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Ethnic Differences in 90-day Post-Stroke Medication Adherence

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Abstract

Background and Purpose: We assessed ethnic differences in medication adherence 3 months post-stroke in a population-based study as an initial step in investigating the increased stroke recurrence risk in Mexican Americans compared with non-Hispanic whites.

Methods: Ischemic stroke cases from 2008–2015 from the Brain Attack Surveillance in Corpus Christi (BASIC) project in Texas, were followed prospectively for three months post-stroke to assess medication adherence. Medications in five drug-classes were analyzed: statins, antiplatelets, anticoagulants, antihypertensives, and antidepressants. For each drug class, patients were considered adherent if they reported never missing a dose in a typical week. Chi-square tests or Kruskal-Wallis non-parametric tests were used for ethnic comparisons of demographics, risk factors and medication adherence. A multivariable logistic regression model was constructed for the association of ethnicity and medication non-adherence.

Results: Mexican Americans (n=692) were younger (median 65 years versus 68 years, p<0.001), had more diabetes (p<0.001) and hypertension (p<0.001) and less atrial fibrillation (p =0.003), smoking (p=0.003), and education (p<0.001) than Non-Hispanic Whites (n=422). Sex, insurance status, high cholesterol, previous stroke/TIA history, excessive alcohol use, tPA treatment, NIHSS score, and comorbidity index did not significantly differ by ethnicity. There was no significant difference in medication adherence for any of the five drug classes between Mexican Americans and Non-Hispanic Whites.

Conclusions: This study did not find ethnic differences in medication adherence, thus challenging this patient-level factor as an explanation for stroke recurrence disparities. Other reasons for the excessive stroke recurrence burden in Mexican Americans, including provider and health system factors, should be explored.

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Keywords

Stroke; medication adherence; disparities; Mexican American

Subject Terms:

Secondary Prevention; Cerebrovascular Disease/Stroke; Ischemic Stroke

Introduction

Stroke is a leading cause of death and disability in the United States[1]. Recurrence is common, accounting for nearly 20% of all strokes[2], and the greatest risk for recurrence is within one year of incident stroke[3]. Compared to first stroke, secondary stroke is associated with greater economic burden, disability, and mortality[4, 5]. Particularly concerning is the fact that racial and ethnic minorities, including Mexican Americans (MAs), have higher stroke recurrence rates than non-Hispanic Whites (NHWs)[6].

Secondary stroke prevention includes identification of risk factors and guideline-concordant treatment including pharmacotherapy[7]. Ischemic stroke patients are often prescribed several classes of medications aimed at managing recurrent stroke risk factors. These classes include antihypertensives, anticoagulants, antiplatelets, and statins[7]. Proper use of these medications can lower recurrent stroke risk by as much as 68%[8–10]. Antidepressants can potentially further reduce stroke risk by improving risk factor management as depressed patients are 1.76 times more likely to be non-adherent to long-term medications[11].

Despite the effectiveness of these medications, post-stroke medication adherence can be as low as 50%[12–14]. Studies of other conditions requiring long-term management, including other cardiovascular conditions, have found particularly low medication adherence in some racial and ethnic minorities including Hispanics[15–18]; however, little is known about post-stroke medication adherence, especially in MAs[13].

In the present study, we examine the prevalence of 90-day post-stroke medication adherence in NHWs and MAs as an initial step to explore whether differences in adherence could contribute to disparate recurrence rates between NHW and MA ischemic stroke patients. If an association between ethnicity and stroke medication adherence is found, subsequent investigations could explore the extent to which improvements in medication adherence might reduce ethnic stroke recurrence disparities.

Materials and Methods

The de-identified data that support the findings of this study are available from the corresponding author upon reasonable request from a qualified investigator as long as it conforms to HIPAA protection, IRB study approvals and data use agreements that the study team has with the participating hospitals.

