World Journal of Pharmacy and Biotechnology
ISSN: 2349-9087
Journal Home Page: www.pharmaresearchlibrary.com/wjpbt

RESEARCH ARTICLE

Assessment of Health Related Quality of Life Indices in Patients on Antidepressant Pharmacotherapy: An Observational Study

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ABSTRACT
Pharmacotherapy with antidepressants and/ or anti-psychotics helps to relieve depression and improve the mental health and overall quality of life of individuals suffering from this disease. There is sufficient data from clinical trials that show the safety and efficacy of these medications. However there is lack of clear guidelines for prescribing these medications and there is a gap in literature on studies which determine the effect of these medications on the overall wellbeing of individuals. This retrospective, observational study used the Medical Expenditure Panel Survey database. Individuals suffering from depression (ICD-9-CM: 296, 300, and 311) and those taking antidepressants and/or antipsychotics since the beginning of the panel were identified. A total of 804 patients met the study inclusion criteria, among which 688 patients were on monotherapy and 116 on add-on/switch therapy. Among patients only on monotherapy, no significant difference was observed in their tendency to show improvement or decline on PCS-12, K6 and PR-MHS scores based on the class of antidepressants. The results of the study may imply that further research needs to be done to determine the reason for SSRIs to show greater improvement on mental health as compared to SNRIs. Similar results in patients on monotherapy and add-on/switch therapy can suggest that their therapy may keep depressive symptoms under control, which can indicate a good clinical decision by the patients' health care providers.

Keywords: Pharmacotherapy, clinical trials, PR-MHS, ICD-9-CM, PR-MHS, Antidepressant

ARTICLE INFO

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ARTICLE HISTORY: Received 26 December 2021, **Accepted** 29 Jan 2022, **Published Online** 22 March 2022

Citation: Gudipalli Bhavani Tejaswini, *et al.* Assessment of Health Related Quality of Life Indices in Patients on Antidepressant Pharmacotherapy: An Observational Study, 2022, 10(1): 5-10.

CONTENTS

1. Introduction

Depression is a mental illness that can be both debilitating and costly to sufferers. It can adversely affect the course and outcome of common chronic conditions, such as asthma, cardiovascular disease, cancer, diabetes, arthritis and obesity.[1] Depression is associated with decrease in functioning and well-being of an individual and increase in number of disability days, utilization of healthcare services and cost.[2-4]Diagnosis and treatment of depression has increased over the past few years among both men and women. A total of $ 22.8 billion was spent to treat depression in the year 2020 as compared to $18.0 billion in the year 2010.

Treatment options for depression include medication, primarily antidepressants, psychotherapy which includes cognitive-behavioral therapy (CBT), interpersonal therapy (IPT) and electroconvulsive therapy. Most common treatments are medications and psychotherapy.[8]This paper will focus on medications, chiefly antidepressants and other atypical antipsychotics which are used for treating depression. According to the Centers for Disease Control and Prevention, during the last 20 years the use of antidepressants has grown significantly making them one of the most costly and the third most commonly prescribed class of medications across the globe.[9] Several different classes of antidepressants are available for treating depression. These include selective serotonin reuptake inhibitors (SSRIs), selective norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs).

This study also assessed the mental health as patient-reported mental health status (PR-MHS) and psychological distress score in individuals suffering from depression. Patients with depressive disorder tend to have worse physical and mental health, role functioning and perceived current health as compared to patients having no chronic conditions.

Also, most participants in clinical trials are recruited by advertisement rather than from representative practices, and they are often selected to have few comorbid disorders, either medical or psychiatric. Furthermore the protocols used in these trials do not represent usual real world clinical practice. There is sufficient data from clinical trials that show the safety and efficacy of these medications. However unlike many other chronic conditions such as diabetes, hypertension, etc there is a lack of clear guidelines for prescribing medications for depression.

