ABSTRACT

In psychosis, appropriate prescribing and administration of medication are keys to patient care. The first generation of antipsychotic drugs is characterized by potent D2 dopamine receptor blockade intended to control positive symptoms of schizophrenia. Second-generation antipsychotic agents, however, are serotonin-dopamine receptor antagonists that block dopamine and 5-HT2A receptors. They have an effect on positive, negative, and cognitive symptoms of psychosis and produce fewer extrapyramidal side effects than do first-generation drugs. Each atypical drug has a distinct pharmacodynamic profile, however, and can be associated with other adverse effects, such as weight gain and lipid abnormalities. An understanding of the association between pharmacodynamic properties and side effects can help psychiatric nurses to better tailor therapies to individual patients. (Adv Stud Nurs. 2004;2[4]:135-145)

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IMPROVING OUTCOMES FOR PATIENTS WITH PSYCHOTIC DISORDERS*

Geoffry W. McEnany, RN, PhD, CS†

Psychotic disorders are complex neurobiologic brain diseases that can potentially result in severe long-term psychosocial and functional impairments. In humans, neurobiologic responses can range from normal adaptive responses, such as logical thought and perceptions, to entirely maladaptive responses, such as thought distortions and hallucinations. The symptoms of psychosis manifest as profoundly maladaptive neurobiologic responses that seriously impair the lives of individuals, their families, and communities. It is important to recognize that these neurobiologic experiences are a dimension of the experience of symptoms in persons living with psychiatric illnesses that manifest with psychotic symptoms. Mitigating influences in the environment, such as social support, create changes in the manifestation of symptoms through complex mechanisms that modulate neurobiology. Herein lies the operational definition of psychiatric illnesses as truly biopsychosocial entities. Like other psychiatric disorders, symptoms of psychotic disorders are influenced by interventions that are biologically based (eg, medications) as well as psychosocially focused, as is the case with many psychotherapies. A combination of therapeutic approaches leads to the best clinical outcomes.

Although psychosis is sometimes present in other psychiatric disorders, such as depression with psychotic features and extreme manic episodes associated with bipolar disorders, schizophrenia is perhaps the most widely recognized psychotic disorder. The symptoms of schizophrenia are frequently categorized as either “positive” or “negative” (see Sidebar “Symptoms of Schizophrenia,” page 137); some clinicians also include a third category. Schizophrenia is classified into 5 categories based on the predominant clinical picture: paranoid, disorganized, undifferentiated, catatonic,
The constellation of symptoms associated with psychosis, however, extends beyond these classic definitions to include cognitive and mood symptoms, attention deficits, impaired memory and decision-making abilities, hopelessness, and suicidal tendency. Figure 1 illustrates how all 5 symptom clusters ultimately lead to social and occupational dysfunction, making schizophrenia among the most devastating and costly mental illnesses.1

**Approaches to Treatment**

The general goals of treatment of schizophrenia are to decrease the frequency, severity, and psychosocial consequences of episodes and to maximize psychosocial functioning between psychotic episodes. The specific goals of treatment depend on the phase of the illness and on other specific characteristics of the patient. For example, those experiencing a psychotic episode for the first time will require a thorough and in-depth evaluation for the clinician to establish a diagnosis and to formulate an effective treatment plan. This process may differ from the process for a patient who has an established diagnosis and a relationship with a group of providers working to manage the symptoms of the illness effectively over time. Many patients with schizophrenia need specific community, supportive, and rehabilitative services to address the impairments in role function associated with their disorder.2 Whether a patient is encountering symptoms of psychosis for the first time or is receiving ongoing care, the role of trusting relationships between a patient and healthcare providers is central to effective treatment and illness management.

**Key Strategies for Managing Schizophrenia**

Treatment of patients with schizophrenia requires an appreciation of the need for a multidimensional approach to care. The need for medications is one facet of the treatment plan but is complemented by a variety of other approaches, including psychosocial interventions that address functional impairments.
occurring over the course of the illness. A comprehensive approach to the treatment of patients with schizophrenia is critical to optimal outcomes. The specifics of standard treatment are articulated in the American Psychiatric Association’s treatment guidelines, which provide clinicians with both the rudiments of treatment planning and benchmarks of effective treatment over time. Such guidelines become the community standard for the treatment of schizophrenic patients and as such should be familiar to everyone engaged in the delivery of treatment to this population.

