Medication Adherence among Stroke Survivors within a Post-stroke Period of Three Months to One Year

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Abstract

Strict compliance with medication is integral to secondary stroke prevention. This study was undertaken to find out medication adherence among stroke survivors and factors associated with it. Cross sectional survey among stroke survivors was conducted. Interview based self-reported medication adherence was defined as consumption at least more than 80 percent of their medications for last two weeks, based on last prescription. Structured interview using pre-tested interview schedule was done to collect other data; stroke survivors (mean age 58.64 ±10.96 years; 25.4% females) with a mean post-stroke period of 6.65±3.36 months participated. Overall medication adherence was 43.8 percent (n=105). Medication adherence was 34.4 percent (n=134), 52.6 percent (n=190) and 56.7 percent (n=224) for antidiabetics, antihypertensives and statins respectively. People less than 45 years of age, urban residents and those with physical and neurological deficits were more adherent to medications. Periodic reminders, financial support to buy medicines and patient education can enhance medication adherence to prevent future strokes.

Adherence to medication is important in the management of chronic diseases and is also a mediator between the treatment and patient outcome. Over 30-50 percent of medicines prescribed for long term illnesses are not taken as directed (Burkhart & Sabate, 2013).

Medication non-adherence is associated with poor control of risk factors (Thorogood, 2004) and risk of death (OR=7.99; 95% CI 6.28 - 10.18) when compared to adherent group (Perreault et al, 2012). Adherence to antihypertensives after stroke have been shown to reduce the incidence of cardiovascular events (Mayor, 2013), hospitalisations and health care costs (Sokol et al, 2013; Cutler et al, 2018). Medication adherence among stroke survivors was suboptimal and it reduces as the post stroke period increases.

The knowledge on medication adherence among stroke survivors can improve the stroke care to prevent stroke recurrence in the community.

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Objectives

This study was set out to find out the adherence to prescribed medications among stroke survivors within a post-stroke period of three months to one year.

Review of Literature

The World Health Organization (WHO) defined adherence as "The extent to which a person's behaviour of taking medication, following a diet, or making healthy lifestyle changes corresponds with agreed-upon recommendations from a health-care provider" (Sebatab, 2003). Attributes of medication adherence are: knowing and agreeing to the medication, communicating and negotiating the regimen and active, continuous involvement and appraisal of the treatment effect. The identified antecedents of medication adherence include a valid prescribed medication regimen, cognitive and action abilities in her/his role as a patient and a level of preparation for medication treatment. The consequences of medication adherence are improving symptom control, decreasing re-hospitalisations and mortality, reducing medical care costs and restoring self-esteem (Bissonnette, 2003).

Medication adherence is a cluster of behaviours simultaneously affected by multiple fac-

tors. According to WHO there are five interacting dimensions of medication adherence. Each dimension will have many factors and many of the factors are not exclusive to one dimension rather they may overlap each other. One or more dimensions can contribute to patients' non-adherence. The five dimensions are: health-care system or team, patient, therapy, condition, or social and economic factors. Improved adherence requires the successful interplay between the patient and those involved in managing his care.

Theories of Medication Adherence

Different theoretical perspectives can be used to explain the behaviour of adherence: biomedical, behavioural, communication, cognitive and self-regulatory etc. Several general theoretical frameworks from the literature in social psychology are useful in understanding adherence (Philip & Leventhal, 2011), The intrapersonal models use mental construct about a health-related domain. Emphasis of these models is on cognitive and behavioural factors such as knowledge, attitude, perception, intention, and expectancies. Examples of intrapersonal models are health belief model, theory of planned behaviour, trans-theoretical model and self-regulatory model. They emphasise the active role of the person. Inter personal models argue that social context of people influences their health. Common sense self-regulation model (CS-SRM) takes the most comprehensive approach to representing the concepts that are proposed to influence adherence behaviour (Philip & Leventhal, 2011). CS-SRM also has the potential to be the most successful at predicting adherence behaviour over a longer period. This theory incorporates the basic concepts of other theories such as severity, susceptibility specific to that illness, ability to perform the treatment and treatment efficacy specific to the illness, experienced symptoms of that illness of a particular patient. Illness identity, causes, timeline, consequences and control belief affect the initial phase of adherence behaviour development. It also incorporates two constructs which are relevant for behaviour maintenance beyond its initiation. As the patient becomes aware of the health threat, forms belief about treatment and his abilities which is influenced by the conflicting information he receives from his environment and his own personal experiences. Based on the belief formed they intent to adhere or non-adhere.

