Propranolol Among Drugs Eyed to Prevent PTSD

BY CHRISTINE KILGORE
Contributing Writer

Over the next several years, victims of car accidents, crimes, or other traumas treated at Boston's Massachusetts General Hospital will be offered a common heart drug—the β-adrenergic blocker propranolol—to potentially help lessen the intensity and impact of traumatic memories.

Participants in this study will be part of a wave of new drug trials aimed at intervening early to alter memory processes and prevent posttraumatic stress disorder (PTSD). Other studies are planned using later intervention to treat PTSD by affecting memory "reconsolidation," the process by which memories that have been reactivated are stored again.

The study at Massachusetts General builds on a pilot study, published in 2002, that suggested that posttrauma administration of propranolol in the emergency room may have a "preventive effect" on subsequent PTSD. (See box.)

Roger Pitman, M.D., who led the pilot study and has a $2.5 million grant from the National Institutes of Mental Health to conduct the larger double-blind randomized study, hopes to recruit at least 100 patients who have experienced a traumatic event and present with tachycardia of at least 80 beats/min. According to Dr. Pittman, most studies addressing the issue of tachycardia as a predictor of PTSD "have been positive."

Propranolol is commonly used to treat high blood pressure and for other cardiovascular purposes. It is also prescribed, albeit less frequently, as an antianxiety therapy adjunct for people with public speaking anxieties, fear of flying, and other phobias. It is the only β-blocker that can cross the blood-brain barrier, Dr. Pitman said.

Patients in his study will be randomized to receive, within 6 hours of the event, a 10-day course of placebo or propranolol followed by a 9-day taper period, said Dr. Pittman, professor of psychiatry at Harvard Medical School, Boston.

A major question faced by investigators concerns the timing of the memory consolidation processes. "We don't know what our window of opportunity is," Dr. Pitman said. "In the most pessimistic estimate, it takes 30 minutes. And it takes at least 30 minutes for propranolol to be absorbed. Some data suggest, though, that the process may take 8 hours."

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Dr. Roger Pitman, professor of psychiatry at Harvard Medical School, Boston, will conduct a study of propranolol for PTSD.

Some physicians believe that it may be more feasible to intervene later and to work on memories that already have formed. The idea here is to reactivate or retrieve the memory and, while it is briefly vulnerable, attempt to weaken it before it is restored.

At the October meeting of the Society of Neuroscience, investigators from the Center for Neural Science at New York University presented preliminary findings that suggested propranolol at least partly disrupts the "reconsolidation" of fear memories, via the amygdala, significantly weakening the memories.

NYU physicians have begun working with others at the multi-institutional Center for the Neuroscience of Fear and Anxiety on testing whether propranolol helps PTSD patients who take it after recalling traumatic experiences.

Dr. Pitman also is planning a study with Karim Nader, Ph.D., a neuroscientist at McGill University in Montreal, in which they will reactivate traumatic memories of PTSD patients and measure the ability of propranolol to reduce the subsequent strength of the memories.

Other physicians have their eyes on the use of selective serotonin reuptake inhibitors (SSRIs) for PTSD prevention.

At Massachusetts General, Mark Pollack, M.D., is testing Lexapro (escitalopram) "at the next potential point of intervention"—in patients who, within a few weeks after trauma, are experiencing acute stress symptoms but do not meet the full criteria for PTSD.

The hope is that the drugs will help interrupt the cycle of increased arousal and anxiety that may presage full-blown PTSD, said Dr. Pollack, director of the hospital's Anxiety and Traumatic Stress Disorders Program. SSRIs are often used (with moderate success) to treat syndromal PTSD.

Physicians at the Center for the Study of Traumatic Stress at the Uniformed Health Services University of the Health Sciences in Bethesda, Md., have started a similar study, administering an SSRI to car accident victims days to several weeks after the event. Robert Ursano, M.D., who chairs the department of psychiatry at the university, is optimistic enough to say that "PTSD may be the first psychiatric illness that we'll be able to prevent."

Investigators are also encouraged by pharmacologic studies aimed at enhancing the process of fear extinction and making it a better adjunct to psychotherapy. One drug of interest is d-cycloserine, which enhances the activity of a protein in the amygdala that is important for fear extinction.

