Family Practice Forum

Tricyclic Antidepressant Drugs in the Ambulatory Treatment of Depression

Robert D. Gillette, MD, and Thomas E. Oxman, MD
Cincinnati, Ohio

Depression is common enough in daily medical practice to justify its nickname, "the common cold of psychiatry."[1] The tricyclic antidepressant drugs (TCAs) have greatly improved the outlook for depressed patients,[2-5] but many physicians are reluctant to prescribe them. In a recent report Keller et al[6] described a group of patients treated for major depression at university medical centers and concluded that these subjects had received TCAs too seldom and minor tranquilizers too often prior to referral. Two editorials in the issue in which the report by Keller et al was published took contrary positions. Lundberg[7] noted that TCAs are more hazardous than minor tranquilizers and may be used by depressed patients to commit suicide. Uhlenhuth[8] expressed the view that benzodiazepine tranquilizers may be suitable for treatment of depression in community settings because of their wide safety margin and low incidence of unpleasant side effects.

The concerns expressed by Keller et al are valid. TCAs should be more widely prescribed, albeit with a high level of knowledge and discretion. Physicians are not afraid of using other hazardous drugs, such as antihypertensive, microbicide, and antineoplastic agents, in appropriate patients with proper precautions. Neither should they avoid TCAs employed properly in selected

From the Departments of Family Medicine and Psychiatry, College of Medicine, University of Cincinnati, Cincinnati, Ohio. Requests for reprints should be addressed to Dr. Robert D. Gillette, Department of Family Medicine, College of Medicine, University of Cincinnati, ML 582, Cincinnati, OH 45267.

patients. Depression is, after all, the only disease known that causes enough suffering to lead its victims, with any degree of regularity, to end their own lives.[9] Patients can kill themselves by TCA overdose, as Lundberg indicates, but this risk can be minimized in two ways: first, by taking a careful history, which includes gentle but thorough questioning about suicidal thoughts and intent; second, by prescribing no more than a seven-day supply of pills at a time during the early weeks of treatment.

Keller et al correctly note that typical benzodiazepine tranquilizers have relatively little antidepressant value. They may give temporary relief of the insomnia and anxiety that may accompany depression, but they do little for the underlying depressive process.[2,10-12] Benzodiazepines are rarely lethal by themselves, but they are frequently involved in deaths associated with multiple drug abuse.[13] All sedative-hypnotics can produce a dose-related decrement in psychomotor performance,[14] anterograde amnesia,[14,15] and psychological dependence.[2] Even if the risks associated with these agents are not great, their risk-benefit ratio is unacceptably high given that their antidepressant value is negligible.

Although the diagnosis and treatment of depressive disorders are addressed in family practice residency programs, many physicians now in practice have not received adequate education in this area and will have to overcome that deficiency through continuing education programs, reading, listening to their depressed patients, and consulting their psychiatrist colleagues. Since the specifics of ambulatory care of depressed patients are available elsewhere,[2-5] only a few of the more important principles of management are summarized here.

Strive for Accurate Diagnosis

The physician should look for reasonable concordance with established diagnostic standards for depressive illness, including at least a two-week history of five or more of the following: change in appetite or weight, sleep disturbance, fatigue, agitation or retardation, loss of interest in usual activities, decreased concentration, self-reproach or guilt, and recurrent thoughts of death or suicide. Patients meeting these criteria are most likely to benefit from TCAs.[3,5]

Evaluate Suicide Risk

Ask the patient about a wish to be dead, any intent to become so, and specific plans the patient may have made. Look for predisposing factors such as recent loss, social isolation, history of substance abuse, lack of hope for the future, or the presence of physical disease that impairs the individual's functional capacity. Determine what support and defense against suicide the patient may be able to derive from family and friends, from religious beliefs, and from other sources. If these psychosocial support systems appear inadequate in relation to the risk of suicide, obtain psychiatric consultation or admit the patient to an appropriate hospital setting.[16]

Fit the Drug to the Patient

Elderly patients are usually treated with relatively small doses, since they may not tolerate amounts suitable for younger people.[17] There has been some concern about prescribing TCAs for cardiac patients, but newer evidence indicates they are generally safe[18-20] and in some instances can reduce ventricular irritability.[21] With cardiac patients, choose the agent with care, follow the electrocardiogram, and adjust the dose in accordance with TCA blood levels.[18,22,23] Amitriptyline should be avoided in patients with heart disease.[24] Orthostatic hypotension is the most common cardiovascular side effect; if it is symptomatic, a change to nortriptyline may be beneficial.[23] Patients with marked agitation and insomnia may benefit from one of the more-sedating TCAs such as amitriptyline, doxepin, or trimipramine. Those requiring more alertness during the day may prefer a less-sedating agent such as desipramine, amoxapine, or protriptyline.

Start the Dose Low and Work Up

The average effective dose of most TCAs (including desipramine, imipramine, doxepin, amitriptyline, and trimipramine) is about 150 mg/d, with doses as high as 300 mg/d required at times. It may be necessary, however, to begin as low as 25 mg daily at bedtime. Patients vary in their tolerance of the common sedative and anticholinergic side effects, and continuing encouragement from the physician may be needed to help the patient persevere in the treatment program. Be sure patients understand that the onset of therapeutic action may be delayed for two weeks or longer. If a patient with poor social support appears to be at risk of hoarding pills with suicidal intent, the physician may wish to measure the TCA blood level after four to seven days of treatment.

