The Interface

ANTIDEPRESSANT ADHERENCE: Are Patients Taking Their Medications?

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This ongoing column is dedicated to the challenging clinical interface between psychiatry and primary care—two fields that are inexorably linked.

ABSTRACT

Depression is a relatively common clinical disorder and can be difficult to effectively treat according to findings from the Sequenced Treatment Alternatives to Relieve Depression study. Given this working terrain, patient adherence with antidepressant therapy is a critical aspect of effective clinical management. However, according to contemporary data (i.e., over the past 10 years), approximately 50 percent of psychiatric patients and 50 percent of primary care patients prematurely discontinue antidepressant therapy (i.e., are nonadherent when assessed at six-months after the initiation of treatment). The reasons behind patient nonadherence to antidepressants are varied and include both patient factors (e.g., concerns about side effects, fears of addiction, belief that these medications will not really address personal problems) as well as clinician factors (e.g., lack of sufficient patient education, poor follow-up). An awareness of the high rates of antidepressant nonadherence among patients hopefully will underscore to the prescriber the importance of carefully exploring patient concerns about these medications and closely monitoring patients while on therapy.

KEY WORDS

Adherence, antidepressants, compliance, nonadherence

INTRODUCTION

According to the findings of the study, Sequenced Treatment Alternatives to Relieve Depression (STAR*D),[1] depressive disorders can be challenging to treat. Indeed, after exposure to four different treatment levels or intervention options, approximately one-third of patients in this study (the largest of its kind) never achieved remission.[1] The potential challenge in treating patients with depression invites the following clinical query—what is the expected antidepressant nonadherence rate among patients in clinical samples, particularly in psychiatric and primary care populations?

The current *Practice Guideline for the Treatment of Patients with Major Depressive Disorder*[2] describes phasic pharmacological

TABLE 1. Sampling of antidepressant adherence studies in psychiatric populations over the past 10 years

FIRST AUTHOR/ YEAR OF PUBLICATION	COUNTRY OF ORIGIN	SAMPLE TYPE/ METHODOLOGY	SUBJECT NUMBER	DEFINITION OF NONADHERANCE	PREVALENCE OF NONADHERENCE
Bambauer/2007[5]	United States	Psychiatric enrollees in a healthcare plan/retrospective review	2405	1. Immediate ATD non-adherence 2. 6-month ATD non-adherence	Immediate: 13.0% 6-month: 49.0%
Yeh/2008[6]	Taiwan	Psychiatric sample/Likert-style survey	181	Estimation of current ATD nonadherence	50.0%
Sawada/2009[7]	Japan	Psychiatric sample/ retrospective chart review	367	6-month ATD nonadherence	55.7%
Shigemura/2010[8]	Japan	Psychiatric sample/internet survey with Likert-style assessment	1151	ATD low-adherence status	33.1%
Lee/2010[9]	Korea	Psychiatric sample/prospective study	76	Medication monitoring system/ 1-month ATD nonadherence rate	48.1%

Note: ATD = antidepressant

treatment of depression with the acute phase lasting 4 to 8 weeks, the continuation phase lasting 4 to 9 months, and a discontinuation phase lasting "several weeks," indicating that the minimum duration of treatment with antidepressants for new-onset depression would seem to be six months, with routine treatment duration of up to one year. Given this guideline, Trivedi et al[3] indicate that only 25 to 50 percent of patients with major depression adhere to treatment.[3] In this same vein, Keller et al[4] indicate that patient adherence with antidepressant medication is poor.

Given this backdrop, we now examine the empirical terrain of antidepressant nonaderence among patients. To do so, we undertook a literature search of the PubMed and PsycINFO databases back to 2001 (i.e., approximately 10 years), entering the following search terms: *antidepressant, compliance, adherence,* and *nonadherence*, and collected studies with patient samples from both psychiatric and primary care settings. Because these types of studies appear to be described with various key words, we may have missed several studies, and therefore refer to our review as a sampling of recent studies. In addition, we excluded studies in foreign languages if data could not be extracted from the English abstract.

ANTIDEPRESSANT NONADHERENCE IN PSYCHIATRIC POPULATIONS

Through a literature search of antidepressant nonadherence in psychiatric populations, we encountered five studies (Table 1).[5–9] One study[5] was from the United States whereas the remaining four studies were from various countries in Asia. Sample sizes ranged from 76 to 2,405 individuals. As expected, the methodologies in these studies varied and included retrospective, current, and prospective designs. Data collection was diverse and obtained through a review of medical records or healthcare data, administered surveys, or utilization of a medication tracking system. In

TABLE 2. Sampling of antidepressant adherence studies in primary care populations over the past 10 years

