

CME Activity

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CME Objectives

After completing this CME activity, the reader will be able to:

- Understand the implications of a new antipsychotic medication being defined as *atypical*: receptor activity, decreased extrapyramidal side effects, and improvement of negative symptoms of schizophrenia
- Understand, based on the case series, the somatic complaints likely to be made by patients using sertindole
- Understand the risks and benefits of sertindole in a treatment-resistant psychotic disorders case series

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In the spirit of full disclosure and in compliance with all Accreditation Council for Continuing Medical Education Essentials, Standards, and Guidelines, all faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows:

Dr. Suppes has received clinical research support from Abbott Laboratories, SmithKline Beecham, Parke-Davis, Glaxo Wellcome, Eli Lilly, and Novartis.

Neither Dr. Lee nor Dr. Knoll has any significant relationship with entities that may have influenced her or his presentation in any way.

Discussion of Investigational Information

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The Atypical Antipsychotic Sertindole: A Case Series

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and Trisha Suppes, M.D., Ph.D.

Background: Psychotic disorders are often difficult to treat with traditional neuroleptics. Sertindole is a new atypical neuroleptic with a broader CNS receptor profile.

Method: Ten patients diagnosed with either schizophrenia or schizoaffective disorder were treated with sertindole for 18 months and observed for changes in Clinical Global Impression scale scores.

Results: Nine patients experienced a reduction of symptoms after 12 months of treatment. Eight patients completed 18 months of treatment, all exhibiting overall improvement. Despite side effects of tiredness, weight gain, headache, nausea, and decreased ejaculatory volume, sertindole was generally well tolerated.

Conclusion: Sertindole appears to be a useful treatment in psychotic disorders. It may present an advantage over traditional neuroleptics in the form of fewer extrapyramidal symptoms and improvement of negative symptoms.

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Schizophrenia and schizoaffective disorder present important challenges to the psychiatric community. Both are common psychiatric illnesses. Schizophrenia affects an estimated 1% to 1.4% of the United States population,¹ while 0.5% to 0.8% suffer a lifetime prevalence of schizoaffective disorder.² Patients with these disorders demonstrate high utilization of both inpatient and outpatient services, loss of productivity, and impaired social functioning. Not surprisingly, these illnesses are associated with high economic costs.³

The dopamine hypothesis for schizophrenia proposes that a dopamine D₂ receptor blockade in the mesolimbic system is a primary catalyst stimulating the antipsychotic effects of neuroleptics. Extrapyramidal symptoms of schizophrenia and related disorders are thought to be produced by a dopamine receptor blockade in the nigrostriatal system.⁴⁻⁶ Limitations of traditional neuroleptics include poorly tolerated side effects such as parkinsonian symptoms (rigidity, bradykinesia, and tremor), dystonias, akathisia, excessive sedation, and tardive dyskinesia, all of which may lead to decreased compliance. Traditional neuroleptics also fail to treat negative symptoms, and possibly worsen them. Despite limitations, traditional neuroleptics such as haloperidol, loxapine, and chlorpromazine have been the treatment mainstay for schizophrenia and related disorders for over 40 years.

The need for improved treatment stimulated development of "atypical" antipsychotic agents. Although no standard definition of an atypical antipsychotic exists, distinguishing features include fewer neurologic side effects, greater efficacy in treating the negative symptoms of schizophrenia, and a broader receptor profile in the brain. Two of these agents, clozapine and risperidone, have been recently approved by the Food and Drug Administration (FDA) for treatment of schizophrenia. The following case series considers a new agent, the atypical neuroleptic sertindole, recently recommended for FDA approval.

Sertindole is believed to be centrally active at 5-HT₂ receptors, α_1 receptors, and D₂ receptor sites. Sertindole's

greatest affinity appears to be at 5-HT₂ receptors (antagonist), with lower effects on α_1 -adrenoceptors (antagonist), and even smaller effects at D₂ receptor sites.⁷ Consistent with the dopamine hypothesis, preclinical studies indicate that for D₂ receptor sites, sertindole has a greater selective antagonist effect on the mesolimbic dopamine neurons than on nigrostriatal neurons.⁸ This selectivity leads to its antipsychotic effects with relatively few motor effects. Studies also suggest that 5-HT₂ activity may enhance antipsychotic effects of atypical neuroleptics while reducing motor side effects.⁹ Given this information, it is predicted that sertindole would improve symptoms of schizophrenia while producing minimal neurologic side effects.

