Geriatric Nursing 38 (2017) 141–145

Contents lists available at ScienceDirect

Geriatric Nursing

journal homepage: www.gnjournal.com

Feature Article

The association between antidepressant use and hemoglobin A1C in older adults

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ARTICLE INFO

Article history:
Received 25 July 2016
Received in revised form
6 September 2016
Accepted 12 September 2016
Available online 11 October 2016

Keywords:
Diabetes
Antidepressants

ABSTRACT

Depression is known to increase diabetes risk and worsen glycemic control in older adults, who already experience high rates of diabetes. The independent impact of antidepressants on glucose control is less clear. Data was drawn from the Health and Retirement Study, a large nationally-representative longitudinal study of retired individuals. Crude and adjusted linear models stratified by diabetes status were used to examine the cross-sectional associations between antidepressant use categorized by subclass and continuous hemoglobin A1C. The sample included 1,153 individuals, most over the age of 70. Antidepressant use was not associated with hemoglobin A1C in any model whether stratified or in the total combined sample. Antidepressants as a class were also not associated with hemoglobin A1C. These findings add to the literature suggesting that antidepressants are not associated with diabetes risk or glycemic control. Prospective studies with larger sample sizes are needed to confirm this finding.

Introduction

The prevalence of antidepressant use among those 60 and older is 15%, which is similar to use among those 40 to 59.[1] However, prior research has found that depression is undertreated among older adults,[2] which may partly be caused by concerns about side-effects. Clinically, it is important to address the possibility of adverse events due to antidepressant use in older adults, as this age group may be more susceptible because of already poorer health,[3] higher numbers on other medications,[3] and metabolic differences.[4] Antidepressants have previously been shown to have other adverse effects in older adults, including increased risk of stroke, heart attack, and mortality.[5] While depression is known to worsen glucose-related health outcomes among the elderly[6,7] who already experience high rates of diabetes and pre-diabetes,[8,9] the independent impact of antidepressants is less clear. Furthermore, another class of psychotropic medications, antipsychotics, has been shown to increase the risk for several cardiometabolic outcomes including diabetes. Hypothesized mechanisms through which antipsychotics may impact glucose levels include weight gain, increased insulin resistance, and higher leptin levels.[10]

The literature on the effects of antidepressants on glycemic outcomes is mixed. Some previous studies have found that antidepressant use is associated with incident diabetes and poorer glycemic control while other findings suggest no association or that some antidepressants may improve glycemic control. One meta-analysis[11] that included a set of trials performed during the 1990s found no significant change in hemoglobin A1C associated with the selective serotonin reuptake inhibitor (SSRI) fluoxetine among individuals with diabetes. On the other hand, a more recent randomized control trial carried out in a sample of adults under 65 with diabetes found that fluoxetine improved hemoglobin A1C, though the association was not statistically significant.[12] The SSRI sertraline was also found to improve hemoglobin A1C among individuals with depression and poorly controlled diabetes[13] and among low income minority individuals with diabetes.[14] Another randomized control trial found the tricyclic antidepressant (TCA) nortriptyline did not improve hemoglobin A1C among individuals with diabetes.[15] A study that measured the association between antidepressant use and several glucose-related measures using a cross-sectional design within a large nationally-representative sample without diabetes found no significant difference in hemoglobin A1C between antidepressant users and non-users.[16] This

No disclosures to report.

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http://dx.doi.org/10.1016/j.gerinurse.2016.09.002

study also found no association when analyses were broken out by subclass or when testing for interactions with age or other characteristics. The association between hemoglobin A1C and antidepressants other than SSRIs and TCAs, such as serotonin-norepinephrine reuptake-inhibitors (SNRIs), has been less well investigated.

The mechanism through which antidepressants may lead to changes in hemoglobin A1C remains unclear. While antidepressants can lead to weight gain or loss,[17] depending on the specific medication, other research has found an association between antidepressants and glucose changes independent of BMI. For example, one study found mood improvements resulting from the use of bupropion led to improved glucose levels independent of changes in self care behaviors or BMI after prolonged use.[18]

The aim of the current study is to preliminarily examine the cross-sectional associations between antidepressant use, as measured by subclass, and continuous hemoglobin A1C among a sample of older adults stratified by diabetes status.