The Brain Attack Surveillance in Corpus Christi (BASIC) project is a population-based surveillance study of stroke in Nueces County in South Texas, USA. Nueces County is a non-immigrant, predominantly urban community of 361,000 people, of whom approximately 63% identify as MA and 30% identify as NHW[19]. Detailed BASIC methods have been published elsewhere[20,21].

Briefly, first-ever and recurrent ischemic stroke patients older than 45 years from 2008–2015 were identified by trained abstractors through active screening of hospital emergency department and inpatient logs for stroke symptoms. This was supplemented by passive screening of both emergency department and inpatient registers utilizing International Classification of Diseases (ICD) 9–10 codes in discharge logs. Only the first stroke captured by BASIC was included. Strokes were then validated by stroke study physicians using source documentation masked to age and ethnicity. Eligible patients were approached by study coordinators for participation in the interview portion of the study. Participant charts were abstracted for demographic and clinical information including age, sex, insurance status, chronic conditions (atrial fibrillation, hypercholesterolemia, diabetes, hypertension, history of stroke/transient ischemic attack (TIA)), current/former smoker status, excessive alcohol use, initial National Institutes of Health Stroke Scale (NIHSS) score, and tissue Plasminogen Activator (tPA) use. If NIHSS was not recorded, it was abstracted from the chart based on symptoms using a previously validated measure[22]. A comorbidity index was calculated as the sum of the following conditions: Alzheimer's, atrial fibrillation, cancer, chronic obstructive pulmonary disease, congestive heart failure, coronary artery disease, excessive alcohol use, dementia, diabetes mellitus, end-stage renal disease, epilepsy, high cholesterol, hypertension, myocardial infarction, Parkinson's, stroke history, and smoking. Soon after the stroke, participants completed a baseline interview, in which they reported their race-ethnicity and highest level of education. If self-reported race-ethnicity was not available, the ethnicity from the medical record was used.

Participants were interviewed again approximately 90 days following stroke. During this interview, subjects were asked to report the medications they were currently taking. For each medication, participants were asked "How often in a typical week do you miss a prescribed dose?" to which they were able to respond Never, Rarely, Occasionally, Often, Very Often, Discontinued, or Don't know[23]. Participants residing in nursing home at the time of the 90-day interview were excluded from the analysis as they are presumably administered their drugs regularly.

This study was approved by the University of Michigan Institutional Review Board (IRB) and the IRBs of both Corpus Christi hospital systems (Christus Spohn Health System and Corpus Christi Medical Center). Informed consent was obtained from the patient or a proxy if the patient was comatose or otherwise unable to give consent.

Data Analysis

Only MA and NHW participants were included in this analysis. Chi-square and Kruskal-Wallis tests were used to compare characteristics of included versus excluded patients by ethnicity. Descriptive statistics and prevalence of non-adherence by drug class were summarized overall and by ethnicity of included participants. To assess ethnic differences in

medication non-adherence, logistic regression models were fit with non-adherence for each drug class as the outcomes. In the crude models, ethnic differences comparing MA and NHW were estimated using an indicator variable of ethnicity. The models were then adjusted for age, sex, NIHSS, insurance (private or Medicare vs uninsured or Medicaid), and education. Age and NIHSS were modeled linearly. Adjustments were made for basic demographic and clinical variables potentially related to medication non-adherence and associated with stroke recurrence as discussed in the American Heart Association Secondary Stroke Prevention Guidelines[7]. To explore whether the use of other medications (a hypothesized proxy for comorbidity) was associated with non-adherence and would need to be adjusted for in the model, we used two separate logistic regression models with number of drug classes and total number of medications (both continuous and categorical) per subject as the predictor, and non-adherence as the outcome. To be consistent with previous research, we defined adherence as never missing a dose in a typical week[23]. To determine whether a more inclusive definition of adherence would change the results, we re-ran the analyses defining adherence as never or rarely missing a dose as a sensitivity analysis. Since we modeled non-adherence as our outcome, this more inclusive definition of adherence resulted in fewer events of non-adherence.