Treatment planning ideally involves patients and their families in an active collaboration, using an integrated approach with appropriate pharmacologic, psychotherapeutic, psychosocial, and rehabilitative interventions. Key strategies include the following:

- Establishing and maintaining a therapeutic alliance
- Monitoring the patient’s psychiatric status
- Providing education regarding schizophrenia and its treatments
- Determining the need for medication and other specific treatments and developing an overall treatment plan
- Enhancing adherence to the treatment plan
- Increasing understanding of and adaptation to the psychosocial effects of the illness
- Identifying and initiating treatment for new episodes as early as possible
- Addressing factors that precipitate and/or perpetuate episodes
- Initiating efforts to relieve family distress and improve family functioning
- Facilitating access to services and coordinating resources among the mental healthcare network and other systems of care.

Appropriate prescribing and administering of medication are keys to patient care. Most patients alternate between acute psychotic episodes and stable phases with full or partial remission (Figure 2). These phases form the structure for integrating treatment approaches.

Historically, pharmacologic treatment of schizophrenia has been directed toward management of positive symptoms, which are believed to arise from excess dopaminergic activity in the mesolimbic pathway. The clinical understanding of the complex constellation of symptoms in schizophrenia, however, has not always been so well understood. Not until the late 1980s was there a clear delineation of positive and negative symptoms in a way that enhanced clinical approaches to symptom management. Nancy Andreasen, in *The Broken Brain*, discussed the dimensions of both positive and negative symptoms. Over time, these symptom clusters have become part of the clinician’s “lenses” through which symptom patterns are better understood. This delineation of positive and negative symptoms also opened the door, from a phenomenologic perspective, to explore the underlying biology that distinguishes these symptom clusters. During the 1990s and into the present, the clinical understanding of the biological dysregulation associated with these distinct symptom patterns has led to more precise biological interventions aimed at the amelioration of both positive and negative symptoms.

### Symptoms of Schizophrenia

**Positive Symptoms**
Excess or distortion of normal function, usually responsive to traditional drugs, manifesting as:
- Delusions and hallucinations
- Disorganization of speech, thoughts, and behavior
- Poor attention

**Negative Symptoms**
A diminution or loss of normal function, usually unresponsive to traditional antipsychotics and more responsive to atypical antipsychotics, manifesting as:
- Restricted range and intensity of emotional expression (affective flattening)
- Reduced thought and speech production (alogia)
- Asociality (anhedonia)
- Decreased initiation of goal-directed behavior (avolition)

### The Dopamine Hypothesis

Significant advances have been made in the understanding of the various dopamine pathways in the brain and the relationship of these pathways to specific symptoms. The 4 pathways are the mesolimbic, mesocortical, nigrostriatal, and tuberoinfundibular. Each pathway plays a different role in the symptom experience of schizophrenic patients. The mesolimbic pathway originates from the midbrain ventral tegmen-
tal area and innervates the ventral striatum (nucleus accumbens), olfactory tubercle, and parts of the limbic system. In schizophrenia, this pathway demonstrates a hyperactive tone (excess dopamine activity); this dopaminergic hyperactivity is associated with the presence of positive symptoms related to the excessive activation of postsynaptic receptors.

The mesocortical pathway also originates from the midbrain ventral tegmental area and innervates areas of the frontal cortex. It has been implicated in aspects of learning and memory. In schizophrenia, this pathway is believed to demonstrate a hypoactive tone, associated with the presence of negative symptoms and cognitive impairment.

The nigrostriatal pathway is involved in control of movement. The tuberoinfundibular pathway projects from the hypothalamus to the anterior pituitary gland and controls prolactin secretion. These pathways are less involved in the pathogenesis of schizophrenia-related symptoms but are potently affected by many of the older or standard treatments aimed at symptom amelioration.

The goal of effective treatment becomes control of both a hyperactive and a hypoactive dopaminergic pathway that simultaneously coexist. The pathways are related to 2 different sets of symptoms: positive and negative.

