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Antipsychotic Use Among Nursing Home Residents Admitted with Hip Fracture

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Abstract

Background/Objectives—Widespread use of antipsychotic medications among skilled nursing home (NH) residents for off-label indications has become a concern of clinicians and policy makers. The objective of this study was to evaluate the association between receiving antipsychotics and the outcomes of a cohort of NH patients with and without presumed delirium after hip fracture.

Design—Population based cohort study.

Setting—11,119 nursing homes nationwide, from 01 January 2000 to 31 December 2007.

Participants—First-time NH admits with hip fracture (N=77,759).

Measurements—The Nursing Home Confusion Assessment Method was utilized to identify residents with no delirium, subsyndromal delirium, and full delirium. Propensity score reweighting was used with analyses stratified by delirium level.

Results—Among patients with no delirium symptoms, about 5 percent (n = 3,250) received antipsychotic drugs. These individuals were less likely to be discharged home (OR 0.68; P < 0.001), had a higher likelihood of death prior to nursing home discharge (OR 1.28; P = 0.03), stayed in nursing homes longer (β 2.83; P = 0.05), and had less functional improvement at discharge (β -0.47; P = 0.03). Receipt of antipsychotics among participants with mild delirium was associated with a lower likelihood of discharge home (OR 0.74; P = 0.03).

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Potential Conflicts of Interest:

Dr. Mor is a co-founder PointRight (formerly LTCQ, Inc.) and currently serves as a member of its Board of Directors.

Conclusion—Among NH residents with hip fracture and no delirium symptoms, use of antipsychotics was associated with worse outcomes, with the exception of rehospitalization. No clear benefits were associated with antipsychotic use for those with presumed delirium.

Keywords

Skilled Nursing Facility; Delirium; Antipsychotics

INTRODUCTION

The use of atypical antipsychotic medications among nursing home (NH) residents has become an important concern. Originally developed as a treatment for psychoses and mood disorders, antipsychotics are widely prescribed to elderly patients for off-label conditions such as those with various forms of dementia.¹⁻⁴ As recently as 2006, nearly one-third of newly admitted NH residents was given at least one antipsychotic medication, 32 percent of which did not have an indication for these drugs as specified by the United States Food and Drug Administration (FDA).⁵

After a review of 17 randomized, placebo controlled trials revealed that the use of atypical antipsychotics in patients with dementia was associated with nearly double the risk of death, the FDA issued a black box warning in 2005, followed by another for all antipsychotics in 2008.^{6, 7} We therefore conducted an exploratory analysis evaluating the use of antipsychotics among a nationwide cohort of first-time NH residents with hip fracture. Hip fracture is among the most common diagnoses associated with NH admission⁸ and is associated with postoperative delirium in more than 40% of cases.⁹ We considered participants who entered NHs for rehabilitation after hospitalization for hip fracture with and without delirium symptomatology, but limited our cohort to those with no other documented co-morbidities. Following hip fracture, it is essential that patients actively participate in rehabilitation to regain functioning. The presence of delirium and/or treatment with antipsychotic medications may compromise patients' ability to do so. We evaluated the association between antipsychotic use and length of stay, discharge home, rehospitalization, death, and functional improvement at discharge while controlling for patient, facility and market characteristics for patients with and without delirium symptomatology.

METHODS

Study Sample

The study population included Medicare fee-for-service beneficiaries aged 65 or older, admitted to NHs between the years 2000-2007 with a diagnosis of hip fracture. We selected only first-time NH admissions that entered facilities from acute care hospitals. Minimum Data Set (MDS) files were examined back to 1998 to ensure that the study participants had no prior NH admissions and were limited to those with a documented discharge disposition. Patients in Hawaii, Alaska, and the District of Columbia were excluded due to the unique geographic characteristics of these markets.¹⁰ During the study period, 562,445 patients were identified as first-time NH admits with hip fracture. Among these patients, only those discharged from hospitals to NHs, with no other documented co-morbidities in the MDS, were selected. Our final sample included 77,759 patients discharged to 11,119 NHs.