METHOD

Presented here is a consecutive case series examining the long-term safety of sertindole, which was added openly to treatment regimens of patients with schizophrenia or other psychotic disorders. Inclusion criteria included meeting DSM-III-R criteria for one of the following primary diagnoses: schizophrenia, schizoaffective disorder, or delusional disorder. Male or female patients between the ages of 18 and 72 years were eligible for study inclusion. Exclusion criteria included pregnant or lactating females, patients receiving methadone, and patients with either a history of substance/alcohol abuse or dependence within 2 months prior to sertindole initiation. All female subjects agreed to use contraception and avoid planned pregnancy throughout the study.

In late 1993, 10 patients were enrolled in the FDA phase 3 medical safety study for 1 year. Five patients were diagnosed as schizophrenic; the remaining five carried a diagnosis of schizoaffective disorder. Diagnosis, based on DSM-III-R criteria, was determined from clinical evaluation and chart review. All patients were from the local mental health authority and had extensive treatment histories and psychiatric hospitalizations. Eight patients had been treated with at least two classes of psychotropic medication prior to study enrollment. After a year of participation, patients were offered a 2-year extension of the study. This case series describes patients' progress during the first 18 months of sertindole treatment.

Study assessment instruments included the Clinical Global Impression scale, parts one (CGI-S) and two (CGI-I).¹⁰ The CGI-S is a clinician-administered scale designed to evaluate the global severity of patient illness. It rates patients' illness of the previous week on a 1 (normal or not at all ill) to 7 (among the most extremely ill) scale. CGI-S scores were assessed prior to starting sertindole,

after 12 months, and after 18 months of treatment. The CGI-I, on the other hand, examines global improvement of illness. This clinician-administered scale rates the illness of the previous week against the baseline score prior to sertindole initiation. The CGI-I is also scored from 1 (very much improved) to 7 (very much worse), with a score of 4 representing no change from baseline. CGI-I scores were assessed after 12 and 18 months of treatment. All CGI-S and CGI-I evaluations were based on monthly clinical interviews and psychiatric assessment.

After sertindole was titrated to a dose no greater than 24 mg daily and all previous neuroleptics were tapered, neuroleptic use other than sertindole was prohibited. The use of adjunctive psychiatric medications (e.g., benzodiazepines, mood stabilizers, antidepressants) and medications used to treat physical ailments was under the discretion of the treating physicians, although guidelines regarding certain medications were established. In particular, caution was advised concerning medications that increased or decreased the metabolism of sertindole or that prolonged the QT interval on electrocardiogram (ECG). Sertindole has been reported to prolong the QT interval in some patients. Additionally, sertindole has α_1 -adrenergic antagonist activity; hence, caution was advised when prescribing drugs with this same activity because patients could develop orthostatic hypotension.

Patient compliance was monitored through a medication diary. Patients or caregivers were instructed to record daily time and dosage of sertindole administration. In addition, an inventory of unused medications was kept by clinicians. To identify potential physical abnormalities, patients received scheduled blood chemistries, electrocardiographs, and physical examinations. Vital signs and weight were recorded at each study visit, and patients were assessed for new and reported side effects and adverse events.

RESULTS

Nine of the 10 patients showed improvement on sertindole treatment (eight patients with a dose of 24 mg/day, one with 20 mg/day). These nine patients demonstrated better control of positive symptoms, and eight of these patients completed 18 months of sertindole treatment. Five of the nine responders were diagnosed as schizophrenic.

At 12 months, Patients 2 and 8 left the study (see Table 1). Although she had responded to sertindole, Patient 2 requested dismissal from the study because of a preference for another neuroleptic. Patient 8 decompensated on sertindole treatment, necessitating hospitalization and an-