**First-Generation Antipsychotic Agents**

First-generation antipsychotic agents, sometimes referenced as conventional or typical, suppress the positive symptoms of schizophrenia by antagonizing D₂ dopamine receptors in the mesolimbic and mesocortical pathways. The dopaminergic activity of these agents, however, extends beyond these pathways, where it can wreak potential havoc. For example, cognition may be impaired due to the suppression of dopamine activity in the cortex. Blocking dopamine activity in the nigrostriatal pathway acutely causes extrapyramidal symptoms (EPS), such as Parkinsonism and acute dystonias as well as tardive dyskinesia. Suppression of dopaminergic neurotransmission in the tuberoinfundibular pathway

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**Table 1. Dopamine Tracks and Effects of Antipsychotics**

<table>
<thead>
<tr>
<th>Site of Dopamine Action</th>
<th>Function</th>
<th>Antipsychotic Effect</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesolimbic</td>
<td>Emotional, intellectual</td>
<td>– hallucinations, delusions, disordered cognition</td>
<td>Diminished cognition</td>
</tr>
<tr>
<td>Mesocortical</td>
<td>Emotional, intellectual</td>
<td>– delusions, hallucinations, negative symptoms, cognitive?</td>
<td>Probable worsening of negative symptoms</td>
</tr>
<tr>
<td>Nigrostriatal</td>
<td>Extrapyramidal system movement</td>
<td>– motor symptomatology</td>
<td>Extrapyramidal effects: Parkinsonism, acute dystonias, tardive dyskinesia</td>
</tr>
<tr>
<td>Tuberoinfundibular</td>
<td>Regulates endocrine functions</td>
<td>– plasma prolactin levels</td>
<td>Hyperprolactinemia</td>
</tr>
</tbody>
</table>

First-generation antipsychotics suppress positive symptoms through potent antagonism of D₂ dopamine receptors in numerous pathways. Their action is nonselective, however, and thus causes side effects in pathways not related to symptom management.

leads to hyperprolactinemia, resulting in impairment of sexual function and fertility (Table 1; Figure 3). Other adverse effects result from the potent antimuscarinic, anti-alpha1-adrenergic, and/or antihistaminergic actions of conventional antipsychotics, including cognitive blunting, orthostatic hypotension, dry mouth, constipation, urinary retention, blurred vision, sedation, and weight gain.

SECOND-GENERATION ANTIPSYCHOTIC AGENTS

The introduction of clozapine in the late 1980s, followed by the second-generation antipsychotic drugs such as risperidone, olanzapine, quetiapine, and ziprasidone, revolutionized the treatment of psychotic disorders. For the first time, nurse clinicians had an opportunity to manage not only the positive symptoms of psychosis but also the debilitating negative symptoms, while achieving positive effects on cognition. Many practice guidelines and consensus statements therefore support the use of atypical antipsychotic medication as the agents of first choice in the treatment of schizophrenia.

Whereas first-generation antipsychotic agents suppress positive symptoms through potent antagonism of D2 dopamine receptors in numerous pathways, the atypical antipsychotic medications have varying effects on multiple neurotransmitters. The atypical agents occupy different tracks in their activity at the D2 receptors. The first is full agonism, achieved with the agent dopamine, resulting in full receptor activity. An antagonist, such as haloperidol or olanzapine, blocks the activity of the receptor, yielding no receptor activity. The newest atypical drug, aripiprazole, acts as a partial agent, marking a significant evolution in this class of antipsychotic agents. As

**Figure 4. TMAP Schizophrenia Algorithm**

Choice of antipsychotic should be guided by considering the clinical characteristics of the patient and the efficacy and side-effect profiles of the medication. Any stage(s) can be skipped depending on the clinical picture or history of antipsychotic failures.

![Diagram](image-url)
such, aripiprazole stabilizes the dopamine membrane and allows for receptor activation—less activation than would occur with a physiologic molecule such as dopamine. The result is a displacement of dopamine when too much is present, reducing dopamine activity and, thus, positive symptoms. If there is too little dopamine activity, a partial agonist triggers activation of the mesolimbic pathway, reversing negative symptoms. Thus, aripiprazole functions as an antagonist under conditions of dopamine hyperactivity to control positive symptoms and functions as an agonist in conditions of dopamine hypactivity to control negative symptoms and offer improvement of cognition with minimal motor or prolactin effects. As a result, hyperprolactinemia and EPS are minimized.9

