

# Medicine Cabinet

## Prescribing medication for Asians with mental disorders

Many recommendations have been made about the drug treatment of medical outpatients with depression.<sup>1,2</sup> In this article, we do not attempt to repeat this guidance. Instead, we begin with a focus on the education of Asian patients who require medication and the clinical principles that guide medication management. Then, we discuss medication for mood and anxiety disorders using the selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines. Finally, we address important clinical issues related to the use of antipsychotic medications.

Using medications to treat Asian American patients with mental disorders can be challenging. Because of the belief that Western medicines may be too strong for their constitution, patients often experiment with medications.<sup>3</sup> Many seek immediate symptom relief because of previous exposure to benzodiazepines. The desire by some Asians to use herbal treatments may result in untoward drug interactions.<sup>4</sup>

Based on our clinical experience in treating Asian American patients, we believe that adopting a culturally

### Summary points

- Start with half the usual recommended starting dose because of possible side effects
- Explain that medications exert their full effects in weeks and not days and that adherence is important in achieving and maintaining positive results
- Minimize the use of benzodiazepines as monotherapy; if they are used jointly with another agent, taper dosage completely after several weeks or taper to the lowest effective dose
- Explain medication treatment using a model that describes the relationships between the brain, brain chemicals, and the restoration of balance to improve symptoms
- Although evidence of the effectiveness of herbal treatments is scant, allow use of some forms (eg, teas, soups) during continuation treatment if patients insist. Caution them, however, about possible interactions between herbs and medication

appropriate model for prescribing medication can help health care professionals manage these concerns and leads to better treatment for Asian American patients.

### PATIENT EDUCATION

Traditionally oriented Asians believe in the concept of maintaining balance (*yin* and *yang*, mind and body, hot and cold), and that this balance is integral to good health.<sup>5</sup> Health care providers should use this concept of balance to explain how medication can help.

- Explain that the patient's symptoms indicate an imbalance in brain chemicals that regulate mood, energy, emotion, and bodily sensations
- Explain that medications restore the balance but time is needed for them to work because the symptoms have been present for some time and stress has depleted the supply of these chemicals
- Emphasize the importance of taking medications daily and that you will work with the patient, starting at a low dose and evaluating its efficacy before increasing the dose
- Tell the patient that some side effects are expected but that they are time limited and generally mild if the proper dosage is used. Consider reframing side effects by saying that they are early indicators that the medicine is attempting to restore balance
- Advise patients to avoid using any herbal medications during this acute period of management. You can say

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**Competing interests:** J-P Chen and K-M Lin received speaker fees/educational grants and travel assistance, respectively, from Pfizer, Inc.; H Chung is Medical Director, Depression and Anxiety Disease Management Team, Pfizer, Inc.

*West J Med*  
2002;176:271-275



Bill Branson/NCI

Careful patient education of Asians who require prescription medication for mental illness is integral to a positive outcome

that while you respect their views, herbal medication use should be discussed when an optimal dose of the medicine has been achieved

- Do not call the psychotropic medication a “sleeping pill.” Instead, explain that symptoms will go away gradually. Family members and others may notice improvement even before the patient does
- To avoid the patient feeling abandoned by you, let the patient know that you will be available to manage the medications and answer questions during the course of treatment, even if you later refer the patient to a specialist

### ANTIDEPRESSANTS FOR MOOD AND ANXIETY DISORDERS

Selective serotonin reuptake inhibitors (SSRIs) are the first line of treatment of mood and anxiety disorders. They have demonstrated efficacy, are better tolerated than tricyclic antidepressants, and are safer in the event of overdose. The Table shows the four most commonly prescribed SSRIs in the US market. Each of these medications is currently approved for the treatment of major

depressive disorder. Several also are approved for use in the treatment of anxiety disorders such as panic disorder and posttraumatic stress disorder.

Although these medications are used by some physicians beyond their approved indications (off-label prescribing), the comfort level of clinicians for this type of prescribing varies by practice specialty. In this brief review, we restrict our discussion to approved indications, because they show that the drug’s efficacy and safety have been reviewed and approved by the US Food and Drug Administration. Any differences between different SSRIs mentioned in the table are directly referenced from the approved product labeling and are only mentioned when the drug is different from the group as a whole.<sup>6</sup>

#### Choice of SSRI

The prescribing clinician should consider the approved indications, individual patient preferences, response to previous treatment, and anticipated side effects when choosing an SSRI to treat mood or anxiety disorders.<sup>7</sup>

- **Efficacy** Optimizing treatment with a single antidepressant agent in primary care is a critical goal. This

