Mentally Ill Face Increased Cardiovascular Risk

BY MARY ANN MOON
Contributing Writer

People who have severe mental illness are at double to triple the risk of dying from coronary heart disease or stroke at all ages, compared with people who are not mentally ill, reported David P.J. Osborn, Ph.D., and his associates.

The social deprivation of the severely mentally ill and their higher rate of smoking do not explain this increased cardiovascular risk, and their use of antipsychotic medications "is only part of the explanation." The exact mechanism underlying this increased vulnerability remains unknown, the researchers said.

Noting that the true burden of physical disease among the severely mentally ill has never been established, Dr. Osborn and his associates at the Royal Free and University College London tried to estimate the risks of heart disease, stroke, and cancer death using data from the United Kingdom's General Practice Research Database. "Precise estimation of the true population risk for CVD [cardiovascular disease] or cancer mortality requires data from large, representative populations followed up for periods long enough to include sufficient observed deaths," they pointed out.

The GPRD covered some 8 million patients treated in 741 general practices throughout the United Kingdom between 1987 and 2002, and the sample included almost all those with severe mental illness at the time.

Compared with more than 300,000 randomly selected, matched control subjects who were free from severe mental illness, the 46,136 subjects with schizophrenia, schizoaffective disorder, bipolar disorder, delusional disorder, or other nonorganic psychoses showed triple the rate of death from coronary heart disease before age 50 and double the rate at aged 50-75 years.

Mentally ill patients may be less likely to present with CVD symptoms, to be correctly diagnosed, to be given correct treatment, and to adhere to treatment.

Similarly, stroke mortality was 2.5 times higher in mentally ill people younger than 50 years and twice as high in those aged 50-75 years than it was in the controls, the investigators said (Arch. Gen. Psychiatry 2007;64:242-9).

In contrast, mortality from six of the seven most common cancers in the United Kingdom—colorectal, breast, prostate, stomach, esophageal, and pancreatic cancers—was no different between the control subjects and the mentally ill. Mortality from the seventh common malignancy, respiratory cancer, initially was higher in the severely mentally ill. However, after the data were adjusted to account for smoking and social deprivation, that difference was no longer significant.

Mentally ill people who did not take antipsychotic medications were at increased risk of coronary heart disease and stroke, and those who did take the medications were at even higher risk. People who took the highest doses were at the highest risk of cardiovascular death.

This dose-response relationship could be attributable to adverse drug effects at higher doses, or it could be that higher doses are simply a marker of the severity of mental illness, which itself may raise mortality risk, Dr. Osborn and his associates said.

The reasons why severe mental illness puts people at higher risk of CVD mortality remain unclear. It is possible that mentally ill patients may be less likely to present with CVD symptoms, to be correctly diagnosed, to be given correct treatment, and to adhere to treatment, the researchers said.

These findings underscore the fact that people with severe mental illness must be monitored for somatic conditions. Although the management of blood pressure, glucose levels, cholesterol levels, smoking, diet, and exercise may be best accomplished in the primary care setting, "psychiatric health care professionals cannot be viewed as exempt from responsibility for physical health monitoring," Dr. Osborn and his associates noted. ■

With Bowel Disease, Parents' Anxiety Worse Than Children's

BY BRUCE K. DIXON
Chicago Bureau

INDIANAPOLIS — Parents of children with inflammatory bowel disease perceive the effects of their children's illness more intensely than do the children themselves, according to Carin L. Cunningham, Ph.D.

"Treating physicians need to be aware of how the parents of children with inflammatory bowel disease are managing, because parental anxiety increases the child's anxiety," Dr. Cunningham said during a poster session at the annual meeting of the Midwest Society for Pediatric Research.

Parents fret that their children may not lead normal lives or participate in normal activities, or that they may not be able to start a family of their own, Dr. Cunningham said in an interview.

"These concerns are most prevalent among parents who do not have IBD themselves," explained Dr. Cunningham, a pediatric psychologist at the Rainbow Babies and Children's Hospital and Case Western Reserve University in Cleveland.

The study examined the health-related quality of life (HRQOL) of children and adolescents with inflammatory bowel disease (IBD), compared with the HRQOL of physically healthy peers, with emphasis on the effects of IBD and steroidal side effects.