Methods

Participants

The Health and Retirement Study (HRS), funded by the Social Security Administration and the National Institute on Aging, is a longitudinal study of the older population in the United States that has collected economic, health, and other data from nationally-representative samples of about 20,000 individuals over the age of 50 every two years since 1992.[19] In 2007, the HRS collected information on prescription drug use as part of the second wave of its Prescription Drug Study that was used to measure the impact of Medicare policy changes implemented in 2006 on the use of prescription drugs. The HRS 2007 Prescription Drug Study is sponsored by the National Institute on Aging (grant number NIA U01AG009740) and was conducted by the University of Michigan.[20] Individuals with low income and those without prescription coverage were oversampled at the time data was collected for the first wave in 2005.[21] The HRS also measured hemoglobin A1C in dry blood spots collected from a random sample of respondents during the 2008 wave of the core survey. Individuals living in a nursing home or with proxy respondents were excluded. Samples were analyzed at either the Biosafe or Flexsite laboratory.[22] All covariate information was obtained from either core survey items collected during the 2008 wave of the study (age, smoking status, diabetes status, having experienced a depressive episode in the past year, and body mass index) or the cross-wave tracker file (gender, race/ethnicity, and education level), both of which are publicly available. A total of 1,153 individuals with complete data were included in both the 2007 prescription drug study and 2008 biomarker samples. The Internal Review Board of the State University of New York at Albany approved the human subject protection of this study.

Variables

The outcome of interest in this study was the association between continuous hemoglobin A1C and exposure to antidepressants including SNRIs, SSRIs, TCAs, other antidepressant subclasses, and multiple antidepressant subclasses. Covariates included gender (male or female), age category (<70, 70–79, 80+), race/ethnicity (African-American, Hispanic, White, or other race/ethnicity), education level (less than high school, high school, or more than high school), smoking status (current smoker or non-smoker), having experienced a depressive episode in the past year (yes or no), and body mass index (<25, 25–29, ≥30). Analyses were stratified by diabetes status (ever or never diagnosed). Depressive episode experience was indicated by responses to a set of items taken from the short form Composite International Diagnostic Interview (CIDI). These 33 items assessed whether the interviewee experienced appetite changes, loss of interest, trouble sleeping, feelings of low mood, and/or other depression symptoms for most or all of the day for two weeks or longer within the past year. The original CIDI was created in the 1980s at the request of the World Health Organization for use by lay interviewers in measuring the prevalence and predictors of depression and other psychological conditions within the general population.[23] The CIDI has been shown to provide a reliable and valid measure of the presence of psychiatric conditions.[24] Short form versions of the CIDI have been shown to provide

Table 1
HRS sample characteristics.

Variable	Category	Frequency	%
Antidepressant subclass	SNRI	12	1.0
	SSRI	70	6.1
	TCA	29	2.5
	Other	16	1.4
	Multiple	21	1.8
	None	1005	87.2
Age category	<70	356	30.9
	70–79	520	45.1
	80+	277	24.0
Gender	Male	485	42.1
	Female	668	57.9
Race/ethnicity	African-American	131	11.4
	Hispanic	102	8.8
	Other race/ethnicity	25	2.2
	White	895	77.6
Education	Less than high school	291	25.2
	High school	441	38.2
	More than high school	421	36.5
Smoking status	Non-smoker	1039	90.1
	Current smoker	114	9.9
Depression status	No depressive episode	1070	92.8
	Depressive episode	83	7.2
BMI category	Under 25	372	32.3
	25 to 29	423	36.7
	30 or higher	358	31.0
Diabetes status	No diabetes	857	74.3
	Diabetes	296	25.7
Total		1153	100.00

TCA = tricyclic antidepressant; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin-norepinephrine reuptake inhibitor.

Table 2
Frequency of specific antidepressants in HRS sample.

Antidepressant	Subclass	Frequency	%
Amitriptyline	TCA	27	15.9
Sertraline	SSRI	22	12.9
Fluoxetine	SSRI	17	10.0
Escitalopram	SSRI	17	10.0
Trazodone	Other	15	8.8
Citalopram	SSRI	13	7.7
Venlafaxine	SNRI	12	7.1
Paroxetine	SSRI	12	7.1
Bupropion	Other	9	5.3
Duloxetine	SNRI	9	5.3
Doxepin	TCA	6	3.5
Nortriptyline	TCA	5	2.9
Mirtazapine	Other	2	1.2
Imipramine	TCA	2	1.2
Nefazodone	Other	1	.6
Amoxapine	TCA	1	.6
Total		170	100.0

TCA = tricyclic antidepressant; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin-norepinephrine reuptake inhibitor.