The specific health belief formed into cognitive representation integrates feedback from time to time. If the performance of the behaviour results in evidence that it works, it confirms the patient's belief and it became coherent. Feedback from behavioural performance motivate behavioural repetition, repetition leads to routinisation and the person acquires a strong behavioural habit. This may motivate multiple behaviour repetition also. The potential barriers to this phase are tempting behavioural alternatives, cost, time, physical limitations, low motivation, too varied daily routine etc.

Measurement of Medication Adherence: There is no gold standard for measuring adherence. Self-reported nonadherence has a high negative predictive value. The widely accepted definition of medication adherence is at least consumption of more than 80 percent of their medications prescribed. This is the cut off accepted by the clinical trials to calculate drug efficiency. The subjective and objective measurements of adherence indicate different aspect of adherence behaviour. The subjective measures determine the belief and barriers to adherence while the objective measures describe how the patient performs the medication regimen. The methods of pill count and electronic devices do not ensure the ingestion of medication by the patient. The questionnaires such as Hill-Bone Compliance Scale, Medication Adherence Rating Scale (MARS) and Brief Medication Questionnaire are validated for specific health conditions. Morisky Medication Adherence scale (MMAS-8) and Medication Adherence Questionnaire (MAQ) have good sensitivity and specificity and are recommended to use in validated conditions with outcome data. The MMAS-8 questionnaire is not in the public domain and not validated for stroke. But the permission to use and validate in stroke was denied.

Prevalence of medication non-adherence among stroke survivors: Medication non-adherence is a major problem in both developing and developed countries. WHO report on non-adherence, estimated that over 30 -50 percent medicines prescribed for long term illnesses are not taken as directed (Sebateb, 2003). A study of over 3,000 patients in Germany reported that 84 percent were still taking aspirin at one year post-stroke, 77 percent oral anticoagulants, but only 61 percent who were prescribed clopidogrel at discharge were still taking it one year later. The reported medication adherence varies widely from 40- 85 percent among stroke survivors (Hamann et al, 2003; Kronish et al 201; Al Shaikh, 2016). The lowest ranges are from studies conducted in China and United States among low income under-privileged groups. No published study is available on medication adherence among stroke survivors is available.

Methodology

It was a cross sectional survey among hospital-based stroke survivors of first episode of stroke within a post-stroke period of three months to one year. The study was conducted the stroke clinic of

Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Thiruvananthapuram, which is a tertiary level referral hospital. The comprehensive stroke care unit admits 450-500 patients per year. The patients are followed up in the stroke clinic on an outpatient basis.

Stroke is defined as "Rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin". Survivors of first episode of stroke refers to the survivors of diagnosed cases of ischaemic stroke, haemorrhagic and transient ischemic attack with evidence of acute infarct. The study population for this cross sectional survey were the survivors of first episode of stroke within a post-stroke period of three months to one year.

The sample size for this study was determined based on the formula: $n=z\alpha^2 p (1-p)/d^2$, where $z\alpha$ = 1.96 at 95% confidence interval, p = prevalence of medication adherence among stroke survivors; taken as 40 percent and d = absolute precision of 7 percent. A sample size of 185 was calculated using Open Epi Software. Considering a non-response rate of 20 percent, the total sample size came out to be 222 participants. To round up, the total sample size estimated for this study was 240 participants.

Sampling criteria: Survivors of first episode of stroke aged 18 and above within a period of three months to one year were recruited for the cross sectional survey during the period, February 2019 to August 2019. Comatose, severely disabled [modified Rankin's Score (mRS) ≥ 5], having multiple coexisting diseases with life expectancy less than six months were excluded from the study.

