggravation of your illness?	3.06±0.57【3.0】	3.06±0.36【3.0】	2.97±0.48【3.0】	3.13±0.50【3.0】	ns
	③ Is the description of your medication helpful in understanding the medication?	3.06±0.57【3.0】	3.03±0.41【3.0】	2.94±0.57【3.0】	3.03±0.55【3.0】	ns
	④ Overall, are you compliant with your medication?	3.16±0.58【3.0】	3.13±0.34【3.0】	3.10±0.60【3.0】	3.06±0.51【3.0】	ns
	⑤ Do you think it is not good to rely on medication?†	2.55±0.81【2.0】	2.61±0.84【2.0】	2.65±0.95【2.0】	2.61±1.09【2.0】	ns
	⑥ Do you think it would be okay to take less medication than you are currently taking?†	2.94±0.73【3.0】	3.16±0.78【3.0】	3.10±0.91【3.0】	3.03±0.75【3.0】	ns
	⑦ Are you worried about the side effects of your current medication?†	3.16±0.90【3.0】	2.90±0.79【3.0】	3.06±0.89【3.0】	3.03±0.91【3.0】	ns
	⑧ Is the act of taking your medication tiresome?†	3.35±0.76【4.0】	3.39±0.62【3.0】	3.52±0.72【4.0】	3.45±0.72【4.0】	ns
	⑨ Are the instructions on how to take your medication easy to understand?	3.35±0.66【3.0】	3.23±0.50【3.0】	3.13±0.72【3.0】	3.32±0.65【3.0】	ns
	⑩ Do you understand why your medication is necessary?	3.29±0.46【3.0】	3.23±0.67【3.0】	3.26±0.63【3.0】	3.39±0.67【3.0】	ns
	⑪ Is the cost of your medication a burden?†	2.90±0.94【3.0】	2.81±0.83【3.0】	2.58±0.89【3.0】	2.48±0.89【2.0】	ns
	Total item scores	33.71±3.52【33.0】	33.29±3.13【33.0】	33.06±4.80【34.0】	33.51±4.48【34.0】	ns

Table 3 shows that change of measure of central tendency in subjects' answer to questionnaires for medication-taking behavior at each of four time points post cerebral infarction and results in Wilcoxon signed-rank test.
†(dagger) shows inverse item.
Data are mean±SD【median】.
Friedman test and with Wilcoxon's signed-rank test after applying the Bonferroni correction *p< .05, **p< .01, ns : no significant.

Table 4 : Classification of change over time in medication compliance total scores

	n (%)	During admission	Post-cerebral infarction			Wilcoxon's signed-rank test
			3 months	6 months	12 months	
Type I : Persistently high medication compliance group	24 (77.4)	15.42±0.83【16.0】	15.67±0.76【16.0】	15.96±0.20【16.0】	15.79±0.51【16.0】	admission< 6 months**
Type II : Persistently low medication compliance group	7 (22.6)	12.57±1.51【12.0】	15.43±0.79【16.0】	13.86±2.11【14.0】	15.29±0.95【16.0】	ns
Mann-Whitney U test		**	ns	**	ns	

Table 4 shows that two groups categorized by the characteristics of changes in the medication compliance total scores at each of four time points, Differences in the medication compliance total scores at each of the four time points were tested using the Mann-Whitney U test.
Friedman test and Wilcoxon's signed-rank test after applying the Bonferroni correction. *p< .05, **p< .01, ns : no significant
Data are mean±SD【median】.

which included 24 patients (77.4%) and was characterized by a high total medication compliance score during admission at 15.42±0.83 that remained high up to 12 months post-cerebral infarction. The medication compliance scores of patients in this group were significantly higher at 6 months post-cerebral infarction than during admission.

Type II was the "persistently low medication compliance group" which included seven patients (22.6%) and was characterized by a total medication compliance score during admission that was about 2 points lower than the mean at 12.57±1.51 and that differed significantly from that of the persistently high medication compliance group. This group did not exhibit any changes over time in medication compliance scores from admission to 12 months post-cerebral infarction.

Mean scores for these two groups differed significantly during admission but were almost the same at 3 months post-cerebral infarction. However, the scores differed significantly again at 6 months, and this difference was reduced by 12 months post-cerebral infarction.