Each atypical drug has its own profile of 5-HT2A receptor blockade. For example, clozapine is an antagonist for 5-HT2, 5-HT6, and 5-HT7 receptors. Ziprasidone is a significant agonist for 5-HT1A, an antagonist for 5-HT1D receptors, and an inhibitor of reuptake for norepinephrine and 5-HT.10 Aripiprazole is a high-affinity antagonist for 5-HT2A receptors and a partial agonist for 5-HT1A receptors; as such, aripiprazole is associated with improvements in negative and depressive symptoms as well as with decreased EPS. Additionally, aripiprazole has no affinity for muscarinic or cholinergic receptors, resulting in low potential for cognitive impairment and other anticholinergic side effects. Aripiprazole’s low-to-moderate affinity for alpha1-adrenergic receptors and histamine H1 receptors yields a low propensity for such adverse effects as orthostasis and a low liability for weight gain and somnolence.11 Because of these pharmacodynamic differences among therapies, it must be stressed that the atypical antipsychotic drugs are not all alike. Patients who do not obtain an adequate clinical response or who experience adverse effects may fare better with an alternate agent.10 The treatment algorithm for selection of antipsychotics used by the University of Texas, published in January 2003 and among the most current available, is presented in Figure 4.12

### ADVERSE EFFECTS

The potential for drug-specific adverse effects of antipsychotic agents is a clear concern for nurse clinicians and for patients. EPS, hyperprolactinemia, somnolence, sedation, and QTc prolongation have been associated with the use of some newer antipsychotic medications. Weight gain, glucose abnormalities that increase the risk for diabetes, and dyslipidemia are also clinical considerations when prescribing these therapies. Table 2 provides a comparison of antipsychotic adverse effects associated with atypical agents.12

### ADHERENCE TO TREATMENT

Nurses, in particular, understand that patient concerns about these adverse effects clearly lead to noncompliance with therapy. The medical literature suggests the primary reason for medication noncompliance in patients with schizophrenia is adverse effects, followed by a dislike of the medication, a perception that medication is not needed and is not effective, and simple forgetfulness.13

Treatment adherence, an important issue for nurses and for patients, is a consequence of the successful negotiation of a plan of care between providers and patients. Adherence differs from compliance because it evokes a different complementarity within the therapeutic relationship. Some would argue that compliance stems from a paternalistic model of care whereby the "provider knows best" and that treatment should be accepted by the patient as a product of the provider’s expert knowledge. Adherence is the consequence of a negotiated rela-

### Table 2. Comparison of Antipsychotic Adverse Effects

<table>
<thead>
<tr>
<th></th>
<th>EPS</th>
<th>TD</th>
<th>Orthostatic Hypotension</th>
<th>Prolactin</th>
<th>Sedation</th>
<th>Weight Gain</th>
<th>Anticholinergic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>+/–</td>
<td>–</td>
<td>+++</td>
<td>+/–</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Risperidone</td>
<td>+/++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+ (+)</td>
<td>+ (+)</td>
<td>+</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+ (+)</td>
<td>++ (+)</td>
<td>++ (+)</td>
<td>++</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>+/–</td>
<td>+/–</td>
<td>+/–</td>
<td>+/– (+)</td>
<td>++ (+)</td>
<td>++ (+)</td>
<td>++</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>+</td>
<td>+</td>
<td>+/–</td>
<td>+/– (+)</td>
<td>+ (+)</td>
<td>+ (+)</td>
<td>+</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>+++</td>
<td>+++</td>
<td>+/–</td>
<td>+/– (+)</td>
<td>+ (+)</td>
<td>+ (+)</td>
<td>+</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>+++</td>
<td>+++</td>
<td>+++/–</td>
<td>+ (+)</td>
<td>+ (+)</td>
<td>+ (+)</td>
<td>+</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>+/–</td>
<td>+/–</td>
<td>+/–</td>
<td>+/– (+)</td>
<td>+ (+)</td>
<td>+ (+)</td>
<td>+/–</td>
</tr>
</tbody>
</table>

EPS = extrapyramidal symptoms; TD = tardive dyskinesia. Adapted with permission from Miller et al. TIMA Procedural Manual Schizophrenia Module. Texas Department of Mental Health and Mental Retardation; 2003.11
tionship where both the patient and the provider share different but equal responsibilities in the outcome of treatment. Using an adherence model, the patient selects a treatment from a variety of options that provides the best fit between symptom manifestation and tolerability of potential adverse effects.