Recommended SSRIs\*

Generic agent	Minimum effective dose, mg	Dose range, mg	Indications	Contraindications and warnings	Precautions	Special populations	Pregnancy
Citalopram hydrobromide (Celexa)	20-40	20-40	Depression	Must not be prescribed with MAOIs		Data in the elderly available for depression; no data in children	Category C
Paroxetine hydrochloride (Paxil)	20, except 40 for panic disorder and OCD	20-60	Depression, OCD, panic disorder, SAD, GAD, PTSD	Must not be prescribed with MAOIs or thioridazine	Short elimination half-life leading to withdrawal-type side effects (discontinuation syndrome)	Data in the elderly available for depression, lower doses recommended; no data in children	Category C
Fluoxetine hydrochloride (Prozac)	20, except 60 for bulimia	20-80	Depression, OCD, bulimia	Must not be prescribed with MAOIs or thioridazine; may cause rash more often than other SSRIs (drug should be stopped if it causes a rash)	Long elimination half-life	Efficacy in the elderly for depression established, lower doses recommended; no data in children	Category C
Sertraline hydrochloride (Zoloft)	50	50-200	Depression, PMDD, OCD, panic disorder, PTSD	Must not be prescribed with MAOIs		Data in the elderly available for depression; efficacy in children with OCD and safety data up to 1 year established	Category C

\*US prescribing information, *Physicians Desk Reference* 2001. SSRI = selective serotonin reuptake inhibitor; OCD = obsessive compulsive disorder; PTSD = posttraumatic stress disorder; SAD = social anxiety disorder; GAD = generalized anxiety disorder; MAOI = monoamine oxidase inhibitor; PMDD = premenstrual dysphoric disorder.

Note: The proprietary names included (in parentheses) are for information only and should not be construed as endorsement of a particular brand by the authors or *wjm* editors.

involves keeping patients on a single-medication regimen for up to 4 to 6 weeks to evaluate response and then adjusting the dose accordingly.<sup>8</sup>

- **Tolerability** Commonly cited side effects of SSRIs include mild anxiety, insomnia, minor gastrointestinal discomfort, and sexual dysfunction. These side effects tend to be time limited and self limited (2 to 4 weeks) and may be dose related.
- **Safety** SSRIs as a class should not be prescribed for patients receiving monoamine oxidase inhibitors (such as phenelzine). Coadministration with antidepressant drugs that increase serotonin causes norepinephrine and other sympathetic precursors to accumulate, which can result in serious, sometimes fatal reactions, including hypertensive crises. Metabolism of psychotropic medications mostly involves cytochrome P450 enzymes. The best studied of these drug metabolizing enzymes is *CYP450 2D6*. Fluoxetine hydrochloride and paroxetine hydrochloride are potent inhibitors of *CYP450 2D6*. Therefore, they are more likely than citalopram hydrobromide or sertraline hydrochloride to cause undesirable drug-drug interactions. This discussion of drug coadministration may be particularly relevant in Asians because evidence suggests that there are more poor and slow metabolizers of *CYP450 2D6* among Asians than in the general US population.<sup>9</sup>
- **Special populations** Sertraline hydrochloride has been proven safe and effective for up to 1 year when treating obsessive-compulsive disorder in children and adolescents.<sup>10</sup> All SSRIs are safe to administer to elderly patients. Fluoxetine hydrochloride has proved effective in treating depression in the elderly. All SSRIs are pregnancy category C, meaning that few data on their safety in pregnancy are available, and they may have teratogenic effects based on high dosages used in animals. Therefore, a careful risk-benefit analysis should be undertaken before prescribing SSRIs in pregnancy. Consultation with a specialist is recommended.

### Use in Asian patients

To minimize potential adverse effects and to increase patient comfort with the idea that medication can be beneficial, we prescribe no more than half the customary starting dose for Asian patients. Reasons why many Asians develop side effects at lower doses compared to other ethnic groups remain unclear but may involve biologic mechanisms (eg, Asians metabolize drugs in the *CYP450 2D6* system more slowly than other ethnic groups and they have a lower body weight) or environmental factors (eg, diet or patient expectation of side effects).<sup>9</sup>

An assessment of the effects of therapy should be made no later than 2 weeks after starting a medication regimen.

This assessment can be done by phone or during an office visit. This contact also allows the health care provider the opportunity to reinforce his or her relationship with the patient.

Explaining to the patient that the effect will not be immediate will increase adherence to the therapy plan. About 60% of patients show a response to the first antidepressant used, and an additional 20% will benefit from an alternative agent if the first agent is not effective.<sup>11</sup>

Self-adjustment of doses of medication is common in traditionally oriented Asian patients. We recommend explaining up front that decisions about and adjustments to dosage should be made together with the prescribing clinician. Although starting with a lower than standard dose is useful to improve adherence and tolerability, the full dose range of a drug should be used to the point of intolerable side effects or suboptimal response before switching to another agent. Although many Asians metabolize psychotropic drugs slowly, some Asian patients are normal or extensive metabolizers at the responsible metabolic pathway for the clearance of the drug and so will have near normal dose levels.

Taking a careful medication history and personal inspection of any medication bottles brought by the patient can be informative. Patients may already be using medications that were obtained from friends or local pharmacies. When this situation occurs, referral to a psychiatrist for consultation is recommended.