2. Methodology

Identification of patients with depression

Individuals having depression were identified using the MEPS HC medical conditions file. This file contains information on observation of each self-reported medical conditions that a MEPS respondent experienced during the data collection year. The participants are asked to report the medical condition that they experienced during the last four to five months since the previous interview in each round of interviews. Medical conditions reported by participants were recorded by interviewers as verbatim text, and were coded by professional coders to fully specified three digits ICD-9-CM codes.[112]According to AHRQ, conditions with ICD-9 codes 296, 300 and 311 were classified as depression.[7] These three ICD-9 codes were used to identify patients with depression.

Medications used to treat depression

Patients taking antidepressants and those who were concomitant users of atypical antipsychotics were identified using the Prescribed Medicines Files. In this study, first the psychotherapeutic agents were identified using the therapeutic classification variable number 242(TC1), which is one of the Multum Lexicon Drug Database variables. [113] The therapeutic sub-classification variable (TC1S1) number 249 and 251were then used to identify antidepressants and antipsychotics respectively. Furthermore the therapeutic sub- sub classification variable (TC1S1_1) number 76(miscellaneous antidepressants), 208 (SSRI antidepressants), 209(tricyclic antidepressants), 306 (phenyl piperazine antidepressants), 307(tetracyclic antidepressants) and 308 (SNRI antidepressants) were used to identify specific classes of antidepressants. Only those patients who were taking antidepressants and/or AAPs since the beginning of apanel were included in the study (using RXBEGYRX variable).

Patients starting medications in the 3rd,4th and 5th round of a panel were also excluded (using PURCHRD and RXBEGMM variable) as their HRQOL, PRMHS and K6 scores were seen in rounds 2 and 4. The drugs that were classified as antidepressants included citalopram, escitalopram, amitriptyline, clomipramine, desipramine, amoxapine, buproprion, doxepine, venlafaxine, desvenlafaxine, paroxetine, imipramine, trimipramine, trazodone, tranylcypromine, sertraline, protriptyline, phenelzine, nortriptyline, nefazodone, mirtazapine, maprotiline, isocarboxazid, fluvoxamine, fluoxetine, doxepin, and desipramine. AAPs included ziprasidone, quetiapine, risperidone, olanzapine and aripiprazole as they have been approved by the FDA for treatment of major depressive disorder or supported with evidence.

Inclusion-Exclusion Criteria

Inclusion criteria

All respondents identified with depression in the 2019-2021 MEPS database files, above the age of 18 years and taking one or more antidepressants and/or antipsychotics were included in the study. Only those respondents who started taking antidepressants and/or AAPs since the beginning of the panel were included in the study.

Exclusion criteria

Patients who purchased medications in the 3rd, 4th and 5th round of a panel for the first time were excluded. Patients

taking AAPs alone were excluded, as they are generally prescribed as monotherapy in patients with bipolar disorder and schizophrenia. Respondents with missing responses on either of the questions of SF-12, K6 and PR-MHS were also excluded.

Health –related quality of life (HRQOL): HRQOL of MEPS participants have been assessed by AHRQ using the Short Form Health Survey-12 version two (SF-12v2). It has two component summary scales, namely the Physical Component Summary (PCS-12) and Mental Component Summary (MCS-12) and their scores range from 0 to 100 where a higher score is indicative of a better HRQOL.

Psychological distress measure

The Kessler Index (K6) scores measure the individuals' non-specific psychological distress in the past 30 days. The scores are based on six mental health related questions (refer Appendix B) that measure the individuals' nervousness, hopelessness, sadness, restlessness, worthlessness, and effortlessness in the past 30 days on a scale of 0 to 4, with 0 being none of the time and 4 being all the time. The values on all these questions give the overall K6 scores. In the present study, the frame work depicts the relationship between depression characteristics, mainly the type of pharmacotherapy and patient-reported outcomes such as HRQOL, PR-MHS and non-specific psychological distress. This model is based on Pearlin's Stress Process Model and the "Biopsychosocial" model of health.