A recent study showed that patients with acrophobia who had exposure therapy combined with d-cycloserine had significantly larger reductions in their symptoms than patients who received placebo (Arch. Gen. Psychiatry 2004;61:1136-44).

Cycloserine could show similar effects for PTSD, said Michael Davis, Ph.D., professor of psychiatry and behavioral sciences at Emory University, Atlanta. "I'm not sure how good propranolol will be in the long run," he said. "If you're trying to get rid of really traumatic fear memories, you need something to block not only the active recollection [of the event], but also the associated fear." ■

Small Studies of Propranolol Set Scene

Dr. Pitman's initial study of propranolol is one of two small pilot studies that looked at use of the drug shortly after a traumatic event.

Forty-one patients were randomized in the emergency department at Massachusetts General Hospital to begin—within 6 hours of a traumatic event—a 10-day course of propranolol (40 mg four times daily) or placebo. Eighteen of the 41 received propranolol.

Patients in the double-blind study were instructed to return 1 and 3 months later for assessment with the Clinician-Administered PTSD Scale (CAPS). At the 3-month follow-up, investigators also measured patients' physiologic responses during script-driven imagery of the traumatic event.

At 1 month, the PTSD rate was 30% in the placebo group (6 of 20 patients who returned for follow-up) and 18% (2 of 11 who returned) in the propranolol group. At 3 months, the CAPS scores did not differ. However, the psychophysiologic testing results suggested that propranolol had an impact.

None of the 8 propranolol patients who participated, but 6 of the 14 participating placebo patients, were physiologic responders, reported Dr. Pitman and his associates (Biol. Psychiatry 2002;51:189-92).

In a second, nonrandomized study of patients treated in the emergency departments of two hospitals in France, 11 patients received propranolol for 7 days (40 mg three times daily), with the first dose administered 2-20 hours after the trauma and with a taper period of 8-12 days; they were compared with 8 patients who refused propranolol but agreed to participate.

PTSD rates, as well as PTSD symptom scores, were higher in the patients who refused the drug (3 of 8) than in patients who took it (1 of 11), reported Guillaume Vaiva, M.D., of the University of Lille (France), and his associates (Biol. Psychiatry 2003;54:947-9).

"The French study showed a significant reduction of PTSD symptoms—we only found a significant trend," Dr. Pitman said.

Emotional Disclosure Focus Helps With Posttraumatic Stress

BY ROBERT FINN
San Francisco Bureau

Santa Fe, N.M. — A focus on emotional disclosure is better than a focus on cognitive restructuring when using a written disclosure paradigm for patients with posttraumatic stress disorder, Denise M. Sloan, Ph.D., reported in a poster presentation at the annual meeting of the Society for Psychophysiological Research.

While some previous studies have suggested that patients with posttraumatic stress disorder (PTSD) can be helped by writing about their experiences, the results have been inconsistent, said Dr. Sloan of Temple University, Philadelphia.

To study this systematically, Dr. Sloan and her colleagues asked 82 undergraduate students with PTSD to write about their experiences in three 20-minute sessions.

The students were randomly assigned to one of three groups. The emotional disclosure group was instructed to write about a traumatic experience with as much emotion and feeling as possible. The cognitive restructuring group was instructed to write about a traumatic experience with a focus on what the experience meant to them and how it changed their lives. The control group was instructed to use no emotions or opinions and to write about how they spent their time.

Before the first session, and again 4 weeks after the completion of all three sessions, participants completed the Posttraumatic Stress Disorder Scale (PDS), the Beck Depression Inventory (BDI), and the Pennebaker Inventory of Limbic Languidness (PILL), a measure of physical symptoms.

Participants in the emotional disclosure group had significantly improved scores on the PDS and the PILL at follow-up, while those in the control and cognitive restructuring groups showed no change in those scores. The emotional disclosure group also had a significant improvement in BDI scores, compared with controls. The cognitive restructuring group showed no significant differences from control subjects at follow-up, Dr. Sloan said.

With the Reliable Change Index, the improvements in PTSD symptom severity and depressive symptoms were shown to be clinically meaningful and not only statistically significant. ■