Given the human propensity for imperfection, total adherence is rare, and partial adherence is most likely the path taken by many patients. In circumstances of nonadherence, the clinician must question what is driving the pattern of nonadherence (eg, cognitive difficulties in understanding the treatment regimen, discomfort with the regimen itself, adverse effects). Both the patient and clinician are responsible for communicating patterns of adherence. The clinician must keep treatment options at the forefront of the discussion with patients, coupled with a willingness to change the regimen to better suit the patient and to deal with the presenting symptoms with greater comfort and effectiveness. Whereas the focus thus far has been on discussing medication side effects in general, some data are presented here to substantiate the discussion from an empirical perspective.

Management of adverse effects provides the greatest challenge to treatment adherence. Adequate management of potential adverse effects is critical for long-term positive outcomes in patients with schizophrenia, both from a subjective and objective stance. Although potential adverse effects related to the extrapyramidal system or from anticholinergic mechanisms may be the source of significant subjective discomfort, other adverse effects, such as hyperlipidemia, may occur silently. In the section that follows, the discussion focuses on a variety of common adverse effects related to the use of antipsychotic medications. Management of these adverse effects is important for overall health maintenance as well as comfort. Failure to deal effectively with potential adverse effects is likely to complicate treatment regimens and may have serious long-term effects, such as type 2 diabetes or cardiovascular complications from antipsychotic medications, and may contribute to morbidity, mortality, and escalating costs associated with treatment.

**EXTRAPYRAMIDAL ADVERSE EFFECTS**

Figure 5 illustrates findings from several clinical trials investigating the use of anti-Parkinsonian medications used concomitantly with atypical antipsychotic agents. Among these atypical agents, risperidone is associated with the highest use of such drugs, followed by olanzapine, ziprasidone, and quetiapine. With the exception of quetiapine, as dose increases, the percentage of patients who require medication to treat EPS also increases. A separate study comparing long-term use of aripiprazole with...
haloperidol, however, shows that aripiprazole, taken at the robust dose of 30 mg, demonstrates a negligible need for such medications as compared with 10 mg haloperidol (Figure 6). This bifurcation in the experience of EPS between aripiprazole and other agents is related to the strength of D₂ antagonism in the nigrostriatal pathway. Aripiprazole’s partial agonism in the nigrostriatal pathway is associated with negligible EPS, enhancing tolerability and comfort for the patient. Treatment of EPS is critical to both comfort and treatment adherence but, given the nature of EPS, the patient may not readily be aware of some dimensions of these adverse effects, such as certain dyskinesias. The clinician must monitor all dimensions of adverse effects; with EPS, the use of standardized instruments may help to monitor these adverse effects over time. If the clinician discusses EPS liability of a given medication before prescribing or administering that medication, it will help the patient to monitor for potential adverse effects and may reduce issues with treatment adherence.

**Serum Prolactin Levels**

Hyperprolactinemia is a potential adverse effect of antipsychotic drugs with mechanisms of action involving D₂ antagonism in the tuberoinfundibular pathway, including conventional and some atypical antipsychotic agents. Hyperprolactinemia can potentially cause amenorrhea, galactorrhea, decreased bone density, increased risk of breast cancer, increased risk of venous thromboembolism, sexual dysfunction, and problems with fertility. Long-term hyperprolactinemia results in gonadal hormone deficiency; thus, its management is an important clinical concern. In a short-term study, aripiprazole was not associated with hyperprolactinemia. Patients treated with aripiprazole experienced a decrease (57% from baseline) in serum prolactin levels; however, the prolactin levels for all but 1 patient in the aripiprazole group remained within normal limits. In contrast, statistically significant increases in serum prolactin were detected in patients taking haloperidol (120% from baseline) as compared with a placebo at all time points.

The greater the capacity of an agent to antagonize D₂ receptors, the greater the liability for changes in prolactin levels. Clinicians must recognize that mechanism of action is always directly related to an adverse-effect profile. Antipsychotic drugs with strong D₂ antagonism are at much greater likelihood of precipitating hormonally driven iatrogenic problems, which are uncomfortable as well as disturbing for the patient. Close monitoring by the clinician and a willingness to change medication strategies in the event of intolerable prolactin-related adverse effects is likely to enhance the patient’s treatment adherence and to improve clinical outcomes.