The HRQOL scores of 49 children and adolescents (aged 10-18 years) with IBD and their parents, who completed the Child Health Questionnaire, were compared with those of healthy children.

"To our knowledge, this is the first study to describe the impact of IBD on HRQOL based on both a standardized measure and a controlled comparison of U.S. children and adolescents with IBD and physically healthy [peers] who were recruited from the same setting," Dr. Cunningham and her associates said.

There are alternative interpretations of the discrepant findings between parent versus child reports of the impact of IBD on HRQOL, according to the investigators. "It is possible that children and adolescents with IBD are coping relatively well with the stressors of their condition and are not experiencing a significant impact of IBD-related problems on their HRQOL."

Another possibility is that young people may deny or minimize the impact of IBD.

The study also found that:

- Caregivers of children with IBD reported that their children's physical and psychological health was more limited and that they experienced more worry and greater interference with their personal time, compared with caregivers of healthy children.
- Children and adolescents with IBD reported worse HRQOL than physically healthy children in only one domain, that of general health.
- Limitations in HRQOL were greatest in children who experienced more frequent IBD-related symptoms together with symptoms of steroidal side effects.

This suggests that children on steroids suffer the most, Dr. Cunningham said. "They become cushingoid, they gain weight, and often there's acne or stretch marks. This results in a lot of teasing from other kids, and these patients tell me they would rather have the pain of the illness than deal with the side effects of steroid medications."

"Guidance counselors in Cleveland-area schools told me that kids will talk about their sex lives and drug use, but they won't open up about IBD, which is a bathroom issue," she added. ■

Experimental Prodrug May Ease Restless Legs, Aid Sleep

BY JEFF EVANS
Senior Writer

CHICAGO — An investigational gabapentin prodrug may be an effective therapy for symptoms and sleep problems associated with restless legs syndrome, Dr. Arthur S. Walters reported at the annual meeting of the American Neurological Association.

The active compound gabapentin has already been shown to improve the sensory and motor symptoms of restless legs syndrome (RLS) and decrease periodic leg movements during sleep, but the drug is approved only for treating epilepsy and postherpetic neuralgia, according to Dr. Walters of the Seton Hall University School of Graduate Medical Education, Edison, N.J.

The gabapentin prodrug XP13512 has several potential advantages over standard gabapentin for treating RLS: The agent has linear pharmacokinetics, doesn't reach a saturation point, and is formulated for sustained release. The capacity for once-daily dosing differentiates gabapentin prodrug XP13512 from the active compound gabapentin (Neurontin), which cannot be manufactured in a sustained-release delivery and must be taken three to four times per day, Dr. Walters discussed on his poster at the meeting.

XenoPort Inc., the drug's manufacturer, has sponsored two phase II, randomized, double-blind trials. One of these trials was a crossover study with 38 patients testing 1,800 mg XP13512 against placebo. The other trial compared XP13512 at 600 mg and 1,200 mg and placebo in 95 patients without any crossover. In both studies, patients had RLS symptoms at least 4 nights during a 7-day baseline period and had a score of at least 15 (out of a possible 40) on the International RLS Study Group rating scale (IRLS). Most patients were white, and mean age was about 50 years.

Compared with patients given placebo, patients treated with the gabapentin prodrug had significantly greater improvement (decreases) in IRLS scores at doses of 1,800 mg (20.4-8.4 vs. 20.4-18.5) and 1,200 mg (22.4-6.3 vs. 22.4-13.5) at the end of the 2-week trial. The patients who received XP13512 at 1,200 mg also had significantly greater improvement than those who received 600 mg. Clinical global impressions of change from both patients and investigators followed the same trend and were significantly in favor of patients who received XP13512, reported Dr. Walters, who received compensation for consulting with XenoPort.

Polysomnographic assessments in the crossover study found that patients had significantly more total sleep time (25 minutes) while receiving the gabapentin prodrug than with placebo. In both studies, patients who received XP13512 had significantly fewer awakenings and spent less time awake per night because of RLS symptoms.

More than 30% of patients who received either 1,200 mg or 1,800 mg of XP13512 experienced somnolence. Dizziness also occurred in 28% of patients at 1,800 mg and in 18% at 1,200 mg. In most cases, the events were transient and mild. Other adverse events occurred at much lower rates, and none were serious. ■