Data Sources

Our analytic file was constructed by merging data from the MDS repository, Medicare enrollment records, the Area Resource File (ARF), and the Online Survey, Certification, and Reporting System (OSCAR). NH resident characteristics were obtained from the initial MDS assessments.¹¹ We also used MDS data matched with the Medicare enrollment file to

identify all first-time NH patients admitted from acute-care hospitals. MDS diagnosis indicators were used to identify residents with hip fracture and no other documented comorbidities. Clinical diagnostic categories on the MDS have been previously validated.^{12, 13}

Facility characteristics were obtained from the OSCAR system, an administrative database which collects and records the results of the state survey and certification process. Data from the ARF provided information on market competition using the county as a proxy.

Delirium Stratification

The Nursing Home Confusion Assessment Method (NH-CAM), a measure developed to mimic the validated Confusion Assessment Method, was utilized to identify residents with no delirium (NH-CAM=0), subsyndromal delirium (NH-CAM=1 or 2), and full delirium (NH-CAM=3).¹⁴ The NH-CAM identifies delirium based on nine variables collected on MDS assessments that CMS has identified as triggers for the condition. Details of the NH-CAM can be found in Dosa et al.¹⁴ Although we know of no MDS 2.0 scales for delirium that have been directly validated against a clinical gold standard, such as the DSM-IV criteria or Confusion Assessment Instrument, the NH-CAM tool has been shown to provide a clear hierarchical risk factor for mortality (hazard ratio of 1.5 to 1.9) and rehospitalization (hazard ratio of 1.1 to 1.3).¹⁴ Additionally, the tool has been shown to be superior to other published MDS 2.0 measures of delirium at stratifying risk of adverse outcomes¹⁴ and has been used previously by others to identify residents with presumed delirium in NH samples.^{15,16}

Outcome Measures

Key outcomes included: discharge home, rehospitalization, death, functional improvement prior to discharge, and length of NH stay. The MDS provides discharge locations and dates for each resident indicating whether the individual was discharged home, rehospitalized, or died in the NH, in addition to other dispositions. Patients' functional improvement was also measured as an outcome by examining changes in Activities of Daily Living (ADL) scores (0-28 scale). This ADL scale is created by summing seven separate items (dressing, eating, toilet use, personal hygiene, transferring, bed mobility and eating), with a higher score being reflective of a larger degree of impairment.¹⁷ A continuous variable was constructed to indicate the absolute improvement over time using the initial ADL assessment and the discharge assessment.

Measure of antipsychotic use—The MDS provides the number of days antipsychotic drugs were received by the resident in the seven days prior to an assessment. We created a dichotomous variable with an affirmative response signifying the receipt of antipsychotic medication on at least one day.

Control Variables—We controlled for resident and facility characteristics, as well as NH market conditions. This is consistent with prior studies of NH quality that examined measures such as hospitalization, functional improvement and discharge location.^{10, 18-23}

At the resident level we controlled for age, gender, race, marital status, cognitive status using a seven point cognitive performance scale (CPS) that has been validated as a good indicator for the Mini-Mental State Examination,²⁴ and baseline functional status as reflected in the patient's Activities of Daily Living (ADL) score at admission.¹⁷ The model also controlled for the number of different medications taken in the previous seven days to further adjust for case-mix. An MDS-based case-mix index was also used as a proxy for severity of illness with a higher score indicating a more severe average acuity profile of the

residents in the facility.²⁵ Approximately 10% of the observations had missing values for this variable, which were imputed with the mean.

At the facility level, we controlled for organizational characteristics of NHs (profit status, chain status, occupancy rates, any special care units, percent Medicare and Medicaid residents, the presence of a nurse practitioner or physician's assistant, and the ratio of registered nurses to total nurses).²⁶

At the market level, we adjusted for NH competition, which has been associated with the quality of care provided in facilities, using the Herfindahl index obtained from the ARF file.²⁷ We also included quarterly time dummies to adjust for temporal trends and seasonal effects.

