

Some See Psychosocial Barriers to Weight Loss

BY SUSAN LONDON
Contributing Writer

SEATTLE — Money and time are the leading barriers to seeking weight-loss treatment among overweight and obese adults, but stigma and a belief that one is too heavy for treatment become more influential barriers as people get heavier.

Little is known from the literature about patterns of treatment seeking for obesity over time, Anna C. Ciao said at an inter-

national conference sponsored by the Academy for Eating Disorders. She also said little is known about barriers that might prevent treatment seeking from taking place.

An anonymous online survey offered to overweight or obese men and women aged 18 years or older addressed some of these issues, according to Ms. Ciao, a graduate student at the University of Hawaii, Honolulu.

The survey asked about seven treat-

ments of increasing intensity (based on level of professional involvement): treatment on one's own by taking steps such as reducing caloric intake, reading self-help books, using self-help online programs, turning to commercial programs such as Weight Watchers, seeking help from professionals other than medical doctors such as nutritionists and psychotherapists, turning to medical doctors, and having weight-loss surgery.

The survey also asked about five barriers

to seeking treatment: money, time, stigma, shame, and a belief that one is too heavy for the treatment.

Of the 154 respondents, 76% were white, 16% were black, 2% were Hispanic, and the rest were of other or mixed ethnicities, Ms. Ciao said at the conference, cosponsored by the University of New Mexico. Eighty-six percent were women. The respondents' mean age was 30 years (range was 18-67 years). Their mean body mass index (BMI) was 33 kg/m² (range was 25-80); 41% were overweight, and 59% were obese.

Among the seven treatments, treatment on one's own was the most commonly sought, desired, and planned. Overall, 77% of respondents had sought this treatment; 36% desired it but had no current plans, and 51% planned to pursue it in the near future. In contrast, surgery was the least commonly sought (8%), desired (18%), and planned (8%) treatment.

"Despite these high levels of endorsement of treatment seeking, a substantial number of people did not say yes to seeking any kind of treatment," Ms. Ciao said. Eleven percent had not sought any of the treatments; in addition, 28% did not desire

BRIEF SUMMARY - Consult full prescribing information before use.

Tofranil-PM®

Imipramine pamoate capsules
(75 mg, 100 mg, 125 mg and 150 mg)
For oral administration
Rx only

Prescribing Information

Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of Imipramine pamoate or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicidality. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Imipramine pamoate is not approved for use in pediatric patients (see WARNINGS: Clinical Worsening and Suicide Risk, PRECAUTIONS: Information for Patients, and PRECAUTIONS: Pediatric Use).

CONTRAINDICATIONS

The concomitant use of monoamine oxidase inhibitors is contraindicated. Hypertensive crises or severe convulsive seizures may occur in patients receiving such combinations. The potentiation of adverse effects can be serious, or even fatal. When it is desired to substitute Tofranil-PM® in patients receiving a monoamine oxidase inhibitor, as long an interval should elapse as the clinical situation will allow, with a minimum of 14 days. Initial dosage should be low and increases should be gradual and cautiously prescribed.

The drug is contraindicated during the acute recovery period after a myocardial infarction. Patients with a known hypersensitivity to this compound should not be given the drug. The possibility of cross-sensitivity to other tricyclic antidepressants should be kept in mind.

WARNINGS

Clinical Worsening and Suicide Risk

Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidal ideation and behavior in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older.

The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences drug-by-drug (placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference) in the number of cases of suicidality per 1000 patients treated) are provided in Table 1.

Table 1	
Age Range	Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated
Increases Compared to Placebo	
<18	14 additional cases
18-24	5 additional cases
Decreases Compared to Placebo	
25-64	1 fewer case
≥65	6 fewer cases

No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide.

It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression.

All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dosage changes, either increases or decreases.

The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of these symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persisting worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for Imipramine pamoate should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose.

Screening Patients for Bipolar Disorder — A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a manic/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that Imipramine pamoate is not approved for use in treating bipolar depression.