Table 1. CGI-S and CGI-I Scores of Patients on Sertindole Treatment*

Patient	Age (y)/ Race/ Sex	Diagnosis	Duration of Illness (y)	Score During Sertindole Treatment ^a					Comments
				CGI-S at Study Entry	CGI-S at 12 Mo	CGI-I at 12 Mo	CGI-S at 18 Mo	CGI-I at 18 Mo	
1	34/W/M	Schizophrenia, chronic paranoid	5	4	4	2	4	2	Began regular exercise, able to tolerate groups of people, decreased thoughts of violence toward animals, no longer openly responding to auditory hallucinations
2	52/W/F	Schizophrenia, chronic undifferentiated	19	4	4	2	NA	NA	...
3	49/W/M	Schizophrenia, chronic paranoid	30	5	4	2	4	2	Much improved hygiene and grooming, increased socialization, began working odd jobs
4	52/W/F	Schizophrenia, chronic paranoid	12	4	4	2	4	2	Markedly improved hygiene and grooming, increased involvement in psychosocial program
5	35/B/F	Schizophrenia, chronic undifferentiated	23	5	4	3	4	3	Improved hygiene and grooming, increased socialization, decreased psychomotor retardation
6	50/W/F	Schizoaffective disorder, bipolar	21	4	3	2	3	1	Improved hygiene and appearance, able to complete additional college work
7	36/W/M	Schizoaffective disorder, bipolar	10	4	4	2	4	1	Improved hygiene and grooming, increased involvement in activities, stated "best he has been"
8	33/W/M	Schizoaffective disorder, bipolar	20	4	5	5	NA	NA	...
9	38/W/M	Schizoaffective disorder, bipolar	13	4	4	3	4	3	Improved hygiene and grooming, able to maintain regular employment, decreased somatic complaints
10	29/W/M	Schizoaffective disorder, bipolar	7	4	4	2	4	2	Improved hygiene and grooming, entered beauty college, improved relationship with family, stopped drug and alcohol use

*Abbreviations: B = black, CGI = Clinical Global Impression scale, F = female, I = Improvement, M = male, NA = not applicable, S = Severity of illness, W = white.

^aCGI-S score range: 1 (normal or not at all ill) to 7 (among the most extremely ill). CGI-I score range: 1 (very much improved) to 7 (very much worse).

other neuroleptic to stabilize his symptoms. In addition, Patient 3 was hospitalized during the 18-month trial of sertindole (see case report below).

At 12 months of treatment, four patients displayed changes from baseline in their CGI-S scores. Patients 3 and 5 demonstrated improvement from a score of 5 (markedly ill) to 4 (moderately ill). Patient 8 showed a de-

terioration in clinical condition from a score of 4 to 5 (moderately to markedly ill). CGI-I scores at 12 months illustrated improvement for nine of the 10 patients. Seven patients were assessed "much improved," two patients as "minimally improved," and one patient (Patient 8) was described as "minimally worse." (See Table 1 for CGI-S and CGI-I scores.)

Table 2. Medication Regimens for Patients at Initiation, at 12 Months, and at 18 Months on Sertindole Treatment

Patient	Prior to Sertindole	At 12 Mo on Sertindole	At 18 Mo on Sertindole	Side Effect
1	Haloperidol D	Sertindole	Sertindole	Decreased ejaculate volume
2	Fluphenazine D thioridazine benztropine	Sertindole thioridazine nortriptyline clonazepam flurazepam diphenhydramine	NA	Insomnia, tiredness, weight gain
3	Perphenazine clonazepam benztropine propranolol	Sertindole trazodone clonazepam	Sertindole trazodone clonazepam	Insomnia, nausea, headache
4	Clozapine valproic acid benztropine hydroxyzine	Sertindole valproic acid trazodone	Sertindole valproic acid trazodone	Daytime sedation, nausea, decreased appetite, drooling
5	Haloperidol D benztropine trazodone alprazolam	Sertindole valproic acid trazodone	Sertindole valproic acid trazodone clonazepam	Insomnia, daytime sedation, headache
6	Haloperidol fluoxetine trazodone	Sertindole fluoxetine doxepin	Sertindole fluoxetine doxepin	Insomnia, decreased energy, increased appetite, weight gain
7	Lithium clonazepam	Sertindole bupropion diazepam	Sertindole lithium trazodone bupropion diazepam	Insomnia, decreased energy, nausea, weight loss, nasal congestion
8	Trifluoperazine lithium valproic acid	Sertindole lithium valproic acid	NA	Daytime sedation, weight gain, drooling
9	Perphenazine clonazepam propranolol	Sertindole sertraline clonazepam diphenhydramine	Sertindole sertraline clonazepam diphenhydramine	Decreased ejaculate volume, weight gain, headache
10	Haloperidol lithium	Sertindole lithium sertraline clonazepam	Sertindole lithium	Decreased ejaculate volume, headache

All eight study patients remaining at 18 months demonstrated persistent clinical improvement (Table 1). Each maintained CGI-S scores identical to those in the 12-month assessment. CGI-I scores also evidenced a continuation of the 12-month ratings, with two patients (Patients 6 and 7) showing further improvement in global functioning from their baseline evaluation. These two patients were rated as "much improved" (CGI-I score of 2) at 12 months and "very much improved" (CGI-I score of 1) at the 18-month scoring. Additionally, five patients showed improved social, occupational, or academic functioning. Each of the patients displayed improved hygiene and self-care.

