Clinicians' Reasons for Antipsychotic Coprescribing

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Background: Prescribing more than 1 antipsychotic is common but has received little supportive evidence in the literature. This study was designed to systematically survey clinicians about their rationale for prescribing more than 1 antipsychotic for specific patients.

Method: Patients with schizophrenia (diagnosed according to ICD-9 criteria from October 1, 1999, to September 30, 2000) at 2 Veterans Administration (VA) medical centers and their prescriptions for antipsychotics (filled within the VA system from June 1, 2000, through September 30, 2000) were identified from administrative databases. Clinicians for each patient with more than 1 antipsychotic prescription were interviewed using a structured questionnaire. After summarizing offered explanations, we compared patients prescribed 2 atypicals with those prescribed an atypical and a conventional.

Results: The treatment of 66 patients was reviewed. The 4 most common reasons for coprescription were reducing positive symptoms (61%), reducing negative symptoms (20%), decreasing total amount of medication (9%), and reducing extrapyramidal symptoms (5%). In 65% of patients (41/63), psychiatric symptoms were thought to have been refractory to antipsychotic monotherapy. In 39% of patients (N = 26), antipsychotic coprescription was intended to be transitional, but in only 46% of these patients (N = 12) had this transition been completed after 6 to 12 months.

Conclusion: Prescribers for patients receiving more than one antipsychotic were frequently able to cite plausible and specific target symptoms they were attempting to address with this practice.

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Prescribing 2 or more antipsychotics in the treatment of schizophrenia occurs in 6.8%[1] to 15.0%[2] of outpatients and in nearly 50.0% of inpatients.[3] However, no large randomized clinical trials have evaluated this practice, and supportive evidence is limited to case reports, small trials, and practitioner experience.[4] With atypical antipsychotics costing thousands of dollars a year per patient,[5] neuroleptic coprescription could result in unnecessary expenditures and increased risk of side effects.

The current study was designed to investigate the clinical rationales for prescribing more than 1 antipsychotic. The types of coprescription of interest were those involving atypical antipsychotics—either 2 atypical antipsychotics or an atypical and a conventional antipsychotic.

METHOD

Patient Population

As part of a national quality-improvement project that used administrative data to investigate adherence to established antipsychotic dosing recommendations, all Veterans Administration (VA) outpatients diagnosed with schizophrenia from October 1, 1999, to September 30, 2000, (federal fiscal year FY00) were identified using an operational definition that required at least 2 outpatient encounters in a specialty mental health outpatient clinic with either a primary or secondary diagnosis of schizophrenia (corresponding to ICD-9 codes 295.00–295.95).[6]

Next, all prescription drug records filled by these patients within the VA system from June 1, 2000, through September 30, 2000, were obtained from the VA Drug Benefit Management System in Hines, Illinois. Since intramuscular neuroleptics are frequently administered without a corresponding written prescription being entered, only prescriptions for oral medications were included in the analysis. In addition, since treatment options following clozapine monotherapy were not well defined, patients receiving clozapine were also excluded. The last prescription for an antipsychotic medication was considered the index prescription, and all prescriptions for the previous week were obtained. Patients who were prescribed 2 atypical medications or an atypical and a conventional were identified as receiving antipsychotic coprescription.

Data Collection

As part of a regional quality-improvement subinitiative, clinicians who had coprescribed antipsychotics

Table 1. Reasons for Antipsychotic Coprescription for All Patients and by Type of Coprescription

Prescriber Response	All Patients (N = 66) N	%	AA (N = 24) N	%	AT (N = 42) N	%	χ^2 Value	p Value
Rationale for coprescription								
Benefits of polypharmacy								
Decreased total amount of medication	6	9	1	4	5	12	1.11	.30
Reduced positive symptoms	40	61	18	75	22	52	3.27	.070
Reduced negative symptoms	13	20	8	33	5	12	4.43	.035
Decreased extrapyramidal symptoms	3	5	0	0	3	7	1.80	.18
Treatment context								
Refractory to monotherapy	41/63	65	18/23	78	23/40	58	2.77	.10
Transition from one to another	26	39	7	29	19	45	0.58	.45
Transition completed	12/26	46	2/7	29	10/19	53	1.19	.28
Inherited from another prescriber	21	32	13	54	34	81	8.68	.0032
Coprescription was indicated	38/48	79	16/21	76	22/27	81	0.20	.65
Past clinical experience								
Experience indicates coprescription is useful	41	62	11	46	30	71	4.25	.040
Disagree with guidelines discouraging coprescription	46	70	15	63	31	74	0.92	.34

Abbreviations: AA = 2 atypical antipsychotics prescribed, AT = atypical and typical antipsychotic prescribed.

