

Psych Diagnoses Up in Deployed Soldiers' Wives

VITALS

Major Finding: 37% of wives whose husbands were deployed received a mental health diagnosis, compared with 30% of wives whose husbands were not deployed.

Data Source: Records of all outpatient medical visits of wives of active-duty Army personnel between 2003 and 2006.

Disclosures: Dr. Mansfield reported no conflicts, but a coauthor reported relationships with Bristol-Myers Squibb and Novartis. Dr. Friedman had no relevant disclosures.

BY MARY ANN MOON

Wives of U.S. soldiers deployed to Iraq or Afghanistan for prolonged periods are at increased risk for receiving mental health diagnoses, compared with wives of non-deployed personnel, according to a recent report.

The higher risk was most apparent for depressive, anxiety, sleep, and acute stress reaction and adjustment disorders, said Alyssa J. Mansfield, Ph.D., of the University of North Carolina, Chapel Hill, and her associates.

"Overall, our data suggest that the mental health effects of current operations are extending beyond soldiers and into their immediate families," the investigators noted.

Dr. Mansfield and her colleagues examined the records of all outpatient medical visits by wives of active-duty Army personnel between 2003 and 2006. This included wives who were treated at military facilities and those who were treated at non-military health centers but used military medical insurance.

Only wives of members of the military who had been in active-duty service for at least 5 years were included in the study "to establish a recent mental health history."

The study sample included 250,626 women who made 6,585,224 outpatient medical visits. Seventeen categories of mental health disorders were assessed. A total of 35% of these wives received at least one mental health diagnosis during the 4-year study.

A total of 37% of wives whose husbands were deployed received a mental health diagnosis, compared with 30% of wives whose husbands were not deployed, the researchers said (N. Engl. J. Med. 2010;362:101-9).

Wives of men who were deployed showed rates of diagnosis that were 24% higher for depressive disorders, 21%-40% higher for sleep disorders, 25%-29%

higher for anxiety disorders, and 23%-39% higher for acute stress reaction and adjustment disorders, compared with wives of nondeployed men.

The rate of mental health diagnosis was significantly associated with length of husbands' deployment. Compared with wives of men who were not deployed, wives of men deployed for up to 11 months used mental health services 19% more often, and wives of men deployed for more than 11 months used mental health services 27% more often.

There were 41 excess cases of any mental health disorder (per 1,000 wives) associated with deployments of 1-11 months, and 61 excess cases of any mental health disorder associated with deployments of more than 11 months.

This represents 3,474 excess mental health diagnoses among nearly 85,000 wives of men deployed for less than 11 months and 5,370 excess mental health diagnoses among more than 88,000 wives of men deployed for a longer period.

"Because the majority of active-duty

Army soldiers are married, and they and their families will eventually receive care outside the military medical system, both the short-term and long-term effects of these findings should be considered" by health care providers both inside and outside of the military, Dr. Mansfield and her associates said.

In an editorial comment accompanying this report, Dr. Matthew J. Friedman of the Veterans Affairs Medical Center in White River Junction, Vt., said the study findings highlight the importance of "developing appropriate programs to fortify wellness and resilience among spouses and children."

"Since social support provides the strongest protection against the development of psychiatric disorders, and since the family is the major source of social support, improvement in the mental health of spouses and children should also pay dividends in improving the mental health of troops throughout the deployment cycle," Dr. Friedman said (N. Engl. J. Med. 2010;362:168-70). ■

More Breast Cancer Deaths With Paroxetine, Tamoxifen

BY BETSY BATES

SAN ANTONIO — Breast cancer patients who took the antidepressant paroxetine during their course of tamoxifen therapy were up to 91% more likely to die from their disease than were those who did not take the two drugs together, according to a retrospective, population-based cohort study conducted in the Canadian province of Ontario.

Investigators used health card identification numbers to track women aged 66 years and older who were treated with tamoxifen for breast cancer. Almost a third of patients were taking an antidepressant during their tamoxifen therapy, including 2,430 who were taking a selective serotonin reuptake inhibitor.

As a class, SSRIs are known to inhibit cytochrome P450 2D6 (CYP 2D6), an enzyme critical for the conversion of tamoxifen to endoxifen, its active metabolite. The ability of SSRIs to interfere with the efficacy of tamoxifen has been theorized, but studies attempting to clarify the issue have reported conflicting results.

In the Canadian study reported at the annual meeting of the San Antonio Breast Cancer Symposium, 1,074 (44.2%) of the women taking an SSRI during tamoxifen therapy had died as of Dec. 31, 2007, when primary data analysis began. After statistical adjustment, investigators found that breast cancer mortality risk increased 24% among women who were coprescribed paroxetine during 25% of their tamoxifen treatment.

If patients took paroxetine for more than half of their tamoxifen course, their

VITALS

Major Finding: Risk of breast cancer death was 24%-91% higher when women took paroxetine while on tamoxifen.