Data analysis

Descriptive statistics were used to describe the population according to their socio-demographic characteristics. The characteristics of patients taking different classes of medications and those who are on monotherapy, combination therapy and those who switch from monotherapy to combination therapy were analyzed for differences using t-tests for continuous variables and chi-square tests for categorical variables. All statistical values were considered significant at a level of significance of $p \leq 0.05$.

3. Results and Discussion

Table 1: Socio-demographic characteristics of study population

Selected Characteristics	N=804(%)	
Gender		
Males	225(27.99)	
Age		
18-45	376(46.77)	
45-64	322(40.05)	
>64	106(13.18)	
Race		
White	487(60.57)	
African American	75(9.33)	
Other	242(30.10)	
Ethnicity		
Hispanic	123(15.30)	
Education Level		
Less than high school	139(17.29)	
High School	300(37.31)	
More than high school	365(45.50)	
Marital Status		
Married	351(43.66)	
Divorced, widowed, separated	263(32.71)	
Never married	190(23.63)	
Person's total income		
No income	83(10.32)	
Less than $25,000	429(53.36)	
$25000-$50,000	181(22.51)	
>$50,000	111(13.81)	
Employment Status		
Employed	406(50.37)	
Insurance		
Any private	443(55.10)	

Public only	268(33.33)	
Uninsured	93(11.57)	
Prescription drug insurance coverage		
Yes	363(45.15)	

Table 2: Patient characteristics stratified by type of pharmacotherapy (Monotherapy or Add-on/Switch therapy)

Selected Characteristics	Monotherapy (N=688)	Add on/Switch therapy(N=116)	P value
	N(%)	N(%)	
Gender			
Males	195 (28.34)	30(25.86))	0.58199
Age			
18-45	316 (45.93)	60(51.72)	0.23
45-64	276(40.12)	46(39.66)	94
>64	96(13.95)	10(8.62)	
Race			
White	422(61.34)	65(56.03)	0.42
African American	61(8.87)	14(12.07)	76
Other	205(29.80)	37(31.90)	
Ethnicity			
Hispanic	106(15.41)	17(14.66)	0.8352
Education Level			
Less than high school	121(17.59)	18(15.52)	0.76
High School	258(37.50)	42(36.21)	42
More than high school	309(44.91)	56(48.28)	
Marital Status			
Married	314(45.64)	37(31.90)	**0.00**
Divorced, widowed, separated	224(32.56)	39(33.62)	**39**
Never married	150(21.80)	40(34.48)	
Person's total income			
No income	64(9.30)	19(16.38)	**0.04**
Less than $25,000	364(52.91	65(56.03)	**13**
$25000-$50,000	163(23.69)	18(15.52)	
>$50,000	97(14.10)	14(12.07)	
Employment Status			
Employed	368(53.49)	37(31.90)	**<0.0001**
Insurance			
Any private	391(56.83)	52(44.83)	0.05
Public only	220(31.98)	48(41.38)	48
Uninsured	77(11.19)	16(13.79)	
Prescription drug insurance			

Table 3: Percentage of individuals showing change in SF- 12, K6 and PR-MHS scores based on monotherapy and add on/switch therapy

Category	Monotherapy			Add on/Switch therapy		
	Improve N(%)	Unchanged N(%)	Decline N(%)	Improve N(%)	Unchanged N(%)	Decline N(%)
SF-12:PCS	128(18.60)	399(57.99)	161(23.40)	23(19.83)	61(52.59)	32(27.59)
SF-12:MCS	213(30.96)	308(44.77)	167(24.27)	37(31.90)	52(44.83)	27(23.28)

PR-MHS	139(20.20)	436(63.37)	113(16.42)	22(18.97)	73(62.93)	21(18.10)
K6 scores	150 (21.80)	415(60.32)	123(17.88)	31(26.72)	66(56.90)	19(16.38)

Table 4: Percentage of individuals on monotherapy showing change in SF- 12, K6 and PR- MHS scores based on the class of antidepressants prescribed.