**Somnolence**

Somnolence greatly affects the patient’s quality of life from a variety of angles: impairment of overall attention, of social interaction, and of activities as well as an embarrassment for the patient. Clinical trial data suggest that olanzapine causes the highest degree of somnolence, followed by quetiapine, ziprasidone, aripiprazole, and risperidone, respectively (Figure 7). However, long-term trials of aripiprazole indicate that the somnolence gradually abates, with a very low incidence of somnolence at 26 weeks and at 52 weeks. These data point to the issue of tolerability over the long term. Tolerability is critical in managing illnesses, such as schizophrenia, that have longer-term trajectories and has clear implications for adherence, thus directly impacting treatment outcome.

**Weight Gain and Diabetes**

Weight gain merits special consideration from clinicians when dealing with medications used in a...
patient’s treatment. Clear discussions about the risk of weight gain must occur with patients prior to their use of any medication. Acceptable weight is defined by a variety of parameters, including culture. Weight has clear implications for the perceptions of others as well as the patient’s self-perception.

Weight gain remains a serious adverse effect of antipsychotic therapy, with clozapine and olanzapine use strongly associated with the most significant weight gain.\textsuperscript{21} Ziprasidone and aripiprazole are reported to have the least incidence of clinically significant weight gain among the atypical antipsychotic agents, according to package labeling. Because type 2 diabetes can result from weight gain (due to associated increased insulin resistance and decreased insulin sensitivity), the risk of diabetes in patients taking antipsychotic medication has been the subject of several clinical trials. The largest of these trials is the Veterans Affairs Retrospective Study, a retrospective analysis of 5837 patients taking olanzapine, risperidone, haloperidol, or fluphenazine over 3 years.\textsuperscript{22} The use of olanzapine was associated with a 37\% increased risk of diabetes as compared with risperidone. No differences in the rates of diabetes were detected with fluphenazine or haloperidol and risperidone.

Iatrogenic comorbidity is preventable, as is the case with weight gain. Selection of an agent with a low risk of weight gain, discussion of the potential implications of a given agent for weight gain, and behavioral strategies to minimize weight gain must be included in the treatment plan using an antipsychotic medication. These efforts can minimize the potential for negative outcomes and the emergence of costly, treatment-bound, and serious consequences.

\textbf{DYSLIPIDEMIA}

Among the potential adverse effects of antipsychotic medications, dyslipidemia is a serious clinical consideration, given its implications for long-term cardiac health. Lipid dysregulation requires the clinician’s close attention because these adverse effects are otherwise silent until the occurrence of a resulting clinical event. In the service of health maintenance and risk reduction, clinicians must be mindful of the potential impact of medications on lipid regulation. As with most adverse effects, the risk for negative outcome can be reduced with the use of behavioral measures, such as diet and exercise, and must be a part of the overall treatment plan.

Elevated cholesterol and low-density lipoprotein (LDL) cholesterol levels are a growing clinical concern, given documented trends related to lipid dysregulation in conjunction with a variety of atypical antipsychotic medications. LDL cholesterol and increased triglycerides have been shown definitively to increase risks for coronary and cerebrovascular disease. Clinical data suggest that patients taking olanzapine are at greater risk for hyperlipidemia as compared with those patients taking risperidone and ziprasidone.\textsuperscript{23-25} Fasting lipids and glucose were also recorded in a 26-week, placebo-controlled trial evaluating time to relapse.\textsuperscript{20} At baseline, patients randomly assigned to receive placebo had the following values: median baseline cholesterol (177 mg/dL), LDL (102 mg/dL), high-density lipoprotein [(HDL), 47 mg/dL], and triglyceride (161 mg/dL). Corresponding values in the patients taking aripiprazole were 191 mg/dL, 113 mg/dL, 47 mg/dL, and 161 mg/dL. Overall, small favorable changes in plasma lipid profiles occurred in both treatment groups, including a reduction in LDL cholesterol, an increase in HDL cholesterol, and a decrease in triglycerides. Use of aripiprazole is associated with actual decreases in LDL cholesterol and triglycerides and increases in HDL cholesterol.\textsuperscript{23} Data presented here are in a comparative fashion, and statistical analyses have not been completed. Data represent trends and should not be construed as statistically significant differences; however, the trends are favorable and merit further attention empirically.