Extreme caution should be used when this drug is given to patients with cardiovascular disease because of the possibility of conduction defects, arrhythmias, congestive heart failure, myocardial infarction, strokes, and tachycardia. These patients require cardiac surveillance at all dosage levels of the drug; patients with increased intracranial pressure, history of urinary retention, or history of narrow-angle glaucoma because of the drug's anticholinergic properties; hypertensive patients or those on thyroid medication because of the possibility of cardiovascular toxicity; patients with a history of seizure disorder because this drug has been shown to lower the seizure threshold; patients receiving guanethidine, clonidine, or similar agents, since Imipramine pamoate may block the pharmacologic effects of these drugs; patients receiving methylenediamine hydrochloride. Since methylenediamine hydrochloride may inhibit the metabolism of Imipramine pamoate, downward dosage adjustment of Imipramine pamoate may be required when given concomitantly with methylenediamine hydrochloride.

Since Imipramine pamoate may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as operating an automobile or machine, the patient should be cautioned accordingly.

Tofranil-PM (Imipramine pamoate capsules) may enhance the CNS depressant effects of alcohol. Therefore, it should be borne in mind that the dangers inherent in a suicide attempt or accidental overdose with the drug may be increased for the patient who uses excessive amounts of alcohol. (See PRECAUTIONS.)

PRECAUTIONS

General
An ECG recording should be taken prior to the initiation of larger-than-usual doses of Imipramine pamoate and at appropriate intervals thereafter until steady state is achieved. (Patients with any evidence of cardiovascular disease

require cardiac surveillance at all dosage levels of the drug. See WARNINGS.) Elderly patients and patients with cardiac disease, ECG changes, pre-excitation of congestive heart failure, stroke.

Psychiatric: Confusional states (especially in the elderly) with hallucinations, disorientation, delusions, anxiety, restlessness, agitation, insomnia and nightmares; hypomania; exacerbation of psychosis.

Neurological: Numbness, tingling, paresthesias of extremities; incoordination, ataxia, tremors; peripheral neuropathy; extrapyramidal symptoms; seizures; alterations in EEG patterns; tremors.

Anticholinergic: Dry mouth, and, rarely associated atropine-like effects: blurred vision, disturbances of accommodation, mydriasis; constipation; paralytic ileus; urinary retention; delayed micturition; delayed ejaculation; dilation of the urinary tract.

Allergic: Skin rash, paresthesias, urticaria, itching, photosensitization; edema (general or of face and tongue); drug fever; cross-sensitivity with desipramine.

Hematologic: Bone marrow depression including agranulocytosis; eosinophilia; purpura; thrombocytopenia.

Gastrointestinal: Nausea and vomiting, anorexia, epigastric distress, diarrhea, peculiar taste, stomatitis, abdominal cramps, black tongue.

Endocrine: Gynecomastia in the male; breast enlargement and galactorrhea in the female; increased or decreased libido; impotence; testicular swelling; elevation or depression of blood sugar levels; increased antidiuretic hormone (ADH) secretion syndrome.

Other: Jaundice (stimulating obstructive); altered liver function; weight gain or loss; perspiration; flushing; urinary frequency; drowsiness, weakness and fatigue; headache; parotid swelling; alopecia; proneness to falling.

Withdrawal Symptoms: Though not indicative of addiction, abrupt cessation of treatment after prolonged therapy may produce nausea, headache and malaise.

Prior to elective surgery, Imipramine pamoate should be discontinued for as long as the clinical situation will allow.

Information for Patients

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with Imipramine pamoate and should counsel them in its appropriate use. A Patient Medication Guide about "Antidepressant Medicines, Depression and Other Serious Mental Illness, and Suicidal Thoughts or Actions" is available for Imipramine pamoate. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking Imipramine pamoate.

Clinical Worsening and Suicide Risk — Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to look for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt, onset, or were not part of the patient's presenting symptoms. Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication.

Drug Interactions

Drugs Metabolized by P450 2D6 — The biochemical activity of the drug metabolizing isozyme cytochrome P450 2D6 (debrisoquine hydroxylase) is reduced in a subset of the Caucasian population (about 7% to 10% of Caucasians are so-called "poor metabolizers"), reliable estimates of the prevalence of reduced P450 2D6 isozyme activity among Asian, African, and other populations are not yet available. Poor metabolizers have higher than expected plasma concentrations of tricyclic antidepressants (TCAs) when given usual doses. Depending on the fraction of drug metabolized by P450 2D6, the increase in plasma concentration may be small, or quite large (8-fold increase in plasma AUC of the TCA).