Category	SSRIs (N=421)			TCAs(N=40)			SNRIs(N=109)			Other Antidepressants(N=118)		
	Improve N (%)	Remains same N (%)	Decline N (%)	Improve N (%)	Remains same N (%)	Decline N (%)	Improve N (%)	Remains same N (%)	Decline N (%)	Improve N (%)	Remains same N (%)	Decline N (%)
SF-12:PCS	71 (16.86)	256 (60.81)	94 (22.33)	13 (32.50)	19 (47.50)	8 (20.00)	24 (22.02)	59 (54.13)	26 (23.85)	20 (16.95)	65 (55.08)	33 (27.97)
SF-12: MCS	150 (35.62)	195 (46.32)	76 (18.05)	15 (37.50)	14 (35.00)	11 (27.50)	25 (22.94)	50 (45.87)	34 (31.19)	40 (33.90)	49 (41.53)	29 (24.58)
PR-MHS	91 (21.62)	260 (61.76)	70 (16.63)	9 (22.50)	24 (60.00)	7 (17.50)	18 (16.51)	76 (69.72)	15 (13.76)	21 (17.80)	76 (64.41)	21 (17.80)
K6 scores	93 (22.09)	256 (60.81)	72 (17.10)	12 (30.00)	22 (55.00)	6 (15.00)	23 (21.10)	64 (58.72)	22 (20.18)	22 (18.64)	73 (61.86)	23 (19.49)

Discussion

This chapter discusses the findings of this study, its implications, limitations and future research. Patients with depressive disorder tend to have worse physical, social, mental health and role functioning as compared to patients having no chronic conditions. After the Medical Outcomes Study, the health-related quality of life (HRQOL) should be the ultimate measure of any kind of intervention in the treatment of depression, our sample was characterized by 72% women which corroborates with the findings of other studies that show that women are more likely to experience depression than males. An average of 47% of patients fell within the age category of 18-45 years. This may be because the average age of onset of depression is at the age of 32. This study is unique as it is one of the few studies that evaluated the effect of various classes of medications used to treat depression in patients on monotherapy alone and in patients who are on monotherapy and add on/ switch therapy on HRQOL and mental health. Moreover, this study has a longitudinal design in contrast to most other studies that are cross sectional in nature. Assessing the above mentioned outcomes in patients only on monotherapy was chosen as a standalone objective as most patients with depression begin therapy with a single antidepressant and resort to augmenting or combining medications if they show partial or noremission. In addition to this, the current study showed similar results for patients on monotherapy versus those on add-on/switch therapy on all the three outcome variables. This may be because outcomes of patients who were on antidepressants since the beginning of the panel in MEPS were evaluated at two different time points. Even though the present study shows no significant difference in improvement in any of the outcome measures among patients on monotherapy and add-on/switch therapy, it can be implied that both the single antidepressant therapy as well as combining antidepressants may provide remission from depression which in turn may maintain the HRQOL and mental health of individuals. None of the groups were found to show significant decline in any of the outcome measures, which may indicate appropriate clinical judgment on the part of the healthcare providers.

4. Conclusion

This retrospective, observational study carried to evolve a consensus on health related quality of life and reduction of psychological distress among the represented subjects has showed a significant association between co- morbidities and HRQOL. Individuals with greater depressive symptoms report more frequent negative social interactions. Patients reporting that their disease state often stops them from having social interactions could be having more severe depression and could be having worse scores in round two of the panel. Further, the pharmacotherapy used to control depression may be working which could result in them reporting better scores in round 4 of MEPS. No causal relationship can be inferred based on the sole findings of this study due to the limitation of the MEPS being a panel design. Hence baseline scores of patients on HRQOL, PR-MHS and K6 could not be considered in the study. Also, in the add-on/switch therapy group we could not distinguish between patients concomitantly using antidepressants or AAPs and those who switch therapies.

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