Prior to study enrollment, nine of the 10 patients were taking at least two psychotropic medications of different

classes. Most patients were taking one or more of the following adjunctive medications: a mood stabilizer, an antidepressant, or an anxiolytic agent. As shown in Table 2, only one patient was taking a neuroleptic alone. After 12 months of treatment, three patients were taking fewer psychotropic drugs, four maintained the same number of medications in their regimen, and three patients increased the number of types of medication. At 18 months, four of eight patients were taking the same number of medications as at study entry. Two patients were taking fewer medications, and two were taking more medications.

Five of 10 patients after treatment with sertindole showed a prolonged QT_c interval (> 0.5 sec) on ECG tests, which subsequently decreased spontaneously (see

Table 3. QT_c Interval Changes in Patients Taking Sertindole*

Patient	QT _c at Study Entry	QT _c at 4 Mo	QT _c at 8 Mo	QT _c at 12 Mo
3	375	508	453	360
5	430	486	505	360
8	435	486	467	539 (486 at 13 mo)
9	360	450	608	464
10	442	481	595	400

*All measurements in milliseconds.

Table 3). Patient 10 was unable to maintain a sertindole dose of 24 mg/day due to a prolonged QT_c interval (> 0.5 sec). However, a dosage adjustment to 20 mg/day normalized the effect. The following adverse events and side effects were also reported (see Table 2). Three of six men experienced decreased ejaculatory volume. Other side effects, all of which were fairly mild and did not impair the patients' ability to function, included periodic headaches (4 of 10 patients), tiredness or decreased energy (3 of 10 patients), and nausea (3 of 10 patients). Weight gain (4 of 10 patients) ranged from 10 to 30 lb (4–14 kg) in the affected patients. Daytime sedation was noted in three patients and insomnia in five patients. However, for these two complaints, causality was difficult to ascertain due to concomitant medications and periodic disruption in sleep-wake cycles. All side effects persisted for at least 2 months.

Case Report: Patient 3

Patient 3 was a 49-year-old man diagnosed with chronic paranoid schizophrenia. This patient's illness had persisted for 30 years and included over six hospitalizations. He had a history of alcohol abuse, but more than 12 years of sobriety at study entry. A closed head injury resulting from a fall was reportedly suffered at age 18. Medical history emphasized chronic obstructive pulmonary disease, anemia, and a grand mal seizure 2 years prior to this study. This seizure was considered a secondary effect of metabolic abnormalities originated by psychogenic polydipsia. Acute exacerbation of this patient's illness was characterized by disorganized thought processes, bizarre and agitated behavior, loud speech, and impaired hygiene. Violent behavior involved a history of fighting, gun collecting, and a stabbing of his brother. This patient's negative symptoms included poverty of thought, blunted affect, and social withdrawal, even during episodes of well-controlled positive psychotic symptoms.

Extensive therapy included electroconvulsive therapy (ECT) in the late 1960s and neuroleptic treatment with haloperidol, perphenazine, and thioridazine. Additional

medication trials utilized lithium, carbamazepine, and methylphenidate. This patient was referred to the sertindole study because of continued psychosis and severe extrapyramidal symptoms. Prior to enrollment, Patient 3 received daily treatment of perphenazine 16 mg, benztropine 4 mg, propranolol 80 mg, and clonazepam 1 mg. At study entry, sertindole was titrated to a daily dose of 24 mg, while perphenazine, propranolol, and benztropine were gradually tapered. During sertindole initiation, the patient decompensated, requiring 1 month of hospitalization. At discharge, psychotic symptoms had subsided, and over the subsequent months, positive symptoms of schizophrenia were held in check. Extrapyramidal symptoms persisted, however, but showed marked improvement over the 18 months of treatment. Social gains included noticeable improvement in hygiene and facilitated employment. This patient had been unemployed for 8 years.