E. Characteristics of the persistently high and low medication compliance groups (Tables 5 and 6)

To investigate the characteristics of the persistently high and low medication compliance groups, the factors associated with patient characteristics and medication-taking behavior-namely level of behavioral control, education on prevention of cerebral infarction recurrence, post-discharge stroke care facility, disease condition, and symptoms-were subjected to intergroup comparison

Table 5 : Subject characteristics by classification of change in medication compliance scores over time

Item		Type I : Persistently high medication compliance group (n=24)	Type II : Persistently low medication compliance group (n=7)	p
<Basic attributes>				
Sex	Male/Female	17/7	5/2	ns
Age (years)	Mean±SD [Range]	66.04±8.23 [64.5]	65.86±9.55 [65.0]	ns
Household family members	Y/N	21/3	7/0	ns
Employment	Prior to admission : Y/N	11/13	4/3	ns
	Post discharge : Y/N	9/15	4/3	ns
<Risk factors for cerebral infarction>				
Disease	Y/N	10/14	4/3	ns
Lifestyle				ns
smoking	Y/N	6/18	2/5	ns
no exercise	Y/N	15/9	4/3	ns
alcohol consumption	Y/N	5/19	2/5	ns
obesity	Y/N	9/15	4/3	ns
<Number of drugs>				
Prior to admission	0/1~2/3~9	11/5/8	3/2/2	ns
After admission	1/2~3/4	8/7/9	2/4/1	ns
<Education on prevention of stroke recurrence>	Y/N	19/5	6/1	ns
<Post-discharge stroke care facility>	Admission hospital/ Primary care doctor	9/15	3/4	ns
<Post-discharge disease symptoms>	Y/N	15/9	3/4	ns
<Awareness of taking medication during admission>		Mean±SD【median】		
① Do you feel the effects of your medication?		2.88±0.74【3.0】	2.86±0.69【3.0】	ns
② Is your medication helpful in preventing aggravation of your illness?		3.13±0.45【3.0】	2.86±0.90【3.0】	ns
③ Is the description of your medication helpful in understanding the medication?		3.13±0.45【3.0】	2.86±0.90【3.0】	ns
④ Overall, are you compliant with your medication?		3.21±0.59【3.0】	3.00±0.58【3.0】	ns
⑤ Do you think it is not good to rely on medication?†		2.50±0.83【2.0】	2.71±0.76【3.0】	ns
⑥ Do you think it would be okay to take less medication than you are currently taking?†		2.88±0.68【3.0】	3.14±0.90【3.0】	ns
⑦ Are you worried about the side effects of your current medication?†		3.13±0.95【3.0】	3.29±0.76【3.0】	ns
⑧ Is the act of taking your medication tiresome?†		3.50±0.66【4.0】	2.86±0.90【3.0】	ns
⑨ Are the instructions on how to take your medication easy to understand?		3.33±0.70【3.0】	3.43±0.54【3.0】	ns
⑩ Do you understand why your medication is necessary?		3.29±0.46【3.0】	3.29±0.49【3.0】	ns
⑪ Is the cost of your medication a burden?†		2.96±0.86【3.0】	2.71±1.25【2.0】	ns
Total item scores		33.92±3.49【33.0】	33.00±3.83【33.0】	ns
<Level of behavioral control>		Mean±SD【median】		
during admission	Supernatural HLC	13.58±4.38【14.0】	12.00±4.04【11.0】	ns
	Internal HLC	24.96±3.59【25.0】	23.43±2.22【24.0】	ns
	Chance HLC	15.04±3.70【15.5】	11.28±5.41【10.0】	*
	Family HLC	22.21±4.33【23.0】	19.71±3.50【20.0】	ns
	Professional HLC	20.42±4.57【20.5】	22.29±1.80【22.0】	ns
12 manths post-cerebral infarction	Supernatural HLC	14.92±3.34【14.5】	12.57±5.35【12.0】	ns
	Internal HLC	23.71±3.46【24.5】	23.29±3.35【23.0】	ns
	Chance HLC	13.92±3.96【15.0】	14.29±8.71【12.0】	ns
	Family HLC	22.71±4.87【23.5】	20.14±5.70【23.0】	ns
	Professional HLC	20.13±2.58【19.5】	21.86±3.93【24.0】	ns

Table 5 shows that differences in basic attributes, disease characteristics, awareness of taking medication and level of behavioral control between high medication compliance group and low medication compliance group.
Categorical variables were tested using the Fisher's exact test, data are number.
Differences in quantitative variables were tested using the Mann-Whitney U test, data are mean±SD【median】. *p< .05, ns : no significant.

