

Correlates of disability in depressed older adults with bipolar disorder

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Abstract

Aims To identify clinical factors associated with disability in depressed older adults with bipolar disorder (BPD) receiving lamotrigine.

Methods Secondary analysis of a multi-site, 12-week, open-label, uncontrolled study of add-on lamotrigine in 57 adults 60 years and older with BD I or II depression. Measures included the Montgomery Asberg Depression Rating Scale (MADRS), Young Mania Rating Scale (YMRS), Cumulative Illness Rating Scale for Geriatrics (CIRS-G), Dementia Rating Scale (DRS), and WHO-Disability Assessment Scale II (WHO-DAS II).

Results Medical comorbidity in this group of elders was substantial, with roughly 60% of subjects having disorders of the vascular, musculoskeletal/integument, and endocrine/metabolic/breast systems. We found significant relationships among mood (MADRS), medical comorbidity (CIRS-G), cognition (DRS), and disability (WHO-DAS II). More severe BPD depression, more medical comorbidity and more impaired cognition were all associated with lower functioning in BPD elders.

Conclusions Our findings fit the paradigm shift that has been occurring in BPD, supporting the notion that BPD is not solely an illness of mood but that it affects multiple domains impacting overall functioning.

Key words: bipolar disorder, elderly, geriatric, lamotrigine, mood stabilizer, anticonvulsant, depression.

Introduction

In the past several years, in the field of psychiatry there has been a paradigm shift in the understanding of bipolar disorder (BPD). Among researchers, BPD is no longer being seen as a disorder solely of cyclical mood episodes interspersed with normal euthymic periods, but rather as a multi-system disease that is chronic and progressive (1, 2). Numerous studies in the past 10-15 years have shown that across the life-span BPD is associated with increased medical comorbidity, cognitive dysfunction, and substantial impairment in everyday function (3-5). Additionally, while suicide contributes to premature mortality in BPD, evidence now reveals that medical comorbidity (cardiovascular and cerebrovascular disease) predominantly contributes to excess mortality, ranging from 35% to 2-fold higher than the general population and higher than major depressive disorder (6). Hence, the paradigm shift in understanding extent and severity of the effects of BPD on an individual has led to broadening of treatment to encompass medical comorbidity, cognitive dysfunction, and everyday function.

The paradigm shift in BPD is relevant to patients across the lifespan and perhaps most acutely to older adults with BPD where the medical comorbidity and cognitive dysfunction are most pronounced. However, older adults with BPD have been a segment of the population of individuals with BPD that have been least studied with this paradigm shift in mind. The reasons for this include long-standing misconceptions that BPD burns out with age, that patients with BPD do not make it into older age because of premature mortality, and funding priorities of national governments and the pharmaceutical industry (7). There is a growing need to understand the healthcare needs of elders with BPD better because this segment of the population is growing and is among the most expensive utilizers of healthcare (8).

We have previously reported on a multi-site open-label, prospective trial of lamotrigine for geriatric bipolar depression (9). In our previous study of lamotrigine in older people with bipolar depression, lamotrigine was associated with improvements in depression, psychopathology and functional status. In a follow-up analysis of the patients enrolled in the trial, we found that lamotrigine appeared to work well in depressed BPD older adults with high levels of cardiometabolic risk and low levels of mania (10).

To understand the relationships among medical comorbidity, cognitive dysfunction, and mood on everyday function better, we carried out secondary analyses of the baseline data collected in our open-label trial of lamotrigine for geriatric BPD depression (9). Our interest was in examining to what extent medical comorbidity, cognitive dysfunction and mood impacted on everyday function and to what extent these domains might be synergistic. While it is well understood that these domains impact on everyday function individually (11), we were interested in exploring whether, when acting together, these domains would have greater than expected impact on an individual with BPD.