In addition, certain drugs inhibit the activity of this isozyme and make normal metabolizers resemble poor metabolizers. An individual who is stable on a given dose of TCA may become abruptly toxic when given one of these inhibiting drugs as concomitant therapy. The drugs that inhibit cytochrome P450 2D6 include some that are not metabolized by the enzyme (quinidine, cimetidine) and many that are substrates for P450 2D6 (many other antidepressants, phenothiazines, and the Type 1C antiarrhythmics propafenone and flecainide). While all the selective serotonin reuptake inhibitors (SSRIs), e.g., fluoxetine, sertraline, and paroxetine, inhibit P450 2D6, they may vary in the extent of inhibition. The extent to which SSRIs/TCAs interactions may pose clinical problems will depend on the degree of inhibition and the pharmacokinetics of the SSRI involved. Nevertheless, caution is indicated in the co-administration of TCAs with any of the SSRIs and also in switching from one class to the other. Of particular importance, sufficient time must elapse before initiating TCA treatment in a patient being withdrawn from fluoxetine, given the long half-life of the parent and active metabolite (at least 5 weeks may be necessary).

Concomitant use of tricyclic antidepressants with drugs that can inhibit cytochrome P450 2D6 may require lower doses than usually prescribed for either the tricyclic antidepressant or the other drug. Furthermore, whenever one of these other drugs is withdrawn from co-therapy, an increased dose of the tricyclic antidepressant may be required. It is desirable to monitor TCA plasma levels whenever a TCA is going to be co-administered with another drug known to be an inhibitor of P450 2D6.

The plasma concentration of Imipramine may increase when the drug is given concomitantly with hepatic enzyme inhibitors (e.g., cimetidine, fluoxetine) and decrease by concomitant administration with hepatic enzyme inducers (e.g., barbiturates, phenytoin), and adjustment of the dosage of Imipramine may therefore be necessary.

In occasional susceptible patients or in those receiving anticholinergic drugs (including antiparkinsonism agents) in addition, the atropine-like effects may become more pronounced (e.g., paralytic ileus). Close supervision and careful adjustment of dosage is required when Imipramine pamoate is administered concomitantly with anticholinergic drugs.

Avoid the use of preparations, such as decongestants and local anesthetics, that contain any sympathomimetic amine (e.g., epinephrine, norepinephrine), since it has been reported that tricyclic antidepressants can potentiate the effects of catecholamines.

Caution should be exercised when Imipramine pamoate is used with agents that lower blood pressure. Imipramine pamoate may potentiate the effects of CNS depressant drugs.

Patients should be warned that Imipramine pamoate may enhance the CNS depressant effects of alcohol. (See WARNINGS.)

Pregnancy

Animal reproduction studies have yielded inconclusive results. (See also ANIMAL PHARMACOLOGY & TOXICOLOGY.)

There have been no well-controlled studies conducted with pregnant women to determine the effect of Imipramine on the fetus. However, there have been clinical reports of congenital malformations associated with the use of the drug. Although a causal relationship between these effects and the drug could not be established, the possibility of fetal risk from the maternal ingestion of Imipramine cannot be excluded. Therefore, Imipramine should be used in women who are or might become pregnant only if the clinical condition clearly justifies potential risks to the fetus.

Nursing Mothers

Limited data suggest that Imipramine is likely to be excreted in human breast milk. As a general rule, a woman taking a drug should not nurse since the possibility exists that the drug may be excreted in breast milk and be harmful to the child.

Pediatric Use

Safety and effectiveness in the pediatric population have not been established (see BOX WARNING and WARNINGS-Clinical Worsening and Suicide Risk).

It is generally recommended that Tofranil-PM® should not be used in children because of the increased potential for acute overdose due to the high unit potency (75 mg, 100 mg, 125 mg, and 150 mg). Each capsule contains Imipramine pamoate equivalent to 75 mg, 100 mg, 125 mg, or 150 mg Imipramine hydrochloride. Anyone considering the use of Imipramine pamoate in a child or adolescent must balance the potential risks with the clinical need.

Geriatric Use

In the literature, there were four well-controlled, randomized, double-blind, parallel group comparison clinical studies done with Tofranil® brand of Imipramine hydrochloride tablets, in the elderly population. There was a total number of 651 subjects included in these studies. These studies did not provide a comparison to younger subjects. There were no additional adverse experiences identified in the elderly.

Clinical studies of Tofranil® brand of Imipramine hydrochloride tablets, in the original application did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Post-marketing clinical experience has not identified differences in responses between the elderly and younger subjects. In general, dose selection for the elderly should be cautious, usually starting at the low end of the dosing range, reflecting greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

(See also DOSAGE AND ADMINISTRATION in Adolescent and Geriatric Patients)

(See also PRECAUTIONS General)

ADVERSE REACTIONS

Note: Although the listing which follows includes a few adverse reactions which have not been reported with this specific drug, the pharmacological similarities among the tricyclic antidepressant drugs require that each of the reactions be considered when Imipramine is administered.

