

Web Site Lets Doctors Tap Evacuees' Rx Data

BY MARY ELLEN SCHNEIDER
Senior Writer

A broad coalition of public and private sector groups has launched a secure Web site where physicians and pharmacists can access medication histories for patients who were evacuated from their homes in the aftermath of Hurricane Katrina.

The Web site—www.KatrinaHealth.org—can be accessed from any location around the country by authorized physicians and pharmacists who are treating evacuees.

The effort is aimed at providing timely information to help physicians renew prescriptions, prescribe new medications, and coordinate care for the hundreds of thousands of people who have been displaced by Hurricane Katrina—many with chronic health conditions.

“With access to [these records] physicians I think can begin to piece together medical histories and avoid drug interactions and renew prescriptions that are vi-

tal to these patients' health,” J. Edward Hill, M.D., president of the American Medical Association said during a telephone briefing to announce the launch of KatrinaHealth.org.

The information in the network comes from electronic databases from commercial pharmacies, government health insurance programs, private insurers, and pharmacy benefits managers in states affected by the storm.

At press time, the network contained more than 1 million patient records representing more than 7 million prescriptions, according to Kevin Hutchinson, president and CEO of SureScripts, an electronic prescribing service provider.

On the Web site, physicians can obtain allergy information; view prescription history as well as drug interaction and therapeutic duplication reports; and query clinical pharmacology drug information. Physicians who want access to the site can contact AMA's 24-hour Unified Service Center at 800-262-3211 to obtain a user name and password. ■

Possible Risks of Paxil in Early Pregnancy Spur Label Change

BY SHARON WORCESTER
Southeast Bureau

New data linking paroxetine use in the first trimester of pregnancy with increased risk of major congenital malformations has prompted changes to the drug's label.

Preliminary results of a retrospective epidemiologic study sponsored by GlaxoSmithKline Inc., the drug's maker, show paroxetine (marketed as Paxil) was associated with more congenital malformations (adjusted odds ratio 2.20) and more cardiovascular malformations (adjusted odds ratio 2.08) than other antidepressants in almost 3,600 pregnant women.

The prevalence of congenital malformations in the study was 4%, compared with about 3% in the general population. The prevalence of cardiovascular malformations was 2%, compared with about 1% in the general population, according to a “Dear Healthcare Professional” letter issued by the company and the Food and Drug Administration. Ventricular septal defects were the most common cardiovascular malformation in the study.

The findings, along with those of two other recent abstracts, warrant the voluntary label change, the company indicated.

In one of the abstracts, Pia Wogelius, Ph.D., of the epidemiology department at Aarhus University Hospital, Denmark, and colleagues reported a link between SSRIs and major congenital malformations, including cardiac malformations. The risk of malformation was increased among women who had prescriptions for SSRIs filled in the 30 days before conception

through the end of the first trimester, compared with those who had no SSRI prescriptions filled in the same period. These data did not specifically look at Paxil use.

The other abstract described a preliminary analysis of data obtained from the National Birth Defects Prevention Study suggesting an association between SSRI use between 1 month before and 3 months after conception and a significantly increased risk of omphalocele. The risk was greatest among paroxetine users, Sura Alwan, a Ph.D. student at the University of British Columbia, Vancouver, reported at the annual meeting of the Teratology Society.

SSRIs' use in that study also was linked with an increased risk of tetralogy of Fallot, she told this newspaper.

The Paxil labeling changes will be in the pregnancy subsection of the “precautions” section of the labels for Paxil and Paxil CR. The new language cites the GSK data but also notes these data conflict with those from previous studies, including those from the Swedish Medical Birth Registry, which showed no increased risk of major malformations in infants born to 708 women exposed to SSRIs—including paroxetine—during pregnancy.