Analytic strategy

For our primary analysis, we used propensity score reweighting to examine the association between antipsychotic drug use and NH quality outcomes.²⁸ Differences in the characteristics of patients who received antipsychotics and those who did not were a concern. Propensity score reweighting creates case and control groups with comparable conditional probabilities of receiving antipsychotic medications. Confounding is mitigated by making the weighted distributions of observable characteristics of the two groups more similar.

We estimated a logit model with an indicator of whether a patient received an antipsychotic drug as the dependent variable to derive predicted probabilities used as the propensity score. Predictors in the propensity score specification included resident characteristics, facility influences and a measure of market competition, all listed in the description of control variables above. Higher order terms and interactions were included to adjust for non-linearity and concomitant effects. Secular trends and seasonal influences were controlled with indicators for year and quarter of admission. Regressions were done separately for each delirium level in order to adjust for varying associations between severity of delirium and outcomes. Logistic models were fitted to calculate odds ratios for binary outcomes and linear models were estimated for continuous outcomes after reweighting the cases and controls.

Since the propensity score is based on observable characteristics, we also used longitudinal models that incorporated resident level outcomes with NH and time fixed effects to control for time invariant facility characteristics and temporal trends. This eliminated key sources of omitted variables bias, such as facility prescribing practice and permanent market differences in the county/state.⁵

Heteroskedastic robust standard errors were adjusted for clustering at the level of the facility. All analyses were carried out using SAS (version 9.1) and STATA SE (version 10). The Institutional Review Board of Brown University exempted this study from review.

RESULTS

Unadjusted outcomes and cohort demographics

Table 1 provides descriptive information of the study cohort by antipsychotic use, stratified by NH-CAM level, with zero indicating an absence of delirium symptomatology. Demographic differences were noted between residents who received antipsychotics and those who did not for each NH-CAM level. Male residents and those with severe cognitive impairment were more likely to receive antipsychotics. Antipsychotic users had higher ADL scores and received more medications. Approximately 10 percent of the cohort (n=7,417)

was identified as having either subsyndromal or full delirium using the NH-CAM. Among hip fracture patients with no observed delirium symptomatology, about 5 percent (n=3,225) received antipsychotic drugs. They were more likely to be rehospitalized, less likely to be discharged home, stayed longer in NHs, and had less functional improvement at discharge. As the NH-CAM level increased, differences in outcomes narrowed between antipsychotic recipients and non-users.

Results for propensity score analysis

Table 2 presents the regression results estimated with propensity score reweighting. Among patients with no delirium symptoms, residents who received antipsychotic drugs were 32% less likely to be discharged home (OR 0.68; $P < 0.001$) and had a higher likelihood of dying in the facility (OR 1.28; $P = 0.03$) compared to those who were not administered antipsychotics. Those receiving antipsychotics also stayed about 3 days longer (β 2.83; $P = 0.05$) and had less functional improvement prior to discharge (β -0.47; $P = 0.03$). Receipt of antipsychotic drugs in the NH was not associated with rehospitalization for this group. Estimates for residents with symptoms suggestive of mild delirium on the NH-CAM showed that those who received antipsychotic drugs were less likely to be discharged home (OR 0.74; $P = 0.03$) compared to those with no antipsychotic use. Among residents with full delirium, receipt of antipsychotics was not associated with a change in outcomes relative to patients who were not given antipsychotic medications.

Models with facility fixed effects showed that NH heterogeneity explained some differences in outcomes between cases and controls. However, adverse effects associated with antipsychotic use were still seen among study participants without delirium after controlling for unobserved heterogeneity between facilities. Estimates from linear regressions indicated that residents who showed no signs of delirium, but received antipsychotic drugs, were less likely to be discharged home (β -0.04, $P < 0.001$), had less ADL improvement prior to discharge (β -0.67, $P < 0.001$), and stayed longer (β 2.62, $P = 0.01$) in the NH relative to residents who did not receive antipsychotics.