Methods

We conducted a multi-site, 12-week, open-label, uncontrolled trial of add-on lamotrigine in 57 adults 60 years and older with BPD I or II depression. Detailed methods of the trial are described elsewhere (9). All subjects met depressive symptom severity criteria of 18 or greater on the GRID version of the 24-item Hamilton Depression Ratings Scale (GRID HAM-D) (12, 13). Individuals with dementia were excluded from the study.

Measures

Mood. We assessed mood with the MADRS (14), GRID HAM-D, and Young Mania Rating Scale (YMRS) (15).

Medical Comorbidity. Medical illness burden was evaluated at baseline with the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) (16). The CIRS-G organises acute and chronic medical burden across

different systems (heart, vascular, etc.), rating burden within each system from “0” (“no problem”) to “4” (“extremely severe/immediate treatment required/severe impairment in function”). Past significant problems that are not currently active are rated as “1.”

Cognition. Cognitive function was assessed with the Dementia Rating Scale (DRS) (17). This instrument has demonstrated sensitivity and specificity in elderly individuals, including those with mood disorders (18). It assesses cognitive function in several domains, including attention, executive function (Initiation/Perseveration), visuospatial ability (construction), abstraction (conceptualization), and memory.

General health/disability status was evaluated with the WHO-Disability Assessment Schedule II (WHO-DAS II) (19). The WHO-DAS II assesses the following domains of function: understanding and communicating, getting around, self-care, getting along with others, household and work activities, and participation in society. The WHO-DAS II is cross-cultural and treats all disorders at parity when determining level of function. The following items from the WHO-DAS II that had a cognitive component were aggregated together: Getting around (s1, s7), life activities (s2), understand/communicates (s3, s6), self-care (s8, s9). These items were used to form a subscale, to focus on everyday function that could be impacted by cognitive impairment.

Statistical Methods. Multiple linear regression models were fitted with WHO-DAS II (or a cognitively-oriented subscale of WHO-DAS II) considered as the outcome measure. Models included adjustment for age and education. A first model considered the full WHO-DAS II scale score, regressed with CIRS-G and MADRS as explanatory variables. This model used all data from 53 subjects. Since the DRS cognitive test data were not collected for all subjects in the sample, this model did not consider DRS.

A second model considered a WHO-DAS II subscale involving the items thought to engage cognitive functioning as measured by DRS. As explanatory variables, we also considered subscales of DRS, specifically those associated with I/P and memory. This allowed for the association of everyday function as measured by the WHO-DAS II items with specific cognitive domains. This second analysis involved 29 subjects.

Results

Baseline characteristics of the subjects (n=57) have been reported previously. In brief, subjects were mean (SD; range) age of 66.5 years (6.7; 60-90), 40% female, 86% Caucasian, mean education of 14.5 years (2.7; 8-23), 77.2% bipolar I and 22.8% bipolar II. Mean CIRS-G was 9.5 (4.7; 2-21), which is consistent with medical severity noted in geriatric samples in mood disorder treatment studies (16). As illustrated in Figure 1, medical comorbidity in this group of elders was substantial, with roughly 60% of the subjects endorsing disorders of the vascular, musculoskeletal/integument, and endocrine/metabolic/breast systems. Individuals were moderately depressed with a mean (SD) MADRS score of 25.3 (8.3) and moderately functionally impaired with a WHO-DAS II subscale scores: Getting around=5.1 (3.0), Self-care=3.5 (2.0), Life activities=2.9 (1.2), Understand/communicate=4.7 (1.9), Participation in society=6.0 (2.0), and Getting Along with people=4.1 (2.1). Married subjects comprised 45% (n=26) of the group, while 45% (n=26) were living alone. Among those with DRS data, there were little differences with the sample as a whole. For instance, for this subgroup, mean (SD; range) age was 66.4 years (6.4; 60-85) and mean (SD; range) education of 14.9 years (2.8; 8-21).

We found significant relationships between everyday function (WHO-DAS II) and medical comorbidity (CIRS-G), cognitive function (DRS memory), and mood (MADRS). See Tables 1 and 2. In the model, a 10 point increase on the MADRS resulted in a 2.3 point increase in the WHO-DAS II, while a 10 point increase in CIRS-G resulted in an 8.1 increase in the WHO-DAS II. We found no interactive (synergistic) effects among the domains on everyday function.