Data collection tools and techniques: Structured interview schedule was used to collect basic sociodemographic data and medication adherence. Self-reported medication adherence was defined as consumption of at least more than 80 percent of their medications for last two weeks, based on their last prescription. The data on medication adherence was collected by interviewing the patient and primary care giver regarding the medication intake history of two weeks. Medication adherence was calculated for five categories of medication; antiplatelets, antihypertensives, antidiabetics, statin and anticoagulants. Overall adherence was defined adherence to all the categories of medication prescribed. The self-reported reasons for non-adherence were also collected from non-adherers.

Analysis: For meeting the objective, the proportion of patients who had consumed at least >80% of their medications for last two weeks, based on their last prescription was reported. Bivariate analysis with medication adherence as outcome variable and patients' characteristics was done to find out the factors associated with medication adherence.

Ethical considerations: The study was undertaken after obtaining clearance from Institutional Ethics Committee of Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala (SCT/IEC).

Results

Characteristics of the Study Participants: A group of 240 stroke survivors within a post-stroke period of three months to one year 240 numbers (n=240) participated. The mean age was 58.64±10.96 years. Females constituted 25.4 percent of the sample. Rural inhabitants were 76.7 percent. Among the participants 32.1 percent belonged to the category of poor households based on government classification. The work or employment status of 44.6 percent was affected by stroke. Nearly 5.4 percent had to go on long leave and 6.3 percent lost their jobs. The other demographic characteristics of the participants are given in Table 1.

Table 1: Demographic characteristics of the study participants

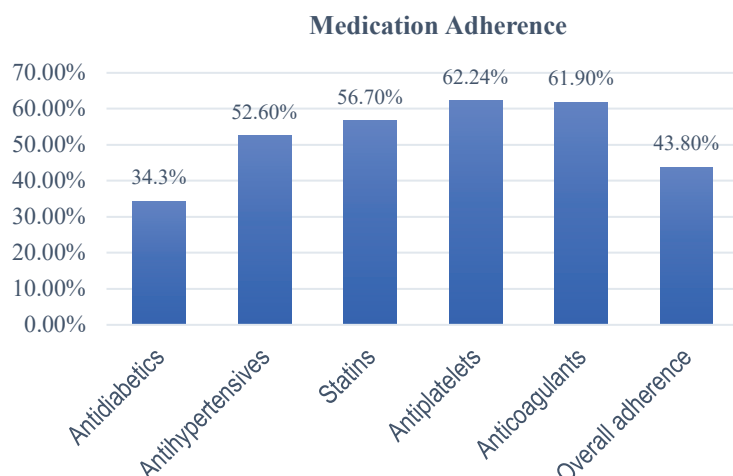| Variables	Categories	n (%)
Age	≤ 45 years > 45 years	31 (12.9) 209 (87.1)
Sex	Male Female	179 (74.6) 61 (25.4)
Place of residence	Rural Urban	184 (76.7) 56 (23.3)
Education of patient	Up to 10th standard Graduate professional	175 (72.9) 50 (20.8) 15 (6.3)
Occupation of patient	Manual laborer Skilled worker Professional Unemployed	141 (58.8) 77 (32.1) 14 (5.8) 8 (3.8)
House hold monthly income (Rupees)	< 1500 1500-5000 ≥5000	88 (36.7) 83 (34.6) 69 (28.8)
Enrolment in health insurance	Yes No	158 (65.8) 82 (34.2)
Nature of insurance	Government Private	134 (84.8) 24 (15.2)
Receiving financial assistance or free outpatient medication	Yes No	64 (26.7) 176 (73.3)
Civil supply card	Yellow Pink Blue White	2 (0.8) 75 (31.3) 82 (34.2) 81 (33.8)