DISCUSSION

This study evaluated the association between receipt of atypical antipsychotics and outcomes of skilled NH patients admitted with hip fracture with and without delirium symptomatology. Among residents with no evidence of delirium symptomatology on admission, those who received antipsychotics had an increased likelihood of death prior to discharge, were more likely to stay longer in NHs, and had less functional improvement.

Among residents showing symptoms of delirium upon admission, those who received antipsychotics did not have statistically different outcomes. In other words, treating presumed delirium for patients with hip fracture with antipsychotics did not appear to benefit these individuals. Rather, antipsychotic use was associated with adverse outcomes for subsyndromal delirium patients, such as a lower likelihood of being discharged home.

The strengths of this study were its use of a nationally representative data source, rigorous statistical tools in the analysis with a homogeneous study population, and examination of clinically and economically important outcomes. All regression models controlled for an expansive set of confounders, in addition to temporal trends. Propensity score reweighting addressed the possibility of selection bias. Facility heterogeneity, such as antipsychotic prescribing culture, was dealt with using facility and time fixed effects. A second major strength is the examination of a skilled NH population that is not easily captured based on secondary data claims such as Medicare Part D. Such claims are limited in their ability to capture medication utilization in the acute-care hospital and skilled NH settings due to the

bundling of payments under Medicare. By matching MDS data with the Medicare enrollment file, however, we were able to identify NH admissions and associated use of antipsychotics.

Several limitations warrant discussion. It is important to note that this exploratory study tests for associations rather than causal inferences. Primary data collection will likely be needed to ascertain whether antipsychotic use alone is responsible for the adverse outcomes described here or whether residual comorbidities are contributing factors. Additionally, data is needed to ascertain whether the effects of specific antipsychotic drugs, dosages and/or duration of use affect outcomes differentially.²⁹

Secondly, we utilized a methodology (NH-CAM) for identifying delirium-like symptoms that has not been validated independently against gold standard diagnostic tools. Although prior studies suggest that the NH-CAM performs well against other commonly used MDS 2.0 tools for identifying delirium including the triggers for the Delirium Resident Assessment Protocol,¹⁴ it is not our intention to presume that residents at various stages of the NH-CAM had clinically defined delirium. Rather, this tool merely implies that they have increased gradations of delirium-like symptoms. Additionally, though care was taken to exclude the confounding effect of dementia within the NH-CAM and in our study, it remains possible that this has influenced our results.³⁰

Finally, though the MDS has been shown to be a reliable data source for numerous items,^{12, 13} we were not able to access the associated hospital claims for study participants. For instance, we relied on MDS diagnoses to identify hip fracture patients. To assess the validity of this approach, we performed a subset analysis of Medicare hospital claims from 2006 and compared hip fracture ICD-9-CM codes (820.X) to the initial MDS assessments from subsequent NH admissions. The estimated positive predictive value was 78.7% (95% CI, 78.3-79.0), indicating a reasonably high reliability to predict hip fracture. Nevertheless, it does indicate that the MDS might incorrectly identify some with hip fracture. If false positives were more likely among cognitively impaired patients, who were more prevalent in one group, this would have introduced bias. Clinically, however, there is no reason to presume that this would occur.

CONCLUSION

This exploratory study shows a negative association between the use of antipsychotics and functional improvement, length of NH stay, and the likelihood of being discharged home, along with an increased risk of death among NH residents with hip fracture and no delirium symptoms. Our results suggest that there were no improvements in the same outcomes, in addition to rehospitalization, among residents with delirium symptomatology who received antipsychotics. Though it is premature to infer that the adverse consequences seen in our results are related exclusively to antipsychotic use, further study is required to better delineate these findings.

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Table 1

Unadjusted outcomes and cohort characteristics.