(of which at least 1 was an atypical and neither were clozapine) were identified at 2 Department of Veterans Affairs medical centers in New England. Each clinician was interviewed individually by a member of the administrative staff at the 2 institutions using a semistructured questionnaire (available on request from the first author).

Investigational review board approval was obtained for the presentation of the results in this article.

Measures

The survey was divided into 4 sections. The first section attempted to validate antipsychotic coprescription as suggested by the administrative pharmacy database.

The second section, and the central focus of the questionnaire, documented the clinician's rationale for antipsychotic coprescription. This section was divided into 6 subsections addressing (1) the justification for coprescription in this patient, (2) whether or not coprescription was intended to be transitional, (3) the provider's expectations of benefit from coprescription, (4) whether the provider disagreed with the general principle that coprescription should be avoided, (5) acceptable alternatives to this treatment, and (6) the role of patient preference in the decision to use more than 1 antipsychotic.

The third section addressed the general characteristics of the patient's treatment, including the prescriber's role on the treatment team, amount of treatment contact, duration of coprescription, and comorbid diagnoses. The fourth and final section documented prescriber characteristics.

Descriptive statistics were employed to characterize the responses of the prescribers. A further analysis was performed to determine whether there were significant differences in responses between patients who received a combination of atypical and typical antipsychotics and those who received 2 atypical antipsychotics.

RESULTS

Validating Dosage and Diagnosis

The treatment of 66 patients, whose clinicians confirmed antipsychotic coprescription, was reviewed at the 2 medical centers. None of these patients were also receiving decanoate at this time. For 42 patients (64%), a typical antipsychotic was coprescribed with an atypical antipsychotic; in the remaining 24 patients (36%), 2 atypical antipsychotics were prescribed.

Although all patients were identified from administrative databases as having the diagnosis of schizophrenia, current clinicians provided varying primary diagnoses: schizophrenia, N = 48 (73%); schizoaffective disorder, bipolar type, N = 7 (11%); schizoaffective disorder, depressed type, N = 7 (11%); and bipolar disorder, N = 4 (6%).

Reasons for Coprescription

Prescriber-observed benefits of coprescription included reduced positive symptoms (N = 40, 61%; Table 1), reduced negative symptoms (N = 13, 20%), decreased total amount of antipsychotic medication (N = 6, 9%), and decreased extrapyramidal symptoms (N = 3, 5%). In 41 of 63 patients (65%), symptoms were thought to have been refractory to antipsychotic monotherapy that the prescriber considered to be of adequate dosage and duration.

In 26 patients (39%), the antipsychotic coprescription was initially intended to be a transition from 1 antipsychotic to another. However, at the time of prescriber interview, from 6 to 12 months after the coprescription was recorded in the pharmacy record, only 12 of the 26 (46%) had completed this transition. Of those that had not completed the transition from 1 antipsychotic to another, reasons given included the presence of symptoms precluding carrying out the transition (N = 3), the patient insisting

that the coprescription be maintained (N = 2), and the patient not being seen often enough to manage the transition (N = 1).

Prescribers indicated that for 21 of 66 patients (32%), coprescription was inherited from another prescriber, while for 38 (79%) of 48 patients, prescribers thought that coprescription was clinically indicated. Among those patients for whom they did not think it was indicated, the leading reasons for coprescription were that the patient insisted (N = 6) or that symptoms precluded transitioning to monotherapy (N = 1).

Providers for 41 patients (62%) stated that experience with other similar patients suggested that antipsychotic coprescription is useful, while providers for 46 of the patients (70%) disagreed with the assertion that prescribing more than 1 antipsychotic should be avoided as an absolute guideline.

Two Atypicals Versus Atypical/Typical Combination

Of the 66 patients in the sample, 24 (36%) received 2 atypical antipsychotics (AA group) and 42 (64%) received a combination of atypical and typical antipsychotics (AT group). Comparison of the AA and AT groups revealed several significant differences. A significantly higher percentage of prescribers for patients in the AA group ($\chi^2 = 4.43$, $p = .035$) thought that coprescription resulted in reduced negative symptoms. There were also trends for prescribers of AA patients to more often assert that their patients' symptoms were refractory to monotherapy ($\chi^2 = 2.77$, $p = .10$) and that coprescription resulted in decreased positive symptoms ($\chi^2 = 3.27$, $p = .070$). Prescribers in the AT group were significantly more likely to state that the coprescription regimen had been inherited from another prescriber ($\chi^2 = 8.68$, $p = .0032$) but also that in their own personal experience, coprescription was useful in some cases ($\chi^2 = 4.25$, $p = .040$).