Results

During the study period November 2008 to December 2015, 2,912 ischemic stroke cases were identified, of which 1,119 were NHW and 1,577 were MA. Of those 2,696 cases, 145 could not be located for the BASIC baseline interview, 566 refused study participation, 73 were interviewed for baseline too late for follow up (>4.5 months post-stroke), and 22 had incomplete data (10 incomplete, 12 previously interviewed in BASIC and therefore excluded per protocol). Of the 1,890 who completed the BASIC baseline interview, 1,636 were alive at the time of the 90-day interview. Of those, 159 could not be located, 143 refused the 90-day interview, 37 had no interview for other reasons, and 39 had incomplete data. Of the remaining 1,258 cases, 144 were living in a nursing home, leaving 1,114 cases for the analysis.

Compared to excluded NHW patients, included NHW patients were younger (68 vs 73 years, $p<0.001$); had lower initial NIHSS (3 vs 4, $p<0.01$), had lower prevalence of atrial fibrillation (16% vs 24%, $p<0.01$) and hypertension (73% vs 79% $p<0.01$); and higher prevalence of high cholesterol (52% vs 43%, $p<0.01$). Compared to excluded MAs, included MAs were younger (65 vs 68, $p<0.001$) and had lower initial NIHSS (3 vs 4, $p<0.05$). Notably, included and excluded MAs and NHWs did not differ by the total comorbidity index (Supplementary Table I-- please see http://stroke.ahajournals.org).

Included patient characteristics are summarized in Table 1. Compared with NHWs, MAs were significantly younger (65 vs 68 years), had less educational attainment, and had higher prevalence of diabetes (47.7% vs 30.8%) and hypertension (85.7% vs 73.5%), all $p<0.001$. NHWs had higher prevalence of current or former smoking (46.1% vs 36.9%) and atrial fibrillation (16.4% vs 10.3%) ($p=0.003$). MAs and NHWs were otherwise similar in sex, insurance, cholesterol, history of stroke/TIA, excessive alcohol use, treatment with tPA, NIHSS, and comorbidity index. Non-adherence was not associated with increasing number

of total medications or by number of medication classes (indicators of comorbidity), so comorbidity was not adjusted for in the multivariable model (Supplementary Tables II and III--please see http://stroke.ahajournals.org). As the total number of medications (continuous) was only marginally nonsignificant, we added this variable into the model in a sensitivity analysis. The results remained largely unchanged, other than the association between insurance status and nonadherence becoming marginally nonsignificant for antiplatelets (Supplementary Table IV--please see http://stroke.ahajournals.org).

Overall non-adherence for each drug class ranged from 14%–20% and did not differ by ethnicity (Table 2). The crude odds of being non-adherent by medication class between MAs and NHWs were not significant (Table 3). The results remained similar after adjusting for age, sex, NIHSS, insurance, and education. Increasing age (per 1-year increase) was associated with a lower odds of being non-adherent for antiplatelets (OR 0.98, CI 0.96–1.00), antihypertensives (OR 0.97, CI 0.95–0.99), and statins (OR 0.98, CI 0.96–1.00). Additionally, non-adherence was less likely in patients having private or Medicare insurance compared to uninsured and Medicaid for antiplatelets (OR 0.60, CI 0.38–0.95), statins (OR 0.59, CI 0.35–0.98), and antidepressants (OR 0.27, CI 0.08–0.84). Sex, NIHSS, and education were not associated with non-adherence.

The sensitivity analysis for more broadly defining adherence to include those who rarely missed a dose, found largely no change in results (Table 4). The numbers of non-adherent events by each medication class using this alternate definition for non-adherence are summarized in Supplementary Table V.