There was little discrepancy in age and education between those with DRS data versus those without. For the second model, MADRS was initially included in this model, but was found not to be significant and subsequently removed. R-square and adjusted R-square for the first model were: 0.382, 0.330; for

the second model the values were 0.577, 0.507 (the difference in the R-squares suggests that cognition can help explain variability in certain items of the WHO-DAS II).

Discussion

In this secondary analysis of the baseline data acquired in an open-label trial of lamotrigine for BPD depression, we found significant relationships between everyday function and medical comorbidity, cognitive function, and mood. More severe BPD depression, more medical comorbidity and more impaired cognition were all associated with lower functioning in BPD elders. A recent review of the literature on comorbidity in older adults with BPD comorbidity concluded that medical comorbidity is common, affecting multiple organ systems with a mean of 3-4 medical conditions (20). The most frequently seen comorbidities in this sample were disorders of the vascular, musculoskeletal, and endocrine/metabolic systems. It appears that the relationships between BPD and medical illnesses are multifactorial, related to shared genetic risk, iatrogenic medication effects, lifestyle and other factors (21-24). With some medical conditions, such as diabetes, there may be a bidirectional relationship between psychiatric and medical illnesses (23, 25).

We found no greater than expected impairment in everyday function among BPD individuals when these domains were looked at together. It appears that multiple factors and not one particular factor impacts functional outcomes. Our findings support the notion that BPD is not solely an illness of mood, but that it affects multiple domains impacting patients overall functioning (1, 2).

While our findings fit the paradigm shift that has been occurring in BPD, some limitations of the findings need to be considered. First, the WHO-DAS II is a self-report and has been criticized for failing to identify relationships between observed cognitive dysfunction and identified functional impairments in schizophrenia (4). Hence, the measure is subject to bias and may underreport deficits in everyday function. Second, the sample studied is a sample of convenience and is biased to patients eligible and willing to undergo a trial of lamotrigine. By design, individuals with dementia were excluded from our study. Consequently, the patients reported may not reflect the larger pool of older adults with BPD. Last, the small sample size resulted in limited power to look at interaction effects among the domains.

Noting the above limitations, our analysis supports the understanding that BPD impacts an individual beyond mood and that treatments need to be directed to address all aspects of the illness for patients to enjoy full and sustained recovery. Our findings emphasize the need to look beyond BPD symptoms in assessment and treatment planning. Given the significant presence of medical and cognitive comorbidities among BPD elders, it is critical that clinicians providing care to these individuals carefully assess for concurrent conditions, use treatments that do not worsen these comorbidities, and coordinate care with other providers to minimize treatment burden and avoid conflicting information or advice (20). Considering the global demographic trends in community and healthcare settings, clinicians in both primary and specialty care will be likely to see and need to provide services to geriatric patients with mood disorders (26, 27). Integrated care that addresses medical illness, mood and cognitive function together are needed to optimize health outcomes for this vulnerable group of patients.