Prescriber Characteristics

The 16 prescribers interviewed represented 13 psychiatrists and 3 advanced practice nurses. Of the psychiatrists, 9 (69%) were board certified. There were no full-time medical school faculty in the sample, but 11 prescribers (69%) had a clinical or adjunct appointment.

For most patients (N = 48, 73%), the provider was acting as the primary provider—defined as being the "mental health treater who sees the patient most frequently," and therefore was likely to have a close familiarity with the patient's treatment.

DISCUSSION

Data presented in this study suggest that it is possible to meaningfully survey the reasons given by prescribers for employing antipsychotic coprescription. Clinicians cited specific target symptoms such as positive and negative symptoms that appeared to benefit from antipsychotic coprescription, occasionally resulting in a decreased total amount of prescribed antipsychotic. In nearly two thirds of patients, symptoms were described as having been refractory to monotherapy. In 39% of patients, antipsychotic coprescription was intended to be temporary as patients were switched from 1 antipsychotic to another; however, an average of 6 months later, the intended switch had occurred in only half of these patients.

In about one third of patients, the coprescription was inherited from another prescriber, while prescribers for nearly 80% of all patients thought that the coprescription was indicated, and 70% thought that blanket prohibitions against this practice were unjustified.

It is perhaps not surprising that clinicians readily justified their reasons for antipsychotic coprescription in selected cases. This may have reflected post hoc rationalization of their behavior, but it may also reflect the fact that, for patients whose symptoms do not respond to monotherapy, the prescription of more than 1 antipsychotic may be clinically justified.

This study has several limitations. First, it relied on each prescriber's recall about the indications for prescribing more than 1 antipsychotic. Clinicians may have thought that their practice was being reviewed for purposes of performance evaluation (although this was explicitly denied in the explanation of the interview) and so may have provided post hoc rationales to address this potential threat. Perhaps if more questions about the history of antipsychotic treatment had been included, there would have been a greater opportunity to explore potential inconsistencies between the clinician's account and the medical record. Second, relatively few patients' treatments were reviewed at the 2 VA medical centers, although the sample did represent every patient receiving at least 1 coprescription for an atypical and a typical or for 2 atypical antipsychotics at these 2 medical centers at a single point in time.

These results can be compared with another recent survey of antipsychotic coprescription within the VA.[7] In that study, the authors reported that the prescribers for patients who received the combination of an atypical and a typical antipsychotic most commonly reported improvement in positive symptoms. They also observed that for 12 (80%) of 15 patients for whom an atypical antipsychotic was added to a typical antipsychotic, the planned discontinuation of the typical antipsychotic was not attempted due to either prescriber or patient unwillingness in the face of symptomatic improvement with the antipsychotic coprescription.

This study represents the second attempt (M.J.S.; D. Leslie, Ph.D.; R.R., manuscript submitted), of which we are aware, to systematically seek out the views of prescribers who have been identified as deviating from a

treatment recommendation for the treatment of schizophrenia, and which, like its predecessor, found that, in the majority of cases, clinicians are able to make a cogent case for the continuation of this practice. Experimental research is needed to see if these rationales are empirically justifiable.

Drug name: clozapine (Fazaclo, Clozaril, and others).

REFERENCES

1. Leslie D, Rosenheck R. Use of pharmacy data to assess quality of pharmacotherapy for schizophrenia in a national health care system: individual and facility predictors. Med Care 2001;39:923–933
2. Wang P, West J, Tanielian T, et al. Recent patterns and predictors of antipsychotic medication regimens use to treat schizophrenia and other psychotic disorders. Schizophr Bull 2000;26:451–457
3. Ereshefsky L. Pharmacologic and pharmacokinetic considerations in choosing an antipsychotic. J Clin Psychiatry 1999;60(suppl 10):20–30
4. Stahl S. Antipsychotic polypharmacy: evidence based or eminence based? Acta Psychiatr Scand 2002;106:321–322
5. Rosenheck R, Leslie D, Sernyak M. From clinical trials to real-world practice: use of atypical antipsychotic medication nationally in the Department of Veterans Affairs. Med Care 2001;39:302–308
6. Leslie D, Rosenheck R. Third Annual Report on Schizophrenia Pharmacotherapy in the VA. West Haven, Conn: Northeast Program Evaluation Center; 2002
7. Tapp A, Wood AE, Secrest L, et al. Combination antipsychotic therapy in clinical practice. Psychiatr Serv 2003;54:55–59