Discussion

Our study found no difference in 90-day post-stroke medication adherence between MAs and NHWs in a large, bi-ethnic community, suggesting that ethnic differences in medication adherence are an unlikely contributor to the higher rate of stroke recurrence in MAs[6]. The association between non-adherence and ethnicity was nonsignificant before and after adjustment for age, sex, insurance status, NIHSS, and education. It also remained nonsignificant with variation in the definition of adherence.

The lack of association of non-adherence and ethnicity is notable as previous studies have reported higher rates of non-adherence to medications for conditions such as hypertension, hypercholesterolemia, and depression in Hispanics compared to NHWs[15,24]. This may be due to overall higher adherence to medications in people with a history of stroke[24]; although reports of medication adherence post-stroke vary widely from 50–95%[12–14, 25]. Most studies reporting rates of post-stroke medication adherence have limited the analysis to NHWs and African Americans[12,25]; however one study reported greater non-adherence in the African American and Hispanic combined group compared to NHWs in people reporting stroke in the past five years[13]. Our study looked at 90-day adherence, as this is the time period for greatest risk for recurrent stroke[26]. However, longer follow-up may be needed to show ethnic differences in non-adherence. We were unable to examine a possible interaction of medication non-adherence, ethnicity and stroke recurrence, such that non-adherence may

confer greater recurrence risk in one ethnic group compared with another. Future studies should consider this.

Aside from ethnicity, we found that having Medicaid or being uninsured was significantly associated with non-adherence to antiplatelets, statins, and antidepressants compared to having private insurance or Medicare. Our finding supports previous research reporting a nearly 60% higher likelihood of adherence comparing those with insurance to those without at 12 months post-stroke[25]. This same study also reported a 47% increased likelihood of adherence comparing those with an adequate income to meet their household needs with those who do not have adequate incomes[25], although the current study does not report participant income data. Together, this suggests a possibility that non-adherence in the underinsured/uninsured group may be related to medication cost. Importantly, one study found overall healthcare system savings associated with medication adherence, reporting that increased pharmacy costs are outweighed by savings from less emergency room and inpatient spending[27]. This could be especially relevant for systems caring for stroke patients, as recurrent strokes are more debilitating and costly than first strokes[4,5]. Insurance companies and hospitals who pay for the cost of readmissions to the hospital for uninsured and underinsured individuals may consider improving post-stroke medication accessibility. Increasing insurance coverage for individuals is also likely to be helpful.

It is tempting for healthcare professionals to point to patient-level behaviors, such as medication adherence, that could contribute to ethnic health disparities[28]. This potentially misguided belief that a minority individual or group is non-adherent to medications could have potentially harmful effects on the treatment of minority patients[29]. Future research should investigate other modifiable factors, including physician behaviors that may contribute to ethnic disparities in stroke recurrence.

There are some important limitations to our study. Our medication adherence data was self-reported and therefore subject to participant social desirability bias, potentially artificially inflating the reports of medication adherence. We expect this would be non-differential by ethnicity and could attenuate associations. Also, we did not have data on whether or for how long a patient was taking a drug prior to the stroke, which has been shown to be associated with adherence[14]. While a few differences exist, there were no ethnic difference in the associations between participation and insurance status and age, variables associated with non-adherence. This implies the ethnic differences in participation were non-differential and might bias the associations towards the null. This study was done in one community and needs to be validated in others.

The large variability in the measurements and definitions of medication adherence is a limitation to the medication adherence literature in general, as it limits effective comparison of findings across studies. In the post-stroke medication literature, there is a large variability in the time adherence is measured relative to date of stroke[12,13,25]. Studies may also use self-report data or prescription refill data to measure adherence, and cut-offs to define adherence vary. In response to this limitation, we conducted a sensitivity analysis using a different cutoff for adherence and found no significant changes to our results. Future work should

come to a consensus upon what is optimal medication adherence, and what is the best method to measure adherence data in patients.