Sertindole was well tolerated by this patient. He experienced insomnia, which was responsive to low-dose trazodone. He also demonstrated on one ECG a prolonged QT_c interval (> 0.5 sec). His baseline QT_c was 0.375 sec at study entry. At 4 months, his QT_c interval was 0.508. By 8 months, the QT_c had decreased to 0.453 and further at 12 months to 0.360 (see Table 3). The QT_c changes were deemed clinically insignificant by the administering cardiologist.

Case Report: Patient 6

Patient 6 was a 50-year-old woman with a 21-year history of schizoaffective disorder, bipolar type. This patient had more than eight psychiatric hospitalizations, but other medical history was unremarkable. Family history included a sister with depression. The patient's illness began in her late 20s with several depressive episodes followed by periods of irritability, paranoid and delusional ideation, aggressive behavior, and auditory hallucinations. At age 40, the patient began experiencing persistent auditory hallucinations in the absence of mood symptoms. She was treated with a variety of medications in-

cluding haloperidol, fluphenazine, lithium carbonate, amitriptyline, tranylcypromine, fluoxetine, nortriptyline, trazodone, trihexyphenidyl, and diphenhydramine. In early 1994, this patient was referred to the study because of persistent hallucinations that interfered with her ability to concentrate. Her current medication regimen included haloperidol 10 mg, fluoxetine 20 mg, and trazodone 200 mg. Once enrolled, sertindole was titrated to 24 mg daily. Haloperidol was tapered off, and trazodone was replaced with doxepin for sleep enhancement. Fluoxetine was continued.

During sertindole treatment, the patient has maintained clinical stability for over 18 months. Her auditory hallucinations were greatly attenuated and no longer disruptive to concentration. In fact, she completed several college courses while working part-time. Hygiene and grooming also improved. She reported no intolerable side effects, but did note increased appetite, weight gain, insomnia, and mildly decreased energy unrelated to depressive symptoms.

DISCUSSION

Nine of 10 patients showed clinical improvement after 12 months on sertindole treatment, as supported by CGI-I scores. Seven of those patients were assessed as clinically "much improved." At 18 months, all remaining eight patients demonstrated global improvement on the CGI-I that was equal to or better than that seen at 12 months.

Two patients required hospitalization during the study. As discussed, Patient 3 began decompensating prior to the initiation of sertindole and continued to decompensate during the initial titration phase. The patient did well with sertindole 24 mg/day, however. The second patient (Patient 8) had a limited response to sertindole, recording a CGI-I score of 5 at 12 months. Exacerbation of symptoms led to hospitalization and required discharge from the study. In addition to Patient 8, Patient 2 also left the study. However, this patient demonstrated an improvement in her overall global functioning while taking sertindole. At 12 months, her CGI-I assessment was a rating of 2 (much improved).

Nine of 10 patients maintained control of positive symptoms. At 18 months, all eight remaining study patients demonstrated improvement in hygiene and self-care. Five of those increased or initiated participation in work, school, or psychosocial programs. The observations about social and occupational functioning support the clinical impression that sertindole improved negative symptoms.

There were no reports of parkinsonian symptoms, dystonia, or akathisia caused by sertindole. This supports theories mentioned in the introduction regarding the receptor profile of sertindole. No medical complications were experienced in relation to a prolonged QT_c interval on ECG seen in five of 10 patients (see Table 3). These changes were transient in all cases, and no subject experienced any clinical symptoms. In four of 10 patients, the prolonged QT_c interval spontaneously decreased during 12 to 13 months of treatment. In one patient, a dose reduction from 24 to 20 mg at 8 months was associated with a normalization of the QT_c 1 week later. Insomnia and daytime sedation were noted by several of the patients, but given the use of other sedating medications and the periodic disruption in sleep-wake cycle, it is difficult to attribute these events to sertindole. It should be noted that weight gain was observed in 40% of subjects. Overall, side effects were well tolerated, and patient compliance was good.

As Table 2 illustrates, after 12 months of treatment, the number of medications prescribed for three of the 10 patients had increased. Two patients were taking more medications at 18 months than they were at study entry. One explanation for the increased number of medications was the closer attention given to treatable symptoms. This closer scrutiny may also have contributed to the overall global improvement demonstrated by these patients.

Results of this case series suggest that a dose of 20 to 24 mg/day of sertindole is able to elicit a clinically meaningful improvement in 80% of subjects over 18 months of treatment. In particular, both positive and negative symptomatology were reduced, while no clinically significant neurotoxicity was observed.

