Pharmacology: Gender-Specific Considerations in the Use of Psychoactive Medications

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INTRODUCTION

This chapter focuses on considerations in prescribing psychoactive medications for women. Women present to physicians more often and have higher rates of anxiety and depression than do men. Psychotropic medications are prescribed for women nearly twice as much as they are for men, but there is little research information on the differences in drug effects between men and women. Among the most frequently prescribed drugs are the anxiolytics and sedative-hypnotics that often fall into the benzodiazepine group and have high abuse potential. Antidepressants and antipsychotics usually do not have abuse potential. However, some anticholinergics, which are prescribed in conjunction with antipsychotics to reduce side effects, can be abused. Stimulants, which are often prescribed for weight control, also have potential for abuse.

LACK OF TREATMENT

The high prescription rates of psychotropic drugs to women are evidenced by data showing that psychiatric diagnoses are twice as prevalent among women as among men (Cooperstock 1978). Women tend to seek medical treatment more often than men, especially for emotional problems. (Some studies show that men tend to deal with their emotional problems by taking drugs on their own.) When women are treated for psychiatric conditions, they often are treated inappropriately (Vranas 1982).

An indication of inappropriate prescribing is demonstrated with major depression, a common problem. Twenty-nine percent of those who suffer from depression take anxiolytics, which can exacerbate depression. Only 11 percent use antidepressant medication, and

69 percent of depressed people receive no medication, even though medication, particularly antidepressants, is known to be efficacious in treating this disorder (Norman et al. 1992). Few women suffering from anxiety syndromes are treated with medication. Even fewer receive behavioral therapy for their problems because most of these problems are treated by a primary care physician, not by a psychologist, psychiatrist, or other psychiatric professional. Despite the concern about overprescribing, many women with psychological and psychiatric problems are not receiving appropriate treatment or medication.

LIMITED RESEARCH ON WOMEN

Little research has been conducted on the effects of psychotropic drugs on women. Most studies are done on laboratory animals. Animal research provides evidence that pharmacologic and pharmacodynamic differences exist between male and female animals when psychotropic drugs are used. However, few studies of this sort are performed with humans.

Most drugs studied in humans involve young men, usually male medical students who volunteer to participate. However, differences exist between men and women in muscle mass and adipose tissue distribution, and all psychotropic drugs are lipophilic or fat-soluble. This is important because the higher fat-to-muscle ratio in women allows more drugs to be stored in body fat and prevent them from getting to the sites where they are active. Therefore, important differences exist and should be considered in terms of how psychotropic drugs should be administered.

The reluctance of most pharmaceutical companies to include women in studies for new medications results from the desire to avoid the potential liabilities that may occur with women (Kinney et al. 1981). There is a fear of litigation, particularly with respect to studies with women of childbearing age. Pharmaceutical companies are concerned about the potential for a lawsuit if a woman were to become pregnant and teratogenesis occurred.

EFFECTS OF THE MENSTRUAL CYCLE ON DRUG ACTION

In the study of drug use by women, the phases of the menstrual cycle are rarely taken into account. The menstrual cycle has dramatic effects

on a woman's body, yet drugs are rarely given with consideration of this fact. Because the hormonal fluctuation encountered during the menstrual cycle may affect the outcome of studies with a particular drug, the desired positive effect might not result. Studies that test new drugs with women usually are conducted with postmenopausal women. Although elderly people often use drugs, high rates of anxiety and depression occur more frequently in women of childbearing age, yet psychotropic drugs are not studied adequately in the younger female population.

Gastrointestinal transit time changes during phases of the menstrual cycle and also can affect how drugs are absorbed into the body. The time sustained-release drugs spend in certain parts of the gastrointestinal tract is critical for absorption. Time changes also can be critical to maintaining therapeutic blood levels in women during various menstrual cycle phases.

Research has demonstrated that women are less responsive to imipramine than are men for treatment of depression (Hamilton and Parry 1983), yet this fact is seldom mentioned in discussions of treatment of depression. Medical professionals also know that older women metabolize benzodiazepines much faster than older men (Greenblatt et al. 1980; Ochs et al. 1981). Women's decrements of liver function are different from men's (Dawkins and Potter 1991). However, this is true only of microsomal oxidation and not of glucuronidation, which is important for the longer-acting benzodiazepines that are metabolized to active metabolites. Some shorter-acting benzodiazepines like oxazepam and lorazepam are directly metabolized to excretable forms; glucuronidation is the process responsible. There is no evidence that benzodiazepine metabolism is altered during the menstrual cycle. Antipsychotics cause tardive dyskinesia and extrapyramidal effects more frequently in women than in men (Halbreich et al. 1984); care must be taken in prescribing these drugs for women.

DRUG TREATMENT DURING PREGNANCY

In treating women with medications, the major concern is pregnancy. For a long time, the placenta was believed to be a protective organ for the fetus and that drugs and other harmful substances would not get through the placenta to the fetus; now it is known that this is not true (Mortola 1989; Paxton 1981). Any drug that gets to the brain will

cross the placenta because the same characteristics that allow a drug to cross the blood-brain barrier also permit it to pass through the placenta.

Several critical issues must be addressed when psychoactive drugs are prescribed to pregnant women. It is necessary to consider the effects of the particular illness and its negative consequences, such as suicide, violence, and decreased functioning, and to weigh these against the potential side effects of the drugs. When women do not get treated for certain disorders, fetal abuse, neonaticide, precipitous delivery, and refusal of prenatal care can occur. The risks of prescribing must be balanced against the risks of not prescribing.

Pregnancy is a continually evolving situation involving significant changes in both the maternal and fetal systems. Those who prescribe medications should keep in mind the importance of the placenta, how it changes during pregnancy, and the profound effects fetal and maternal system changes have on pharmacokinetics and pharmacodynamics. For example, during methadone treatment, blood levels of methadone drop precipitously in the later stages of pregnancy. Various approaches have been taken to counteract this drop, from increasing the dose of methadone to splitting the dose (Wittman and Segal 1991).

An institutional review board that wishes to study a drug in pregnant women demands that the drug show clear efficacy in a nonpregnant population first. Therefore, if phase 2 or phase 3 studies with a new drug have not demonstrated efficacy, pregnant women are not included.

EFFECTS OF DRUGS ON THE FETUS

Neonatal withdrawal is primarily believed to be associated with drugs like methadone, sedative-hypnotics, and alcohol; however, most psychoactive drugs, including antidepressants and antipsychotics, given to a woman during pregnancy will produce a kind of withdrawal syndrome after the newborn is delivered.

When these drugs are prescribed for pregnant women, withdrawal syndromes in neonates must be addressed because most psychoactive drugs will produce withdrawal symptoms and the infants often are premature and small for gestational age. It is vital to remember that the use of drugs is riskiest to the fetus during days 18 to 55 of fetal development (Schardein 1993, p. 5).

THE FUTURE

Little is known and much must be learned about the relationship between women and drugs. A review of the literature reveals how few studies have examined the effects of psychotropic drugs on women, particularly pregnant women. This field is wide open and needs more work. Research in this area becomes even more important because, more often than men, women have problems for which psychotropic drugs are prescribed. How to treat women appropriately must be better understood. A mixture of behavioral therapies and pharmacotherapies may provide the best treatment for these problems and needs closer examination.

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