We also caution patients about taking herbal or other pharmaceuticals that exert a psychotropic effect. Immigrant Asian patients may have medicines from their native country that they or others have retained, some of which are psychotropic agents that have been rebranded and sold



Ask patients to bring in all medications that they are taking and inspect them closely

as medicines for “nerves” or for restoring vitality. The effects of such agents can confound the clinical picture, and their use may lead to untoward drug-drug interactions. If the patient insists on continuing their use, we recommend their use only after reaching an optimal dosage of the prescribed regimen or in continuation therapy with consultation from the provider.

Because sleep relief is important to patients, a sedating serotonergic agent such as trazodone hydrochloride (25 to 50 mg) or a benzodiazepine (see below for special considerations) can be prescribed until the antidepressant medication is effective.

### ANXIOLYTICS AND HYPNOTICS

Adding an anxiolytic or hypnotic agent to the SSRI regimen to treat mood and anxiety disorders can be helpful for patients with insomnia or agitation. Relief of these symptoms using SSRIs alone generally takes 1 to 2 weeks, whereas symptom relief is almost immediate (although short-lived) with benzodiazepines.

#### Choice of agent

Commonly used benzodiazepines are diazepam, alprazolam, lorazepam, and clonazepam. When benzodiazepines are used in conjunction with antidepressants, frequent monitoring is recommended to avoid the development of tolerance and dependence that are associated with chronic benzodiazepine use. The dosage of benzodiazepines should be tapered when the SSRI starts to have an effect (2 to 4 weeks).

#### Use in Asian patients

For many immigrant patients, benzodiazepines have already been prescribed in their country of origin to treat mood and anxiety disorders. In many cases, more than one benzodiazepine is prescribed and long-term tolerance and dependence may occur. In some Asian countries, benzodiazepines are available without a physician’s prescription.

If possible, benzodiazepine use should be avoided by patients with a history of or ongoing problem with substance abuse.

When a benzodiazepine must be used to control an acute panic attack, clonazepam (FDA approved) is preferred. Clonazepam has an intermediate onset and is longer acting, and therefore carries less potential for abuse, than alprazolam (fast onset and short-acting) and diazepam (fast onset).

“Start low and go slow” is the rule of thumb when starting benzodiazepine therapy in Asian patients because initial oversedation can be avoided and Asians may have slower metabolism of benzodiazepines.<sup>12</sup> The need for

continued benzodiazepine use should be reassessed frequently.

### ANTIPSYCHOTIC MEDICATION

The primary care clinician usually does not initiate therapy with an antipsychotic medication except in emergency circumstances. In general, patients with psychotic symptoms should be referred to a psychiatrist for consultation and evaluation. Primary care practitioners should, however, have a working knowledge of the common first-line antipsychotic agents. Because many Asian patients have poor access to mental health specialty treatment, primary care physicians often see patients who are receiving these medications and occasionally adjust doses when the patients are receiving routine medical care.

#### Choice of agent

The two main classes of antipsychotic medication are:

- Conventional antipsychotics (dopamine receptor antagonists), such as chlorpromazine and haloperidol
- Atypical antipsychotics (serotonin-dopamine antagonists), such as clozapine, olanzapine, quetiapine, risperidone, and ziprasidone

Although both classes improve the positive symptoms of psychosis (hallucinations and delusions), atypical antipsychotics also improve negative symptoms (apathy, anhedonia, social withdrawal). The side effects of conventional antipsychotics are shown in the Box. Atypical antipsychotics may have significantly fewer side effects,

#### Side effects of conventional antipsychotics

- Sedation
- Anticholinergic effects
- Blurred vision
- Dry mouth
- Dry skin
- Constipation
- Extrapyramidal effects
- Acute dystonic reactions (acute muscle contractions of limbs and body)
- Parkinson-like symptoms of rigidity and tremor
- Akathisia (a sense of restlessness or inability to sit or stand still)
- Tardive dyskinesia
- Catatonia (a state of near mutism and little affective response to stimuli)
- Orthostatic hypotension (sudden changes in blood pressure related to position, resulting in fainting spells and falls)

especially extrapyramidal symptoms, and they are less often associated with tardive dyskinesia (a disabling, disfiguring movement disorder that may occur with long-term exposure to antipsychotic medication). Because of a better side effect profile and the effect on negative symptoms, we believe that atypical agents are the first-line treatment for psychosis.

### Use in Asian patients

Similar to their response to antidepressants and benzodiazepines, Asian patients often respond to lower doses of antipsychotic medication. They may also experience side effects at lower doses than are seen in other ethnic groups.<sup>13-16</sup> When initiating treatment in Asian Americans, we prescribe a starting dose that is approximately one-half the standard recommended dose. Lower final dosages should not be strictly assumed for every individual Asian patient because some may require the full typical doses.

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