Our study also has strengths. There are very few studies that have looked at racial/ethnic differences in post-stroke medication adherence, and of those most are limited to differences between African Americans and NHWs[12,25]. We examined medication non-adherence 90-day post-stroke using a large sample of MAs and NHWs, allowing identification of even small differences in medication non-adherence by ethnicity and also the ability to correct for many potential confounders.

The study also looked at post-stroke adherence to antidepressants, the confidence intervals for non-adherence to antidepressants were large, indicating the estimate of the effect is unstable. Although this drug class is not generally thought of as central for secondary stroke prevention, it is known that post-stroke depression is highly prevalent[30] and 90-day post stroke depression is a predictor of 15 month post-stroke functional outcome[31]. Given the high prevalence of post-stroke depression, future studies need to investigate the association of the use of antidepressants post-stroke and stroke recurrence.

Summary/Conclusions

We found no ethnic differences in medication adherence 90-days post-stroke. However, prevalence of non-adherence for both ethnic groups is high, leaving room for improvement. Future research should target other patient, provider and health system-level variables that may contribute to the large stroke recurrence disparity in MAs and NHWs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Baseline characteristics of included participants

	Overall (N=1114)		MA (N=692)		NHW (N=422)		
	N or Median	% or (Q1, Q3)	N or Median	% or (Q1, Q3)	N or Median	% or (Q1, Q3)	P
Age	66	(58, 77)	65	(57, 75)	68	(60, 79)	<0.001
Female	560	50.3	353	51.0	207	49.1	0.53
Total Insured	1000	89.8	616	89.0	384	91.2	0.24
Education							
Less than HS	184	16.5	174	25.2	10	2.4	<0.001
HS	511	45.9	339	49.1	172	40.8	
Vocational/some college	267	24	128	18.5	139	32.9	
College or more	151	13.6	50	7.2	101	23.9	
Atrial fibrillation	140	12.6	71	10.3	69	16.4	<0.01
High Cholesterol	577	51.8	357	51.6	220	52.1	0.86
Diabetes	531	47.7	401	57.9	130	30.8	<0.001
Hypertension	903	81.1	593	85.7	310	73.5	<0.001
History of Stroke or TIA	297	26.7	189	27.3	108	25.7	0.54
Current/former smoker	449	40.4	255	36.9	194	46.1	<0.01
Excessive alcohol	84	7.5	48	6.9	36	8.6	0.32
Treated with TPA	136	12.2	75	10.8	61	14.5	0.07
NIHSS *	3	(1, 6)	4	(2, 8)	3	(1, 7)	0.12
Comorbidity index †	3	(2, 5)	3	(2, 5)	3	(2, 5)	0.17

MA= Mexican American, NHW=Non-Hispanic White, HS= High school, TIA= transient ischemic attack, TPA=tissue plasminogen activator, NIHSS=National Institute of Health Stroke Scale

Chi-square test for categorical variable, Kruskal-Wallis non-parametric test for continuous variables

* NIHSS 0.36% missing

† Comorbidity 0.27% missing

Table 2.

Prevalence of Non-adherence by Medication Class

	Overall			MA			NHW		
	N	Missed	%	N	Missed	%	N	Missed	%
Antiplatelets	914	184	20.1	574	117	20.4	340	67	19.7
Anticoagulants	173	27	15.6	82	13	15.9	91	14	15.4
Antihypertensives	917	158	17.2	585	107	18.3	332	51	15.4
Statins	819	146	17.8	504	98	19.4	315	48	15.2
Antidepressants	177	25	14.1	105	16	15.2	72	9	12.5

MA=Mexican Americans, NHW=Non-Hispanic Whites, Missed=non-adherent

Table 3.