(Table 5). The only difference was in the Chance HLC score at admission, which was significantly higher in the persistently high medication compliance group.

Awareness of taking medication was compared between groups at 3, 6, and 12 months post- cerebral infarction, but there were no significant differences between any of the variables at any of these

Table 6 : Correlation between medication compliance at each time point in patients in each type of medication compliance group

	<Medication compliance>							
	During admission		Post-cerebral infarction					
			3 months		6 months		12 months	
	High group	Low group	High group	Low group	High group	Low group	High group	Low group
<Awareness of taking medication>								
① Do you feel the effects of your medication?	.200	-.112	.264	.075	.254	-.544	.312	.233
② Is your medication helpful in preventing aggravation of your illness?	-.012	-.476	.332	.000	.550**	-.312	.305	.342
③ Is the description of your medication helpful in understanding the medication?	-.180	.289	.252	.001	.377	-.312	.040	.373
④ Overall, are you compliant with your medication?	-.141	.748	-.091	.002	.080	.000	.137	.833*
⑤ Do you think it is not good to rely on medication?†	-.150	.609	.073	-.065	.136	.073	-.074	-.473
⑥ Do you think it would be okay to take less medication than you are currently taking?†	-.236	-.231	.180	-.516	.238	.365	-.010	.511
⑦ Are you worried about the side effects of your current medication?†	-.222	-.648	-.135	.529	-.016	.476	-.152	.322
⑧ Is the act of taking your medication tiresome?†	.509*	.722	.375	-.342	.370	.073	.165	.529
⑨ Are the instructions on how to take your medication easy to understand?	.318	.661	.407*	.342	.103	.000	.093	.322
⑩ Do you understand why your medication is necessary?	-.173	.805*	.276	.342	.110	.147	.093	.882**
⑪ Is the cost of your medication a burden?†	.280	-.079	-.131	.367	.144	.010	-.015	.174
Total item scores	.079	.148	.280	.152	.318	.093	.088	.141
<Level of behavioral control>								
Supernatural HLC	.290	.716					.362	-.132
Internal HLC	-.122	.817*					.086	.639
Chance HLC	.281	.727					.057	.677
Family HLC	-.178	-.500					-.213	.422
Professional HLC	-.275	.000					-.099	.475

Table 6 shows that the factors associated with medication compliance in each medication compliance group at each of four time points and Spearman's rank correlation coefficient.
Spearman's rank correlation coefficient *p< .05, **p< .01
"High group" indicates persistently high medication compliance group and "Low group" indicates persistently low medication compliance group.

time points. There were also no intragroup changes over time in awareness of taking medication or HLC scale scores. In the HLC subscales, Internal HLC scores were the highest of the five subscale scores in both groups.

Next we investigated the factors associated with medication compliance in each group during admission (Table 6). Medication compliance during admission in the persistently high medication compliance group was characterized by a strong association with the perception that taking medication was bothersome. There was also a strong association with the perception that the medication regimen was easy to understand at 3 months, and the perception that medication is useful in preventing disease at 6 months post-cerebral infarction. In the persistently low medication compliance group, there was a strong association with understanding the need for medication during admission and Internal HLC. At 12 months post- cerebral infarction, there was a strong association with the perception of being good at taking medication and understanding the need for medication.

DISCUSSION

A. Characteristics of the study subjects

Lacunar infarction accounted for 60% of cerebral infarction type, with a mean onset age of 66.0 years, and the youngest patient with this cerebral infarction type aged 49 years. Lacunar infarction is reportedly less neurologically severe at admission and onset age is earlier than in other cerebral infarction types (20) and is believed to be characteristic of first mild cerebral infarction patients. Approximately half of the patients had cerebral infarction risk factors and were taking medication prior to cerebral infarction onset. While the presence of cerebral infarction risk factors differs according to the disease type, approximately 60% to 70% of patients have hypertension, 20% to 30% have diabetes mellitus, and 15% to 30% have dyslipidemia (28), indicating that the risk factor rate was slightly low in the present study.