The conflicting data make it difficult to establish a causal relationship between SSRI use and major congenital malformations. Due to the lack of adequate and well-controlled studies in humans, Paxil maintains its Pregnancy Category C status, according to GSK. However, the company said physicians should discuss the findings with their patients. Results of the GSK study are posted at the company's Clinical Trial Register at <http://ctr.gsk.co.uk/welcome.asp>. ■

DRUGS, PREGNANCY, AND LACTATION

Reviewing the Safety of SSRIs

Over the past few years, several studies have addressed the reproductive safety of the selective serotonin reuptake inhibitors. Recent studies have focused on the risk for neonatal discontinuation syndrome or symptoms of perinatal jitteriness associated with maternal use of SSRIs during the latter portions of pregnancy. Estimates of risk of first-trimester exposure to SSRIs derive from data accumulated over the last 15 years, which support the absence of major congenital malformations associated with first-trimester exposure. Data on the teratogenicity of SSRIs come from relatively small cohort studies and larger, international teratovigilance programs, and they have cumulatively supported the reproductive safety of fluoxetine (Prozac) and certain other SSRIs. These include a Scandinavian-based registry study of 375 women exposed to citalopram (Celexa) in the first trimester, which failed to indict SSRI as a teratogen. A recent meta-analysis conducted by researchers at the Motherisk Program in Toronto supported the absence of teratogenicity associated with first-trimester exposure to a number of SSRIs.

Another recent report from the Swedish Medical Birth Registry failed to identify higher rates of congenital malformations associated with prenatal exposure to a number of SSRIs, including fluoxetine, citalopram, paroxetine (Paxil), and sertraline (Zoloft).

But at the Teratology Society's annual meeting in June, investigators from the University of British Columbia, Vancouver, reported an increased risk of omphalocele and craniosynostosis associated with first-trimester exposure to SSRIs. Using data from the National Birth Defects Prevention study, they compared data on 5,357 infants with selected major birth defects with 3,366 normal controls and interviewed mothers about exposures during pregnancy and other possible risk factors. Children with chromosomal anomalies or known syndromes were excluded.

They found an association between exposure to any SSRI during the first trimester and omphalocele (odds ratio of 3). Paroxetine accounted for 36% of all SSRI exposures and was associated with an odds ratio of 6.3 for omphalocele. Use of any SSRI during the first trimester was also associated with having an infant with craniosynostosis (odds ratio of 1.8). No association was noted between SSRI use and the other classes of major malformations studied.

This preliminary unpublished report is also described in a letter to physicians from GlaxoSmithKline, which markets paroxetine as Paxil. The letter also in-

cludes additional data from an uncontrolled study of SSRI use during pregnancy, which noted a twofold increased risk in overall congenital malformations and cardiovascular malformations (most were ventricular septal defects) in offspring exposed to paroxetine, compared with other SSRIs. These data were derived from an HMO claims database.

Many clinicians who prescribe SSRIs may be confused by the volley of new reports that suggest some potential teratogenic risk associated with this class of compounds. Indeed, previous reports fail to describe such an association. Many more recent findings derive from either retrospective data sets taken from HMO claims data or from case-control studies, which also have certain methodologic limitations, compared with prospective cohort studies.

These recent findings of increased risk with prenatal SSRI exposure are inconsistent with earlier findings. Nevertheless, large case-control studies can uncover an association not previously identified because of the inadequate statistical power of previous cohort studies, which were not large enough to detect an infrequent anomaly.

Even if we assume the associations from the new case-control study are true and that they are indeed causal, an odds ratio of 6.4 is associated with an absolute risk for omphalocele of only 0.18%. Absolute risk is of far greater clinical value than relative risk and should be taken into account before patients are arbitrarily counseled to discontinue antidepressants during pregnancy.

The new findings are not necessarily cause for alarm. Patients who are planning to conceive and are at significant risk for depressive relapse associated with antidepressant discontinuation may benefit from switching to an antidepressant for which there are the most data supporting reproductive safety. These include fluoxetine, citalopram, escitalopram (Lexapro), as well as the older tricyclics.

However, for women who present when pregnant and still taking SSRIs, including paroxetine, discontinuation should not be arbitrarily pursued. Abrupt discontinuation of antidepressants can threaten maternal affective well-being. That is an unacceptable outcome, which can be stated absolutely.

DR. COHEN directs the perinatal psychiatry program at Massachusetts General Hospital, Boston, which offers information about pregnancy and women's mental health at www.womensmentalhealth.org. He is a consultant to manufacturers of several antidepressant drugs, including SSRIs.



BY LEE COHEN,
M.D.