Data Source: Retrospective, population-based cohort study of 2,430 women.

Disclosures: Dr. Kelly reported no relevant financial disclosures.

breast cancer mortality risk rose to 54%. Patients who took both drugs for 75% of the time they received tamoxifen had a 91% risk of breast cancer mortality.

The results were significant only for paroxetine, and not for other SSRIs—including fluoxetine, sertraline, fluvoxamine, or citalopram—that were taken concurrently with tamoxifen, reported Dr. Catherine M. Kelly at the meeting.

Dr. Kelly hypothesized that the explanation lies in the degree to which various SSRIs inhibit CYP 2D6. "Paroxetine is the only SSRI that is an irreversible—or 'suicide'—inhibitor of CYP 2D6," she said in an interview.

The dose-response curve of the study, with escalating mortality risk paralleling time on paroxetine, adds significant weight to the findings with regard to paroxetine, marketed as Paxil by Glaxo-SmithKline.

The company did not respond to a request for a comment on this study.

Fluoxetine is also a potent inhibitor of CYP 2D6, but was not shown to increase breast cancer mortality in the study, said Dr. Kelly, who was with the University of Toronto Sunnybrook Health Sciences Centre while conducting the study and is currently a breast medical oncology fellow at the University of Texas M.D. Anderson Cancer Center in Houston. ■

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INDICATIONS AND USAGE

PATADAY™ solution is indicated for the treatment of ocular itching associated with allergic conjunctivitis.

CONTRAINDICATIONS

Hypersensitivity to any components of this product.

WARNINGS

For topical ocular use only. Not for injection or oral use.

PRECAUTIONS

Information for Patients

As with any eye drop, to prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use. Patients should be advised not to wear a contact lens if their eye is red.

PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% should not be used to treat contact lens related irritation. The preservative in PATADAY™ solution, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and whose eyes are not red, should be instructed to wait at least ten minutes after instilling PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% before they insert their contact lenses.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Olopatadine administered orally was not carcinogenic in mice and rats in doses up to 500 mg/kg/day and 200 mg/kg/day, respectively. Based on a 40 µL drop size and a 50 kg person, these doses were approximately 150,000 and 50,000 times higher than the maximum recommended ocular human dose (MROHD). No mutagenic potential was observed when olopatadine was tested in an *in vitro* bacterial reverse mutation (Ames) test, an *in vitro* mammalian chromosome aberration assay or an *in vivo* mouse micronucleus test. Olopatadine administered to male and female rats at oral doses of approximately 100,000 times MROHD level resulted in a slight decrease in the fertility index and reduced implantation rate; no effects on reproductive function were observed at doses of approximately 15,000 times the MROHD level.

Pregnancy: Teratogenic effects: Pregnancy Category C

Olopatadine was found not to be teratogenic in rats and rabbits. However, rats treated at 600 mg/kg/day, or 150,000 times the MROHD and rabbits treated at 400 mg/kg/day, or approximately 100,000 times the MROHD, during organogenesis showed a decrease in live fetuses. In addition, rats treated with 600 mg/kg/day of olopatadine during organogenesis showed a decrease in fetal weight. Further, rats treated with 600 mg/kg/day of olopatadine during late gestation through the lactation period showed a decrease in neonatal survival and body weight. There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human responses, this drug should be used in pregnant women only if the potential benefit to the mother justifies the potential risk to the embryo or fetus.

Nursing Mothers:

Olopatadine has been identified in the milk of nursing rats following oral administration. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in the human breast milk. Nevertheless, caution should be exercised when PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% is administered to a nursing mother.

Pediatric Use:

Safety and effectiveness in pediatric patients below the age of 3 years have not been established.

Geriatric Use:

No overall differences in safety and effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS

Symptoms similar to cold syndrome and pharyngitis were reported at an incidence of approximately 10%.

The following adverse experiences have been reported in 5% or less of patients:

Ocular: blurred vision, burning or stinging, conjunctivitis, dry eye, foreign body sensation, hyperemia, hypersensitivity, keratitis, lid edema, pain and ocular pruritus.

Non-ocular: asthenia, back pain, flu syndrome, headache, increased cough, infection, nausea, rhinitis, sinusitis and taste perversion. Some of these events were similar to the underlying disease being studied.

DOSAGE AND ADMINISTRATION

The recommended dose is one drop in each affected eye once a day.

HOW SUPPLIED

PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% is supplied in a white, oval, low density polyethylene DROP-TAINER® dispenser with a natural low density polyethylene dispensing plug and a white polypropylene cap. Tamper evidence is provided with a shrink band around the closure and neck area of the package.

NDC 0065-0272-25

2.5 mL fill in 4 mL oval bottle

Storage:

Store at 2°C to 25°C (36°F to 77°F)
U.S. Patents Nos. 4,871,865; 4,923,892; 5,116,863; 5,641,805; 6,995,186

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