	No Delirium n = 70120 (90.4%)			Subsyndromal n = 6738 (8.7%)			Full Delirium n = 679 (0.9%)		
	Antipsychotics Yes (4.6 %)	Antipsychotics No (95.4%)	P value	Antipsychotics Yes (10.4 %)	Antipsychotics No (89.6 %)	P value	Antipsychotics Yes (22.6 %)	Antipsychotics No (77.4 %)	P value
Outcome Variables									
Length of stay (mean (± SD))	42.7 (53.6)	32.0 (36.1)	<0.001 ***	41.0 (55.0)	38.6 (44.1)	0.19	40.7 (60.0)	37.0 (47.2)	0.42
Activities of Daily Living (ADL) improvement (mean (± SD))	2.3 (4.2)	3.8 (4.4)	<0.001 ***	2.7 (4.4)	3.7 (4.6)	<0.001 ***	2.2 (4.9)	3.3 (4.3)	0.04 *
Discharged home (%)	53.9	79.0	<0.001 ***	51.5	68.6	<0.001 ***	40.5	53.0	<0.01 **
Rehospitalization (%)	16.9	7.7	<0.001 ***	14.0	10.3	<0.01 **	19.0	15.6	0.33
Death (%)	10.9	3.2	<0.001 ***	12.1	7.3	<0.001 ***	16.3	10.3	0.04 *
Sociodemographic Characteristics									
Age (mean (± SD))	83.8 (7.0)	82.6 (7.6)	<0.001 ***	85.0 (7.0)	84.2 (7.5)	0.01 *	84.7 (6.2)	85.7 (6.8)	0.08
Male (%)	27.1	21.5	<0.001 ***	33.0	24.3	<0.001 ***	37.3	30.7	0.12
Married (%)	33.3	33.02	0.72	32.7	30.0	0.14	36.4	32.4	0.35
Race (%)									
White, non- Hispanic	91.8	93.4	<0.001 ***	94.4	94.7	0.77	95.4	94.8	0.77
Black, non-Hispanic	4.0	2.8	<0.001 ***	2.3	2.5	0.70	3.9	2.3	0.27
Other	4.2	3.9	0.33	3.3	2.8	0.45	0.7	2.9	0.11
Functional Status									
Cognitive Performance Scale (CPS) (%)									
Less impairment (CPS = 0,1,2)	37.3	87.57	<0.001 ***	25.2	63.4	<0.001 ***	11.9	21.4	0.01 *
Moderate impairment (CPS = 3,4)	44.8	10.39	<0.001 ***	55.9	30.8	<0.001 ***	64.2	60.3	0.38
Severe impairment (CPS = 5,6)	18.0	2.04	<0.001 ***	18.9	5.8	<0.001 ***	23.8	18.3	0.13
Case Mix reimbursement									
Baseline activity of daily living (ADL) score (0-28) (mean (± SD))	19.6 (5.1)	15.7 (4.8)	<0.001 ***	19.6 (4.7)	17.7 (4.7)	<0.001 ***	20.1 (4.2)	19.6 (4.6)	0.22
The number of medications received (mean (± SD))	10.0 (3.8)	8.4 (3.8)	<0.001 ***	10.0 (5.2)	8.1 (3.9)	<0.001 ***	10.4 (4.2)	8.6 (4.1)	<0.001 ***

Note:
 * (p < .05),
 ** (p < .01),
 *** (p < .001).

No delirium (NH CAM = 0), Subsyndromal (NH-CAM = 1 and 2), full delirium (NH-CAM = 3)

Table 2

Regression results using propensity score reweighting

Delirium Level	Discharged Home		Rehospitalization		Death		Activities of Daily Living (ADL) improvement		Length of stay	
	Odds Ratio	P value	Odds Ratio	P value	Odds Ratio	P value	Point Estimate	P value	Point Estimate	P value
No Delirium	0.68	<0.001 ***	1.25	0.08	1.28	0.03 *	-0.47	0.03 *	2.83	0.05 *
Subsyndromal	0.74	0.03 *	0.9	0.52	0.93	0.66	-0.32	0.41	-0.82	0.75
Full Delirium	0.72	0.19	1.12	0.73	1.06	0.86	-1.06	0.26	6.94	0.26

Note:

* (p < .05),

** (p < .01),

*** (p < .001)

The variables used to estimate the propensity score are described in the text. Regression estimates for the other covariates are not shown but are available upon request from the authors.