Crude and Multivariable Models of the Association of Ethnicity and Medication Non-adherence 90 days post-stroke

	Multivariable Models				
	Antiplatelets (n=914)	**Anticoagulants (n=173)**	**Antihyperten-sives (n=917)**	**Statins (n=819)**	**Antidepress-ants (n=177)**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
MA (v NHW)	0.92 (0.64–1.33)	1.13 (0.43–2.97)	1.00 (0.67–1.49)	1.15 (0.76–1.73)	1.20 (0.45–3.22)
Age	0.98 (0.96–1.00)	0.97 (0.94–1.02)	0.97 (0.95–0.99)	0.98 (0.96–1.00)	0.97 (0.93–1.02)
Female (v Male)	0.83 (0.60–1.15)	1.11 (0.47–2.62)	0.94 (0.66–1.33)	1.07 (0.74–1.54)	1.01 (0.39–2.60)
NIHSS	0.99 (0.95–1.03)	0.93 (0.85–1.02)	0.98 (0.94–1.02)	0.97 (0.93–1.01)	1.00 (0.92–1.08)
Private and Medicare (v none and Medicaid)	0.6 (0.38–0.95)	1.13 (0.24–5.33)	0.71 (0.43–1.16)	0.59 (0.35–0.98)	0.27 (0.08–0.84)
HS education	1.02 (0.61–1.71)	1.55 (0.36–6.76)	1.20 (0.70–2.05)	1.29 (0.73–2.27)	1.49 (0.27–8.18)
Vocational/some college	0.96 (0.54–1.72)	1.43 (0.29–7.12)	0.74 (0.39–1.40)	0.79 (0.40–1.53)	1.01 (0.15–6.76)
College or more	0.72 (0.36–1.43)	1.59 (0.25–10.22)	0.76 (0.36–1.60)	0.81 (0.37–1.77)	0.75 (0.08–7.14)
Crude: MA (v NHW) *	1.04 (0.75–1.46)	1.04 (0.46–2.36)	1.23 (0.86–1.78)	1.34 (0.92–1.96)	1.26 (0.52–3.03)

MA=Mexican American, NHW=Non-Hispanic White, NIHSS=National Institute of Health Stroke Scale, HS= High school

No high school is the reference category for education

Adherence defined as never missing a dose

Estimates obtained from a logistic regression

* Obtained from crude model and limited to cases with complete data on variables included in adjusted model

Table 4.

Sensitivity Analysis for Multivariable Model of Association of Ethnicity and 90-day Medication Non-adherence

	Multivariable Models				
	Antiplatelets (n=914)	**Anticoagulants (n=173)**	**Antihyperten-sives (n=917)**	**Statins (n=819)**	**Antidepress-ants (n=177)**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
MA(v NHW)	0.93 (0.59–1.49)	0.74 (0.18–3.02)	1.19 (0.66–2.16)	1.36 (0.72–2.56)	2.75 (0.73–10.33)
Age	0.99 (0.97–1.01)	0.94 (0.89–1.00)	0.97 (0.94–0.99)	0.97 (0.94–1.00)	0.97 (0.92–1.02)
Female (v Male)	1.07 (0.71–1.62)	2.48 (0.58–10.53)	1.26 (0.76–2.09)	2.03 (1.16–3.55)	0.61 (0.20–1.89)
NIHSS	0.99 (0.95–1.03)	0.98 (0.86–1.11)	0.99 (0.94–1.04)	0.97 (0.91–1.03)	0.99 (0.90–1.09)
Private and Medicare (v none and Medicaid)	0.42 (0.24–0.72)	-	0.47 (0.25–0.89)*	0.26 (0.13–0.49)	-
HS education	1.13 (0.60–2.15)	-	1.72 (0.76–3.91)	1.12 (0.50–2.54)	-
Vocational/some college	0.73 (0.34–1.55)	-	0.63 (0.22–1.79)	0.33 (0.11–1.00)	-
College or more	0.83 (0.35–1.95)	-	1.14 (0.37–3.46)	1.33 (0.45–3.89)	-

MA=Mexican American, NHW=Non-Hispanic White, NIHSS= NIH Stroke Scale, HS=high school

No high school is reference category for education

Adherence defined as never or rarely missing a dose