While this case series was small, its results indicate that sertindole may effectively treat psychotic illnesses. The advantages of sertindole over traditional neuroleptics include the absence of parkinsonian symptoms and akathisia and the improvement in negative symptoms. Sertindole may offer patients novel and efficacious reduction of extrapyramidal symptoms and negative symptoms. Controlled trials in the long-term utility of sertindole are needed to further evaluate its maintenance treatment potential with schizophrenia and schizoaffective disorder.

Drug names: alprazolam (Xanax), amitriptyline (Elavil and others), benzotropine (Cogentin and others), bupropion (Wellbutrin), carbamazepine (Tegretol and others), chlorpromazine (Thorazine and others), clonazepam (Klonopin), clozapine (Clozaril), diazepam (Valium and others), diphenhydramine (Benadryl and others), doxepin (Sinequan and others), fluoxetine (Prozac), fluphenazine (Prolixin and others), flurazepam (Dalmane and others), haloperidol (Haldol and others), hydroxyzine (Atarax and others), loxapine (Loxitane), methylphenidate

(Ritalin), nortriptyline (Pamelor and others), perphenazine (Trilafon), propranolol (Inderal and others), risperidone (Risperdal), sertraline (Zoloft), thioridazine (Mellaril and others), tranylcypromine (Par-nate), trazodone (Desyrel and others), trifluoperazine (Stelazine), tri-hexyphenidyl (Artane and others), valproic acid (Depakene and others).

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Instructions

Psychiatrists may receive 1 hour of Category 1 credit toward the American Medical Association Physician's Recognition Award by reading the article starting on page 410 and correctly answering at least 70% of the questions in the quiz that follows.

1. Read each question carefully and circle the correct corresponding answer on the Registration form.
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1. Sertindole is considered an atypical antipsychotic because it is:

- a. A dopamine receptor antagonist
- b. A serotonin receptor antagonist
- c. An α -adrenergic receptor antagonist
- d. All of the above
- e. None of the above

2. Use of sertindole increases:

- a. Extrapyramidal side effects (e.g., dystonia and akathisia)
- b. The severity of negative symptoms
- c. Answer a only
- d. Answers a and b only
- e. None of the above

3. Sertindole use over 12 to 18 months in 10 patients was associated with:

- a. Clinical improvement of psychiatric symptoms in most cases
- b. Psychosocial gains
- c. Improved hygiene
- d. All of the above
- e. None of the above

4. Some of the side effects observed with sertindole are:

- a. Insomnia
- b. Weight gain
- c. Daytime sedation
- d. Decreased ejaculate volume
- e. All of the above

5. When asked, most patients:

- a. Would most likely continue taking sertindole
- b. Believed sertindole was clinically helpful to them
- c. Described side effects, but felt these were tolerable because of helpful clinical effects
- d. Believed sertindole decreased symptoms of their illness more effectively than usual antipsychotics
- e. All of the above

6. This case series described patients with psychotic illnesses who responded inadequately to at least two different classes of typical antipsychotics. When given sertindole:

- a. Positive symptoms decreased
- b. Negative symptoms decreased
- c. Most patients needed 20 to 24 mg daily
- d. Most patients' clinical improvement was evident from psychosocial gains and the CGI change scores
- e. All of the above

7. In this medical safety study of sertindole:

- a. The ECG QT_c initially increased in some patients
- b. The ECG QT_c normalized in these patients over 1 year of treatment
- c. No adverse events were noted that were related to changes in the ECG QT_c
- d. All of the above
- e. None of the above

Circle the one correct answer for each question.

1. a b c d e
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3. a b c d e
4. a b c d e
5. a b c d e
6. a b c d e
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5. Achievement of educational objectives:

A. Enabled the reader to understand the implications of a new antipsychotic medication being defined as *atypical*: receptor activity, decreased extrapyramidal side effects, and improvement of negative symptoms of schizophrenia. _____

B. Enabled the reader to understand, based on the case series, the somatic complaints likely to be made by patients using sertindole. _____

C. Enabled the reader to understand the risks and benefits of sertindole in a treatment-resistant psychotic disorders case series. _____

6. This CME activity provided a balanced, scientifically rigorous presentation of therapeutic options related to the topic, without commercial bias. _____

7. Please comment on the impact that this CME activity might have on your management of patients.

8. Please offer additional comments and/or suggested topics for future CME activities.

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