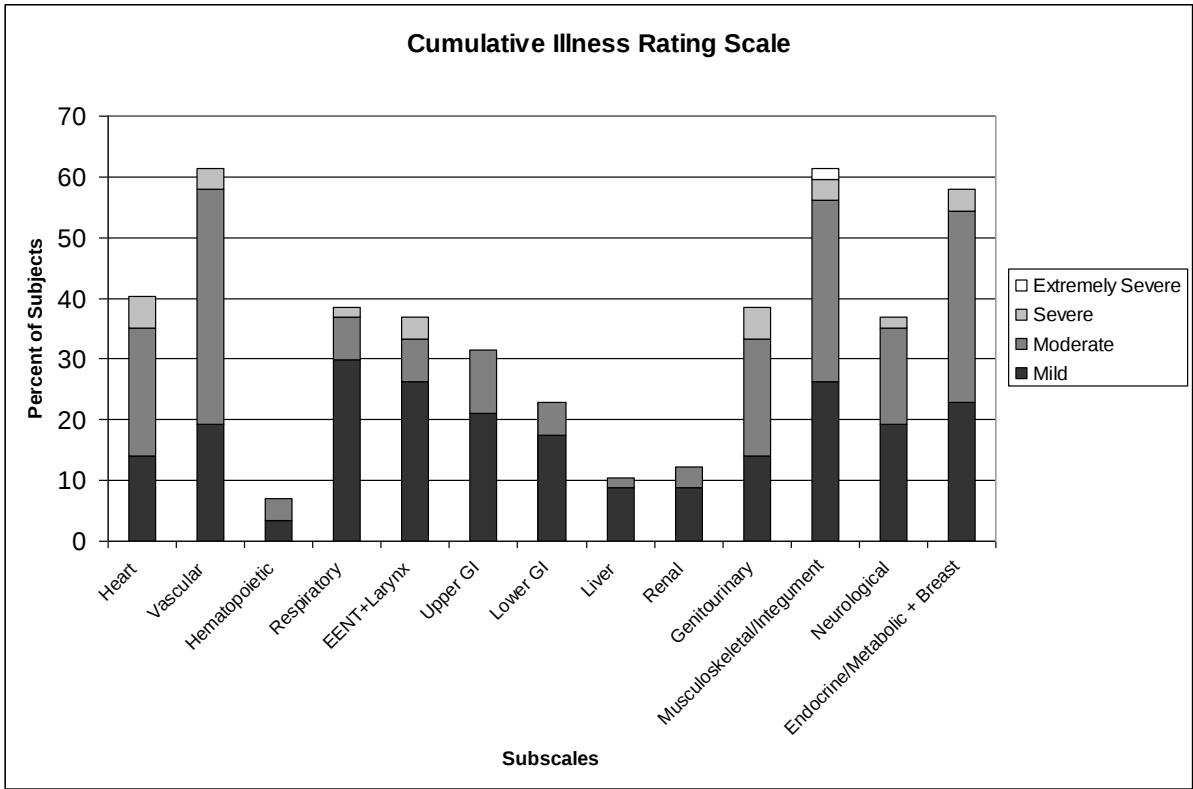
Table 1. Parameter estimates for the regression model incorporating medical burden (CIRS-G) and depression (MADRS) scores on everyday function (WHO-DAS II) among 53 older adults with bipolar disorder

	β	Std. Error	t	Sig.	95% Confidence Interval (β)	
					Lower Bound	Upper Bound
Intercept	30.726	12.147	2.530	.015	6.303	55.149
Cumulative Illness Rating Scale-Geriatric (CIRS-G)	.808	.206	3.921	<.001	.394	1.223
Montgomery-Asberg Depression Rating Scale (MADRS)	.230	.109	2.111	.040	.011	.450
Education	-1.033	.333	-3.103	.003	-1.703	-.364
Age	.001	.134	.011	.992	-.267	.270

Table 2. Parameter estimates for the regression model incorporating cognition (DRS I/P and DRS Memory) and medical burden (CIRS-G) scores on everyday function (WHO-DAS II cognitively-oriented subscale) among 29 older adults with bipolar disorder

	β	Std. Error	t	Sig.	95% Confidence Interval (β)	
					Lower Bound	Upper Bound
Intercept	75.658	17.949	4.215	<.001	38.528	112.788
Cumulative Illness Rating Scale-Geriatric (CIRS-G)	.490	.223	2.198	.038	.029	.951
DRS Initiation/Perseveration Subscale	-.097	.209	-.461	.649	-.529	.336
DRS Memory Subscale	-2.014	.664	-3.035	.006	-3.388	-.641
Education	-.531	.282	-1.886	.072	-1.114	.051
Age	-.054	.108	-.504	.619	-.277	.168

Figure 1. Cumulative Illness Rating Scale-Geriatric (CIRS-G) scores in 57 older adults with bipolar disorder



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