Medication Adherence

Fig 1: Adherence to five categories of medication and overall adherence

Ischaemic stroke patients constituted 83.8 percent of the participants. The mean NIHSS score at ictus was 6.5 (5.9) and the mean mRS score at ictus was 1.2 (1.3). The mean NIHSS score at recruitment was 1.2 (2.2). Majority of the participants were with a post stroke period of three months to six months. The mean cost of medication per week was Rs. 377.96 (minimum 100; maximum 2000). Majority (68.5%) had medical insurance which covered their inpatient treatment expenditure, in which 84.8 percent had insurance provided from government agencies. Only 26.7 percent (n=64) had any form of assistance to cover the expenditure of their prescribed medications. In which 40.6 percent were getting reimbursement for their outpatient care and 59.4 percent were getting free medications from government hospitals. Nearly 90 percent of the patients received discharge education from the hospital at the

Table 2: Self-reported reasons for medication non-adherence

Self-reported reasons for medication non-adherence	Frequency (n)	Percentage (%)
Side effects	39	16.3
No need for medications	11	4.6
Forgetfulness	56	23.3
Journeys	37	15.4
Financial problems	84	35

Table 3: Anti-diabetic medication adherence for injectable and oral medication

Adherence	Injectable		OHA		Total	
	n	%	n	%	n	%
Yes	6	15.4	40	42.1	46	34.3
No	33	84.6	55	57.9	88	65.7
Total	39	100	95	100	134	100

time of discharge from hospital during index stroke. The discharge education was received from multiple sources by individual patients. The discharge education was received from treating physician by 77 percent, 43 percent received from nurses and 80 percent received it from other sources like physiotherapist and research coordinators. The components of discharge education included diet (67.5%), physical activity (77.1%), follow up care (60%) and regular intake of medication (79.2%).

Medication Adherence

Adherence to five categories of medications and overall adherence is shown in Figure 1 and self reported reasons for non adherence in Table 2. Adherence to anti-diabetic medication, separately for injectable and oral medication is given in Table 3. Medication adherence was highest for antiplatelet medications; the anticoagulants ranked second. Adherence was least for anti-diabetic medications. Overall medication adherence among stroke survivors was 43.8±6.27. The adherence to insulin therapy was very poor compared to oral hypoglycaemic agents. The most frequently reported reason (self-reported reasons among non-adherent participants) for medication non adherence was financial issue. Simple forgetfulness was reported by stroke survivors as a reason for their non-adherence to medications.

Medication adherence was high among those aged 45 years or below but the difference was not statistically significant. Higher medication adherence was observed among urban residents and people belonging to the category Above Poverty Line (APL) based on classification of government. Those who had more severe stroke in terms of neurological and functional disability were more adherent to medication. Presence of moderate to severe neurological disability at recruitment was also associated with medication adherence. The post-stroke period was not significantly associated with medication adherence. Medication adherence was not significantly different among stroke survivors for the other characteristics of the patients assessed in this study. The patients' characteristics and medication adherence are given in Table 4.

Discussion

This cross sectional survey revealed that adherence to medications intended to control risk factors and prevent stroke recurrence was very low (43.8%). The reported medication adherence varies widely in studies ranging from 40 percent to 85 percent (Hamann et al, 2003; Kronish et al, 2013; At Shaikh et al, 2016). The findings of this

Table 4: Patients' characteristics and medication adherence (N=240)

Variables	Categories	Adherence* Yes (n=105)		χ² value	p value
		n	%		
Age	≤ 45	18	58.1	1.94	0.085
	> 45	87	41.6		
Sex	Male	73	40.8	2.52	0.112
	Female	32	52.5		
Place of residence	Urban	31	55.4	3.99	0.046
	Rural	74	40.2		
Education of patient	High school	74	42.30	0.56	0.453
	Higher secondary and above	31	47.70		
Occupation	Skilled worker	43	47.3	0.73	0.393
	Unskilled worker	62	41.60		
Monthly income	<1500	37	42.05	0.654	0.721
	1500-5000	35	42.17		
	≥5000	33	47.83		
Enrolled in health insurance	Yes	74	46.84	1.789	0.181
	No	31	37.80		
Getting financial assistance for medication	Yes	30	46.86	0.346	0.556
	No	75	42.61		
Nature of civil supply card (dichotomized)	BPL	26	33.77	4.592	0.032
	APL	79	48.47		
Post stroke period	3-6 months	63	44.05	0.258	0.879
	6-9 months	14	45.16		
	9-12 months	28	41.17		
NIHSS at ictus	0-4	43	47.70	8.859	0.031
	5-15	44	44.44		
	16-20	12	60.00		
	21-42	6	85.71		
NIHSS at review	0-4	93	41.70	5.355	0.021
	5-15	12	70.58		
mRS	≤ 2	61	39.10	3.912	0.033
	> 2	44	52.38		
Received discharge education from hospital	Yes	95	45.24	1.512	0.219
	No	10	33.33		