FIRST AUTHOR/YEAR OF PUBLICATION	COUNTRY OF ORIGIN	SAMPLE TYPE/ METHODOLOGY	SUBJECT NUMBER	DEFINITION OF NONADHERANCE	PREVALENCE OF NONADHERENCE
Demyttenaere/2001[10]	Belgium	Primary care sample/prospective study	272	6-month ATD nonadherence	53.0%
Hansen/2004[11]	Denmark	Primary care sample/ retrospective review	4860	No ATD prescription filled for first 6 months	33.6%
Cantrell/2006[12]	United States	Managed care sample/ retrospective study	22,947	6-month ATD nonadherence	57.0%
Akincigil/2007[13]	United States	Health plan pharmacy claims/retrospective study	4312	4-month ATD nonadherence	49.0%
Bambauer/2007[5]	United States	Primary care enrollees in healthcare plan/ retrospective review	7982	1. Immediate ATD nonadherence 2. 6-month ATD non-adherence	Immediate: 18.0% 6-month: 53.0%
Hansen/2007[14]	Denmark	National registry/ retrospective study	Unknown	6-month ATD nonadherence (no refill after 6 months)	25.2%
Sheehan/2008[15]	United States	Managed care sample/ retrospective study	266,665	6-month ATD nonadherence	67.4–87.6% depending on ATD type
Vanelli/2008[16]	United States	Pharmacy records/retrospective study	211,565	First 30-days ATD nonadherence	38.8% in those without previous ATD exposure
Kennedy/2008[17]	United States	Medicare beneficiaries/ retrospective study	Unknown	Failure to fill/refill at least one ATD prescription	5.4%
Hrique/2009[18]	France	Primary care sample/ retrospective clinical interview	632	6-month ATD nonadherence, patient's initiative	58.1%
Bulloch/2010[19]	Canada	General population sample/survey	2497	Inadequate or missed doses during a typical treatment month with ATDs	45.9%
Serna/2010[20]	Spain	Prescription database/retrospective review	7525	4-month ATD nonadherence	56.0%
Fortney/2011[21]	United States	Primary care VA sample/prospective study	395	1. Never filled prescription 2. 6-month ATD nonadherence	4.8% 12.2%

Note: ATD = antidepressant; VA = Veterans Affairs

addition, across these studies, investigators used differing definitions of *nonadherence*. In summarizing findings, the overall nonadherence rates for antidepressant prescriptions ranged from 13 percent (at the outset of prescription) to 55.7 percent. In averaging those studies that examined antidepressant nonadherence at six months (2 studies), the nonadherence rate was 52 percent.

ANTIDEPRESSANT NONADHERENCE IN PRIMARY CARE POPULATIONS

Through a literature search of antidepressant adherence in primary care populations, we encountered considerably more studies (Table 2).[5,10–21] Of these 13 studies, seven were from the United States and six were from various other countries (the majority from Europe). Sample sizes ranged from 272 to 266,665 individuals. As expected, there were various methodologies in these studies, as well, including retrospective approaches, current patient impressions, and prospective designs. Data were elicited through a review of patient or pharmacy records, pharmacy claims, or national registries. In these studies, investigators used differing definitions of antidepressant nonadherence, as well. The overall nonadherence rates for antidepressant prescriptions ranged from 5.4 to 87.6 percent. In parceling out the eight studies that examined nonadherence during a six-month period,[5,10–12,14,15,18,21] the averaged rate of antidepressant nonadherence was 46.2 percent (in determining this overall average, we used an averaged percentage for the range presented in the Sheehan et al study,[15] which resulted in a rate of 77.5%).

COMPARISON OF SAMPLES

Given the limitations imposed by the variations in methodology, in comparing the six-month antidepressant nonadherence rates between psychiatric populations (52%) and primary care populations (46.2%), the percentages are very close. Findings indicate that approximately one-half of patients, either from psychiatric or primary care settings, will be nonadherent to antidepressant treatment. Interestingly, note that in both the Kennedy study[17] and the Fortney study,[21] rates of nonadherence were surprisingly low at 5.4 percent and 4.8 percent, respectively. Both of these low rates occurred in clinical populations with government-sponsored insurance (e.g., Veterans Administration, Medicare beneficiaries). This deviation from the general findings warrants further investigation (i.e., does low-cost or no-cost insurance improve antidepressant adherence?).

REASONS FOR PATIENT NONADHERENCE TO ANTIDEPRESSANTS

There appears to be a broad range of reasons why patients discontinue antidepressants prematurely. Bulloch and Patten[19] found that simply forgetting was the main reason for patient non-adherence. Fortney et al[21] found that side effects were a commonly reported reason for antidepressant discontinuation. Kennedy et al[17] found that lower adherence was associated with higher cost of the medication, medications not covered by insurance, the patient perception that the medication was not necessary, and patient's fears of side effects. Deterrents to adherence may also include medication-induced sexual dysfunction;[22] patient fears that antidepressants will be difficult to discontinue after being taken for a long time, and concerns that antidepressants may alter personality;[23] patient belief that antidepressants do not really solve a person's problems;[24] delayed onset of medication action;[25] poor instruction by the clinician about the antidepressant;[26] specific personality characteristics of patients such as extraversion[27] and/or Cluster B[28] or other personality disorder symptoms;[29] patient substance abuse;[29] patient fears of addiction;[30] lower patient depression severity;[31] complicated titration or dosing schedule of the medication;[32] lack of follow-up care by the clinician;[32] and low patient motivation.[32] How these factors load with regard to specific clinical populations (e.g., psychiatric vs. primary care) remains unknown. Suffice it to say that there are numerous reasons why patients prematurely discontinue antidepressant therapy.

CONCLUSIONS

From our sampling and review of studies examining patient antidepressant nonadherence over the past 10 years, we can draw two general conclusions: 1) about 50 percent of patients discontinue antidepressant therapy prematurely; and 2) this percentage does not meaningfully differ between psychiatric and primary care populations. We may also conclude that patients prematurely discontinue antidepressant therapy for a number of possible reasons, some patient-related (e.g., side effects, misperceptions about the medication) and some clinician-related (e.g., poor instruction by the clinician about the medication, lack of follow-up care). Appreciating the high nonadherence rate to treatment with antidepressants will hopefully underscore the importance of

carefully educating patients about this type of treatment, exploring questions and possible misperceptions that patients may have, and consistently monitoring patients for medication adherence.

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