Cardiovascular: Orthostatic hypotension, hypertension, tachycardia, palpitation, myocardial infarction, arrhythmias, heart block, ECG changes, precipitation of congestive heart failure, stroke.

Psychiatric: Confusional states (especially in the elderly) with hallucinations, disorientation, delusions; anxiety, restlessness, agitation; insomnia and nightmares; hypomania; exacerbation of psychosis.

Neurological: Numbness, tingling, paresthesias of extremities; incoordination, ataxia, tremors; peripheral neuropathy; extrapyramidal symptoms; seizures; alterations in EEG patterns; tremors.

Anticholinergic: Dry mouth, and, rarely associated atropine-like effects: blurred vision, disturbances of accommodation, mydriasis; constipation; paralytic ileus; urinary retention; delayed micturition; delayed ejaculation; dilation of the urinary tract.

Allergic: Skin rash, paresthesias, urticaria, itching, photosensitization; edema (general or of face and tongue); drug fever; cross-sensitivity with desipramine.

Hematologic: Bone marrow depression including agranulocytosis; eosinophilia; purpura; thrombocytopenia.

Gastrointestinal: Nausea and vomiting, anorexia, epigastric distress, diarrhea, peculiar taste, stomatitis, abdominal cramps, black tongue.

Endocrine: Gynecomastia in the male; breast enlargement and galactorrhea in the female; increased or decreased libido; impotence; testicular swelling; elevation or depression of blood sugar levels; increased antidiuretic hormone (ADH) secretion syndrome.

Other: Jaundice (stimulating obstructive); altered liver function; weight gain or loss; perspiration; flushing; urinary frequency; drowsiness, weakness and fatigue; headache; parotid swelling; alopecia; proneness to falling.

Withdrawal Symptoms: Though not indicative of addiction, abrupt cessation of treatment after prolonged therapy may produce nausea, headache and malaise.

OVERDOSAGE

Deaths may occur from overdosage with this class of drugs. Multiple drug ingestion (including alcohol) is common in deliberate tricyclic overdose. As the management is complex and changing, it is recommended that the physician contact a poison control center for current information on treatment. Signs and symptoms of toxicity develop rapidly after tricyclic overdose. Therefore, hospital monitoring is required as soon as possible.

Children have been reported to be more sensitive than adults to an acute overdosage of Imipramine pamoate. An acute overdose of any amount in infants or young children, especially, must be considered serious and potentially fatal.

Manifestations

These may vary in severity depending upon factors such as the amount of drug absorbed, the age of the patient, and the interval between drug ingestion and the start of treatment. Clinical manifestations of overdose include cardiac dysrhythmias, severe hypotension, convulsions, and CNS depression including coma. Changes in the electrocardiogram, particularly in QRS axis or width, are clinically significant indicators of tricyclic toxicity.

Other CNS manifestations may include drowsiness, stupor, ataxia, restlessness, agitation, hyperactive reflexes, muscle rigidity, atetoid and choreiform movements.

Cardiac abnormalities may include tachycardia, and signs of congestive failure. Respiratory depression, cyanosis, shock, vomiting, hyperpyrexia, mydriasis, and diaphoresis may also be present.

Management
Obtain an ECG and immediately initiate cardiac monitoring. Protect the patient's airway, establish an intravenous line, and initiate gastric decontamination. A minimum of 6 hours of observation with cardiac monitoring and observation for signs of CNS or respiratory depression, hypotension, cardiac dysrhythmias and/or conduction blocks, and seizures is necessary. If signs of toxicity occur at any time during this period, extended monitoring is required. There are case reports of patients succumbing to fatal dysrhythmias late after overdose; these patients had clinical evidence of significant poisoning prior to death and most received inadequate gastrointestinal decontamination. Monitoring of plasma drug levels should not guide management of the patient.

Gastrointestinal Decontamination — All patients suspected of tricyclic overdose should receive gastrointestinal decontamination. This should include large volume gastric lavage followed by activated charcoal. If consciousness is impaired, the airway should be secured prior to lavage. Emesis is contraindicated.