B. Factors associated with changes over time in medication-taking behavior up to 12 months after initial mild cerebral infarction onset

The present study involved a prospective, longitudinal survey

if changes in medication-taking behavior from cerebral infarction onset to 12 months post- cerebral infarction in patients who had experienced a mild first cerebral infarction. The study results showed that even among patients who had previously forgotten to take their medication, their cerebral infarction and hospitalization motivated them to adhere to their medication regimen, with the number of patients who decided to stop taking their medication decreasing to zero at 12 months post-cerebral infarction.

Several longitudinal studies of medication-taking behaviors in ambulatory cerebral infarction patients (16), chronic heart failure patients (14), and ischemic heart disease patients (15) have found that approximately half of all study patients inadvertently forgot to take their medication, and that 10% to 20% of patients stopped taking their medication based solely on their own decision. This finding is consistent with the medication compliance behavior of patients during admission in the present study. At 12 months after cerebral infarction onset, almost all patients had perfect medication compliance to their medication regimen, but this medication compliance may have decreased again from 12 months onwards. Even though motivation for medication compliance increases after important events such as cerebral infarction onset and hospitalization, one can infer that medication compliance to medication instructions will decline over time.

Meanwhile, the study findings did not reveal any changes in awareness of taking medication at 12 months post-cerebral infarction, but there was an increase in the perceived burden of medication costs. Continuing medication after release from hospital involves multiple financial burdens for the patients, such as transport fees to attend the stroke care facility, outpatient medical expenses, and the cost of drugs to manage various risk factors of diseases. Approximately half of the patients felt that it was not good to rely on medication while they were hospitalized, pointing to the need to consider the patient's financial burden as a risk factor for decreased adherence.

C. Associated factors of each characteristic of changes in medication compliance over time

Cluster analysis of changes over time in medication compliance up to 12 months after cerebral infarction onset was used to classify patients into two groups. Patients in the persistently high medication compliance group managed to maintain medication compliance from admission until 12 months post-cerebral infarction. Conversely, patients in the persistently low medication compliance group had low medication compliance during admission which gradually improved over time but failed to reach the level of the persistently high medication compliance group. There was no difference between these two groups in their awareness of taking medication, but there was a difference in their level of behavioral control during admission.

Patients in both groups realized that their level of behavioral control in terms of health behavior was determined by their own actions rather than that of physicians or other stakeholders. Meanwhile, patients with high compliance perceived that their health are influenced by chance and fate significantly more than those with low compliance.This finding suggests that patients, who perceive cerebral infarction onset as an unpredictable event and consider that it will be difficult to control their own health only by themselves in the future, were more likely to adhere to their medication regimen in order to prevent cerebral infarction recurrence. The subjects of present study were patients who had experienced cerebral infarction for the first time, so we speculate that they would not have enough knowledge that recognize previous lifestyles as causes and results of cerebral infarction at admission. Behind the value that stroke patients attach to the behavior of taking anti-thrombotic medication is the shock of having a fearful stroke experience and of their subsequent recovery (17). Moreover, patients with a high level of behavioral control exhibit a sense of responsibility towards their poor health (29). This finding shows that medication compliance is an essential behavior for preventing cerebral infarction recurrence, but it is also necessary to understand the causes of cerebral infarction onset and how patients perceive their future cerebral infarction rehabilitation and to investigate ways to assist patients based on the theory of planned behavior in order to prevent patients from experiencing excessive fear, unnecessary concern, and an overly strong sense of responsibility.

We investigated the associated factors at each of the four time points from cerebral infarction onset to 12 months post- cerebral infarction in patients belonging to the persistently low and high medication compliance groups. In the persistently low medication compliance group, understanding the need for medication was strongly related to medication compliance. As stated above, patients in this group perceived the impact of chance and fate on how they controlled their health behavior to a lesser extent than their counterparts in the persistently high medication compliance group. There was also a relationship between Internal HLC and medication compliance during admission. This finding suggests that even patients with low medication compliance behavior during admission were capable of maintaining medication compliance once they recognized that they could prevent cerebral infarction recurrence through their own actions. Patients with good medication compliance at 12 months post-cerebral infarction also perceived that they were good at taking their medication. This result could be attributed to patients having evaluated their own medication-taking behavior. Rather than being a cognitive or behavioral trait of adhering to the instructions of medical professionals, this outcome was attributed to patients having understood the aim of their treatment and engaging in their cerebral infarction rehabilitation while monitoring their health behavior.