Keep Close Contact With the Patient

A continuing supportive physician-patient relationship should be the norm, with more structured psychotherapy added in some cases.[25] The time between visits should be no greater than one week until benefits are apparent, and interim telephone contact may be indicated. As Balint noted two decades ago,[26] the physician-patient relationship is therapeutic in itself, especially if the practitioner is, by inclination and training, a perceptive, willing listener.

Clinical experience indicates that concerned, competent family physicians and other primary practitioners can and should manage the majority of ambulatory depressed patients and that tricyclic antidepressant drugs should be an important part of their armamentarium.[27,28]

References

1. Roberts RE, Vernon SW: Depression in the community: Prevalence and treatment. Arch Gen Psychiatry 39: 1407, 1982
2. Baldesserini RJ: Chemotherapy in Psychiatry. Cambridge, Mass, Harvard University Press, 1977
3. Cassem NH: Depression. In Hackett TP, Cassem NH (eds): Massachusetts General Hospital Handbook of General Hospital Psychiatry. St. Louis, CV Mosby, 1978, pp 209-225
4. Perry PJ, Alexander B, Liskow BI: Psychotropic Drug Handbook, ed 3. Cincinnati, Harvey Whitney Books, 1981
5. Wharton RN, Kornfeld DS: The management of depression. In Kornfeld DS, Finkel JB (eds): Psychiatric Management for Medical Practitioners. New York, Grune & Stratton, 1982, pp 107-136
6. Keller MB, Klerman GL, Lavori PW, et al: Treatment received by depressed patients. JAMA 248:1848, 1982
7. Lundberg GD: Antidepressant drugs as a cause of death: A call for caution and data. JAMA 248:1879, 1982
8. Uhlenhuth EH: Depressives, doctors, and antidepressants. JAMA 248:1879, 1982
9. Guze SB, Robin E: Suicide and primary affective disorders. Br J Psychiatry 117:437, 1970
10. Schatzberg AF, Cole JO: Benzodiazepines in depressive disorders. Arch Gen Psychiatry 35:1359, 1978
11. Covi L, Rickels K, Lipman RS, et al: Effects of psychotropic agents on primary depression. Psychopharmacol Bull 17:100, 1981
12. Klerman GL: Anxiety and depression. In Burrows GD, Davies B (eds): Handbook of Studies on Anxiety. New York, Elsevier/North-Holland Biomedical Press, 1980, pp 143-164
13. Finkel BS, McCloskey KL, Goodman LS: Diazepam and drug-associated deaths. JAMA 242:429, 1979
14. Johnson LC, Chernik DA: Sedative hypnotics and human performance. Psychopharmacology 76:101, 1982
15. Dundee JW, Lilburn JK, Nair SG, et al: Studies of drugs given before anesthesia. XXVI: Lorazepam. Br J Anaesthesiol 49:1047, 1977
16. Allen JR, Allen BA: Guide to psychiatry: A handbook for health professionals. New York, Medical Examination, 1978, pp 162-168
17. Nies A, Robinson DS, Friedman MJ, et al: Relationship between age and tricyclic antidepressant plasma levels. Am J Psychiatry 134:790, 1977
18. Glassman AH, Bigger J: Cardiovascular effects of therapeutic doses of tricyclic antidepressants: A review. Arch Gen Psychiatry 38:815, 1981
19. Ayd FJ: Guidelines for treating cardiac patients with tricyclic and tetracyclic antidepressants. Int Drug Ther Newslett 13:9, 1978
20. Veith RC, Raskind MA, Caldwell JH, et al: Cardiovascular effects of tricyclic antidepressants in depressed patients with chronic heart disease. N Engl J Med 306:954, 1982
21. Bigger JT, Giaiding EGV, Perel JM, et al: Cardiac antiarrhythmic effect of imipramine hydrochloride. N Engl J Med 296:206, 1977
22. Amsterdam J, Brunswick D, Mendels J: The clinical application of tricyclic antidepressant pharmacokinetics and plasma levels. Am J Psychiatry 137:633, 1980
23. Roose SP, Glassman AH, Siris SG, et al: Comparison of imipramine- and nortriptyline-induced orthostatic hypotension: A meaningful difference. J Clin Psychopharmacol 1:316, 1981
24. Jefferson JW: A review of the cardiovascular effects and toxicity of tricyclic antidepressants. Psychosom Med 37:160, 1975
25. Weissman MM: The psychosocial treatment of depression. Arch Gen Psychiatry 36:1261, 1979
26. Balint M: The Doctor, His Patient and the Illness, ed 2. London, Pittman Medical, 1964
27. Oxman TE, Smith R: Consultation-liaison psychiatry within a family practice. Soc Psychiatry 17:101, 1982
28. Parron DL, Solomon F. Mental health services in primary care settings: Report of an Institute of Medicine Conference, April 2-3, 1979. National Institute of Mental Health (Rockville, Md): Series DN, No. 2. DHHS publication No. (ADM) 80-995. Government Printing Office, 1980