*Outcome variable; Abbreviations: OR- Odds Ratio; CI- Confidence Interval; APL-Above Poverty Line; BPL-Below Poverty Line; NIHSS- National Institute Health Stroke Scale; mRS- modified Rankins Scale.

study in a low and middle income country are in agreement with those done among other low and underprivileged groups. A study conducted using validated adherence measure in a low income setting found out an adherence level of 40 percent among stroke survivors (Kronish et al, 2013). We used consumption of more than 80 percent of all the category of prescribed medications during last two weeks as an indicator of adherence. Our study result is similar to the one done using validated measure. We could reduce the recall bias as we had assessed the medication intake status of last two weeks only.

In this study the overall adherence, that is adherence to all the categories of medication prescribed for a patient was 43.8 percent. We had assessed adherence to individual categories of medication, which showed a highest adherence rate to antiplatelets (62.24%) and least adherence to anti-diabetic medication (33.3%). Adherence to anticoagulants was also higher compared to other categories (61.9%).

Adherence to antidiabetic medication was assessed separately for injectable and oral hypoglycaemic agents. Adherence to insulin was at least 15.4 percent. Even with a valid prescription people tend to alter the dose and timings and even skip the doses or take medications based on the perceived need. They tend to alter the dose based on their diet, physical activity, 'gut feeling', availability of insulin and accessories for injection and availability of personnel to administer insulin. Stroke patients who experienced feeding problems tend to alter the dose for fear of inadequate diet and over medication. Those who are taking OHA were more adherent 42.1 percent. The lower adherence to injectable agents created a lower overall adherence to anti diabetic medication. This result is contradictory to the result of a study conducted among patients on insulin in Chennai which reported an adherence of 80 percent to insulin (Sankar et al, 2015). But a community-based study conducted among rural inhabitants of Kerala showed and adherence of 26 percent to anti diabetic medication. They have also reported significantly different levels of medications adherence among those who receive OHA and insulin. Studies conducted in other countries showed an adherence level of 60 percent for insulin therapy (Alsayed & Ghoraba, 2018).

The effect of age, gender, income and education on medication adherence was inconsistent and varied in studies conducted in different settings. We found statistically non-significant higher adherence among females and those with higher education and professionals. In our present study, there was a significant difference between medication adherence among people belonging to poor and non-poor households. A study done in a developed country among stroke survivors also found no effect of income on medication adherence (Aziz et al, 2018). A systematic review of 21 studies showed almost similar level of poor medication adherence among patients with free medication and with different payment schemes (Al Shaikh et al, 2016). In contrast to

some qualitative study findings, we could not get any significant difference in adherence between those have care giver support and those without (Perreault et al, 2013; Al Shaikh et al, 2016). The most common self-reported reason for non-adherence was simple forgetfulness. Studies done in both developing and developed countries showed similar results Kronish et al, 2013; Al Shaikh et al, 2016). Presence of neurological deficits was associated with higher adherence. The initial step in the process of development of medication adherence behaviour is perceived need of medicine. The disability caused by stroke and subsequent perceived poor state of health thus remained a major facilitator for medication adherence.