Cardiovascular — A maximal limb-lead QRS duration of ≥ 0.10 seconds may be the best indication of the severity of the overdose. Intravenous sodium bicarbonate should be used to maintain the serum pH in the range of 7.45 to 7.55. If the pH response is inadequate, hyperventilation may also be used. Concomitant use of hyperventilation and sodium bicarbonate should be done with extreme caution, with frequent pH monitoring. A pH >7.50 or a $pCO_2 < 20$ mmHg is undesirable.

Dysrhythmias unresponsive to sodium bicarbonate therapy/hyperventilation may respond to lidocaine, bretylium, or phenytoin. Type IA and IC antiarrhythmics are generally contraindicated (e.g., quinidine, disopyramide, and procainamide).

In rare instances, hemoperfusion may be beneficial in acute refractory cardiovascular instability in patients with acute toxicity. However, hemodialysis, peritoneal dialysis, exchange transfusions, and forced diuresis generally have been regarded as ineffective in tricyclic poisoning.

CNS — In patients with CNS depression, early intubation is advised because of the potential for abrupt deterioration. Seizures should be controlled with benzodiazepines, or, if these are ineffective, other anticonvulsants (e.g., phenobarbital, phenytoin). Phenytoin is not recommended except to treat life-threatening symptoms that have been unresponsive to other therapies, and then only in consultation with a poison control center.

Psychiatric Follow-up — Since overdosage is often deliberate, patients may attempt suicide by other means during the recovery phase. Psychiatric referral may be appropriate.

Pediatric Management — The principles of management of child and adult overdoses are similar. It is strongly recommended that the physician contact the local poison control center for specific pediatric treatment.

ANIMAL PHARMACOLOGY & TOXICOLOGY

A. Acute Oral LD₅₀

Mouse 2165 mg/kg

Rat (F) 1142 mg/kg

(M) 1807 mg/kg

Rabbit 1016 mg/kg

Dog 693 mg/kg (Emesis ED₅₀)

B. Subacute
Two three-month studies in dogs gave evidence of an adverse drug effect on the testes, but only at the highest dose level employed, i.e., 90 mg/kg (10 times the maximum human dose). Depending on the histological section of the testes examined, the findings consisted of a range of degenerative changes up to and including complete atrophy of the seminiferous tubules, with spermatogenesis usually arrested.

Human studies show no definitive effect on sperm count, sperm motility, sperm morphology or volume of ejaculate.

Rat
One three-month study was done in rats at dosage levels comparable to those of the dog studies. No adverse drug effect on the testes was noted in this study, as confirmed by histological examination.

C. Reproduction/Teratogenic:
Oral: Imipramine pamoate was fed to male and female albino rats for 28 weeks through two breeding cycles at dose levels of 15 mg/kg/day and 40 mg/kg/day (equivalent to 2 1/2 and 7 times the maximum human dose).

No abnormalities which could be related to drug administration were noted in gross inspection. Autopsies performed on pups from the second breeding showed no pathological changes in organs or tissues; however, a decrease in mean litter size from both matings was noted in the drug-treated groups and significant growth suppression occurred in the nursing pups of both sexes in the high group as well as in the females of the low-level group. Finally, the lactation index (pups weaned divided by number left to nurse) was significantly lower in the second litter of the high-level group.

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‘Feeling too heavy may reflect ... an expectation that weight-loss treatment may not work for them.’

MS. CIAO

any, and 25% had no plans for any. However, she noted, respondents were limited to the treatments listed on the survey.

Of the five barriers to treatment, the most commonly cited overall was money, and the second most commonly cited was not having enough time. "In general, money and time were cited as barriers for the more intensive types of treatments, like commercial programs, other professionals, and medical doctors," Ms. Ciao said. Most respondents reported no barriers to three less-intensive treatments: treatment on one's own, self-help online programs, and self-help books.

BMI was correlated with the total number of barriers sought but not with the number desired or planned.

"Heavier people sought a greater number of treatments in the past but didn't necessarily plan to seek or desire to seek more treatments in the future," Ms. Ciao said. That disconnect might suggest "suggest some discouragement from the failed weight-loss attempt," she said.

BMI also was correlated with the total number of barriers across treatments, indicating that heavier people perceive more barriers to treatment generally, she said. Moreover, BMI was correlated with stigma and being too heavy for treatment individually. "Feeling too heavy may reflect a sort of anticipated failure or an expectation that weight-loss treatment may not work for them," Ms. Ciao said.

Ms. Ciao reported that she had no conflicts of interest in association with the study.