The reason why patients in the persistently high medication compliance group perceived the task of taking medication as bothersome needs to be identified and this perception reduced. The process of recovering from acute-stage stroke involves multiple aspects of subjective experience, and changes in physical function and movements are closely associated with the transition to these aspects (30). A 1-year follow-up study on changes over time in self-esteem after stroke onset found that self-esteem up to 6 months after stroke was associated with the patient's actions and activities of daily living and was subsequently associated with emotional support (31). Cerebral infarction patients therefore repeatedly experience physical impairments and adapt to their daily lives over time while experiencing mental and physical changes. Amidst these mental and physical changes, patients are also faced with the challenge of engaging in behaviors to prevent cerebral infarction recurrence. Adapting to changes in disease pathology and routine lifestyle as well as psychological changes after cerebral infarction onset therefore needs to be perceived in separate stages. The reason why patients perceive the task of taking medication to be bothersome may also change over time so health care personnel involved in the patient's recovery, namely stroke rehabilitation centers and primary care physicians or home care providers, need to undertake a multilateral assessment and provide support for medication taking and other behaviors geared towards preventing cerebral infarction recurrence.

In patients who adhered to their medication regimen from admission, there was a strong association between medication compliance and the perception that medication is useful for preventing disease at 6 months post- cerebral infarction. This finding suggests that patients associated the behavior of taking medication with the benefits of medication, and this attitude informed their subsequent behavior. A previous study found that behaviors to prevent cerebral infarction recurrence among mild cerebral infarction patients were characterized by a perceived decline in the risk of cerebral

infarction recurrence and a tendency to discontinue self-management once the patient was able to perform daily activities independently (32). Anti-thrombotic medication to prevent cerebral infarction recurrence is a lifelong prospect and is intended to prevent new cerebral infarction onset rather than being a symptomatic or replacement therapy. Health care providers must therefore assist patients to properly understand the effects of this medication and to maintain medication compliance.

D. Role of practical nursing care in preventing cerebral infarction recurrence

The study findings suggest that when providing education to intial cerebral infarction patients on how to prevent recurrence, it is possible to assess the patient's cognitive and behavioral traits of medication-taking during admission. Patients can be classified to some extent according to their current medication compliance, their own health perception and attitude towards treatment, and their perceived behavioral control. Support should then be provided in a manner that meets the individual attitudes of patients in each group. A more important issue is that health care providers should not forget that cerebral infarction patients continue to experience physical and mental changes over time and that they are undergoing a process of rebuilding through their rehabilitation, and nurses should provide close support for prevention of cerebral infarction recurrence that is commensurate with the patient's rehabilitation stage. As such, there is a need to establish a personalized, ongoing nursing intervention program capable of contributing to the prevention of cerebral infarction recurrence.

E. Study limitations and issues

This study used a longitudinal design to investigate patients who experienced their first mild cerebral infarction but who had various physical impairments so the study population was small and is not sufficient to make general statements. Moreover, the follow-up period of cerebral infarction patients was from admission to 12 months post-cerebral infarction. Accordingly, future studies are needed to investigate patients with different levels of cerebral infarction severity over a term of more than 12 months post- cerebral infarction in order to obtain useful resources for the development of prevention of cerebral infarction recurrence programs. The subjects of present study were patients who agreed to participate, it is possible that selection participants are biased toward results on medication-taking behavior. It is also possible that the telephone interviews conducted over time by the study investigators acted as an intervention towards maintaining medication compliance.

CONCLUSIONS

1. We investigated the medication-taking behaviors of 31 first mild cerebral infarction patients up to 12 months after cerebral infarction onset and found that medication compliance improved over time compared to during admission. On the other hand, there were no changes over time in awareness of taking medication.

2. Cluster analysis based on changes over time in medication compliance revealed that patients could be classified into a "persistently high medication compliance group" and a "persistently low medication compliance group." Assessing the perception of health behavioral control among patients in the persistently high medication compliance group showed that their perception was influenced by chance and fate to a greater extent than their counterparts in the persistently low medication compliance group.

3. By assessing actual medication compliance and patient perception of health behavioral control during admission, we were able to identify patient characteristics, thus suggesting the need for education on prevention of cerebral infarction recurrence and medication guidance based on individual cognitive and behavioral traits.

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