Recommendations

This study had identified certain areas which require further explorations. A validated instrument to measure medication adherence is lacking in the public domain. Future studies can be undertaken to create a tool which accurately measures the medication adherence level and can be validated among stroke population. We have noticed adherence to insulin therapy was very low. Future qualitative studies can be undertaken to find out the perceptions and attitude of patients receiving insulin therapy. This study identified factors associated with medication adherence among stroke survivors; based on that, interventions can be designed and validated so that it can be widely utilised to improve medication adherence.

Nursing Implications

Nurses working in the clinical area can contribute to increase patient's adherence to their prescribed medication. Since forgetfulness is the common reason identified in almost all the settings, periodic reminders to care giver reminding or through text messages can help. An immediate care giver can be entrusted with this rile while discharging the patient. At every clinic visit people should be screened and asked for side effects of medication. Misconceptions about side effects of medications should be corrected through awareness programmes. Planned discharge education can be given to all patients regarding importance of adherence to medication and risk control.

Conclusion

In our study medication adherence among stroke survivors between three months to one year was very low. Since forgetfulness is the common reason identified in almost all the settings, periodic reminders in the form of care giver reminder or text messages to the care giver can help. At every clinical visit people should be screened and asked for side effects. Misconceptions about side effects of medications should be corrected by awareness programmes.

References

1. Burkhart PV, Sabaté E. Adherence to long-term therapies: Evidence for action. *Journal of Nursing Scholarship*: (Official publication of Sigma Theta Tau International Honor Society of Nursing) 2003; 35(3): 207

2. Thorogood M. Southern Africa stroke prevention initiative (SASPI) study. Bulletin of the World Health Organization 2004; 82: 503-508

3. Perreault S, Yu A, Cote A, et al. Adherence to antihypertensive agents after ischemic stroke and risk of cardiovascular outcomes. *Neurology* 2012; 79: 2037-43

4. Mayor S. Non-adherence to medication increases stroke risk in patients with high blood pressure. *BMJ* 2013; 347: f4586

5. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care* 2013; 43: 521-30

6. Cutler RL, Fernandez-Llimos F, Frommer M, et al. Economic impact of medication non-adherence by disease groups: a systematic review. *BMJ Open* 2018; 8: e016982. doi: 10.1136/bmjopen-2017-016982

7. Sebateb E. Adherence to long term therapies: Evidence to action. World Health Organisation. Geneva; 2003, p 3-45

8. Bissonnette JM. Adherence: A concept analysis. *Journal of Advanced Nursing* 2008; 63(6): 634-43

9. Philip LA, Leventhal H. Using Habit Theory and Commonsense Self-regulation Theory to Improve Medication Adherence Assessment. Graduate School-New Brunswick Rutgers. The State University of New Jersey; 2011

10. Hamann GF, Weimar C, Glahn J, et al. Adherence to secondary stroke prevention strategies - results from the German Stroke Data Bank. *Cerebrovascular Disease* 2003;15: 282-88

11. Kronish IM, Diefenbach MA, Edmondson DE. Key barriers to Medication Adherence in survivors of strokes and transient ischemic attacks. *Journal of General Internal Medicine* 2013; 28 (5): 675-82

12. Al Shaikh S, Quinn T, Dunn W, et al. Predictive factors of non-adherence to secondary preventative medication after stroke or transient ischaemic attack: A systematic review and meta-analyses. *Eur Stroke J* 2016; 1(2): 65-75. doi: 10.1177/2396987316647187

13. Sankar UV, Lipska K, Mini GK, et al. The adherence to medications in diabetic patients in rural Kerala, India. *Asia Pac J Public Health* 2015; 27(2): NP513-23. doi: 10.1177/1010539513475651

14. Alsayed KA, Ghoraba MK. Assessment of diabetic patients' adherence to insulin injections on basal-bolus regimen in diabetic care center in Saudi Arabia 2018: Cross sectional survey. *J Family Med Prim Care* 2018; 2(8): 1964-70

15. Aziz H, Md Hatah E, Makmor Bakry M, Islahudin F. How payment scheme affects patients' adherence to medications? A systematic review. Dove Medical Press 2018; 10: 837-50