\textbf{FROM THEORY TO PRACTICE: CLINICAL IMPLICATIONS}

Adverse effects of some antipsychotic agents include EPS, weight gain, hyperprolactinemia, hyperlipidemia, and type 2 diabetes. Evidence of these symptoms may warrant a switch to another antipsychotic medication. Clinical instrumentation is always a helpful supplement to the clinical assessment and judgment of the nurse. A variety of established instruments can be used (see Sidebar “Rating Scales,” page 144).\textsuperscript{26}

\textbf{EXTRAPYRAMIDAL MONITORING}

Whether a patient is or is not currently taking antipsychotic medications, it may be helpful to conduct a baseline assessment of potential dyskinetic movements or other EPS. These symptoms may be a consequence of previous treatment or the effects of other influences, such as aging (some dyskinetias may be related to normal aging). A baseline evaluation
using a standardized instrument provides a foundation against which future assessments can be compared. For those patients taking antipsychotic medications, a routine assessment of EPS and dyskinesia is critical and should be done regularly. In some states, these evaluations are mandated by law.

**Metabolic Monitoring**

In a study of the adverse effects associated with clozapine, Henderson recommends baseline measurements before treatment and at 6-month intervals for fasting plasma glucose, glycosylated hemoglobin, and lipid levels. Those patients with significant risk factors must be monitored more closely. Weight and body mass index also should be measured.

**Prolactin Monitoring**

The normal range of prolactin for nonlactating individuals is between 1 µg/L and 25 µg/L (male and female differences). The effects of hyperprolactinemia usually occur when the prolactin level ranges between 30 µg/L and 60 µg/L or greater. Although measurement of baseline prolactin levels is not common, monitoring for the clinical effects of altered prolactin is crucial. The clinician must be aware of the constellation of potential effects from hyperprolactinemia and be willing to make the necessary adjustments in the medication regimen to mitigate the adverse effects and enhance the patient’s comfort.

**Conclusion**

Nurse clinicians must strive to achieve therapeutic goals for patients with psychosis and remain mindful of the adverse effects associated with many antipsychotic medications. Because of the various pharmacodynamic properties of atypical antipsychotic agents, each medication manifests a profoundly individual safety and tolerability profile. Olanzapine and clozapine are most notably associated with weight gain, diabetes, and lipid abnormalities. Risperidone is associated with dose-related EPS and hyperprolactinemia. Aripiprazole has demonstrated a favorable comprehensive safety and tolerability profile with respect to both metabolic and nonmetabolic adverse effects.

The goal of therapy is to stabilize symptom patterns, minimize positive and negative symptoms, and prevent relapse. Only by matching the physical and clinical characteristics of each patient with the therapy best suited to that individual profile can these goals be achieved without compromising a patient’s overall health status.

**Rating Scales Used in the Diagnosis of Schizophrenia and in Assessing Effectiveness of Medication**

**Abnormal Involuntary Movement Scale (AIMS)**
A standardized physical examination using 12-item scale for assessment of medicine-induced abnormal movements, including tardive dyskinesia.

**Brief Psychiatric Rating Scale (BPRS)**
A standardized rating scale used to assess the severity of psychiatric symptoms, particularly psychotic symptoms. The scale has 18 items; each is assessed on a 7-point scale, from absent to extremely severe, and covers positive and negative symptoms.

**Clinical Global Impression (CGI)**
Used to assess overall severity of illness or degree of improvement. Comprising 3 components: Severity of Illness, Global Improvement, and Efficacy Index. Low scores indicate improvement.

**Positive and Negative Syndrome Scale (PANSS)**
A standard rating scale used in trials to assess symptom severity. The scale has 30 items; each is assessed on a 7-point scale from absent to extreme. It is divided into subscales covering both positive (PANSS-P) and negative symptoms (PANSS-N).

**Scale for the Assessment of Negative Symptoms (SANS)**
A standardized scale used to assess the negative symptoms of schizophrenia. Assessments are made using a 6-point scale covering a range of negative symptoms.

Data from the Association of the British Pharmaceutical Industry Web site.

**References**


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