

Letter to the Editor

The Many Uses of Bupropion and Bupropion Sustained Release (SR) in Adults

Sir: Bupropion is an antidepressant originally approved by the U.S. Food and Drug Administration (FDA) in 1989 for the treatment of depression.¹ Its unique mechanism of action among antidepressants is thought to be due to reuptake of dopamine and norepinephrine.² In 1997, the FDA approved bupropion sustained release (SR) for the treatment of smoking cessation.³ Bupropion has been used to treat a number of conditions, and the following discussion will review those off-label uses.

It appears that bupropion may be an effective antidepressant across a wide spectrum of depressive conditions. Weihs et al.⁴ found bupropion to be a safe and effective agent in the treatment of depression in the elderly. In addition to having a favorable side effect profile, bupropion has been shown to have positive results in treating anxiety associated with depression compared with sertraline and fluoxetine.⁵⁻⁷ The most common side effects of bupropion described in a series of studies include headache, dry mouth, and nausea when compared with placebo.⁸ Two important clinical issues noted in the studies were that sexual dysfunction was reported by less than 1% of patients and that a dose-associated weight loss was found in all 3 studies.⁸ Bupropion has also been associated with weight loss in overweight and obese women in a recently published study.⁹

Dysthymic disorder, a chronic low-grade depression, is often treated with antidepressants.¹⁰ In an open-label study of 21 adults diagnosed with dysthymia, 71.4% responded to bupropion SR treatment with no dropouts due to side effects.¹¹

Bipolar depression can be a debilitating phase of the illness with associated morbidity and increased risk of suicide.¹² Mood stabilizer monotherapy is insufficient for the majority of bipolar patients.¹³ In the Expert Consensus Guideline Series for the medication treatment of bipolar disorder, bupropion is the treatment of choice for mild-to-moderate depression.¹⁴ It is also a preferred agent in the treatment of severe melancholic and atypical depression associated with bipolar disorder.¹⁴ Bupropion was associated with lower rates of inducing mania than desipramine in a prospective, double-blind trial.¹⁵ It may also be associated with milder manic states than other antidepressants.¹⁶ Bupropion may also be a promising adjunct to lithium in rapid-cycling bipolar patients.¹⁷

Up to 46% of patients do not adequately respond to treatment with antidepressants.¹⁸ Clinicians are left with either switching or augmenting options. Bupropion appears to be a safe and effective agent when added to selective serotonin reuptake inhibitors (SSRIs).¹⁹ Mischoulon et al.²⁰ reported that bupropion was the most widely chosen augmentation agent in a survey of 801 clinicians in the United States and Canada.

Sexual dysfunction may occur in up to 75% of patients taking antidepressants.²¹ In head-to-head trials, bupropion SR has also been shown to have a significantly lower rate of sexual dysfunction than sertraline and fluoxetine.²²⁻²⁴ Bupropion has been used successfully to treat antidepressant-induced sexual

dysfunction in a number of studies.²⁵⁻³⁰ Bupropion SR may also be a useful agent in treating orgasmic dysfunction in nondepressed patients.³¹ It has been reported to be a treatment option for women diagnosed with hypoactive sexual desire disorder.³²

Initial results of an open-label study involving bupropion in the treatment of social phobia appear to be promising.³³ Canive et al.³⁴ looked at bupropion's efficacy in treating posttraumatic stress disorder (PTSD). They found bupropion decreased depressive symptoms, but no significant changes in symptoms of intrusion and avoidance were noted. Almai et al.,³⁵ in an open trial evaluating bupropion SR in the treatment of PTSD, noted that 89% of the patients completing the study reported a marked improvement in reexperiencing, avoidance, numbing, and hyperarousal symptoms.

Bupropion may offer a valuable treatment option in adults with attention-deficit/hyperactivity disorder (ADHD), which may occur in as many as 4.7% of adults.³⁶ As early as 1990 in an open-label trial, Wender and Reimherr³⁷ reported that bupropion treatment was beneficial in adults with ADHD. Wilens et al.³⁸ conducted a double-blind, placebo-controlled, randomized, parallel 6-week trial comparing bupropion SR with placebo in adults with ADHD. The results showed that bupropion SR was associated with significant changes in ADHD symptoms, with 76% reporting improvement compared with 37% taking placebo. Based on Clinical Global Impressions scale screens, 52% of patients taking bupropion reported being much improved compared with 11% treated with placebo. Kuperman et al.³⁹ in a randomized, double-blind, parallel study compared bupropion, methylphenidate, and placebo. The group treated with bupropion reported a 64% response rate based on the Clinical Global Impressions scale versus a 50% response rate in the methylphenidate group and a 25% response rate in the placebo-treated group. There are at least 2 other double-blind, placebo-controlled studies and 1 open-label study in adults demonstrating bupropion SR to be effective in reducing ADHD symptoms.⁴⁰⁻⁴²

To date there is 1 double-blind, placebo-controlled crossover study evaluating the efficacy of bupropion in the treatment of neuropathic pain, which showed promising results with 73% of patients experiencing pain relief on bupropion SR.⁴³

In a case report, bupropion SR has been shown to be of value when combined with behavior modification in treating smokeless tobacco use.⁴⁴ Bupropion has been helpful in reducing cravings associated with cocaine use in an active-controlled study, an open-label trial, and a case report,⁴⁵⁻⁴⁷ but showed no advantage in 2 other reports.^{48,49} In another case report, bupropion SR therapy and participation in a 12-step program showed positive results in reducing cravings associated with methamphetamine use.⁵⁰

Bupropion appeared to be superior to placebo in a double-blind, controlled study of patients with bulimia.⁵¹ However, 4 patients suffered grand mal seizures during treatment, and it is recommended that bupropion not be used in patients with any history of seizures, anorexia nervosa, bulimia, or major head injury.¹ It is also recommended that when physicians are pre-

scribing medications in an off-label use that informed consent be obtained acknowledging the off-label use.

Bupropion appears to have a number of uses in a variety of conditions, in addition to its FDA indications. It is recommended that physicians using bupropion in an off-label condition document the patient.

Dr. Berigan reports no financial affiliation or other relationship relevant to the subject matter of this letter.

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Timothy R. Berigan, D.D.S., M.D.
Palo Verde Behavioral Health Professionals
Tucson, Arizona

Book Review

W. Clay Jackson, M.D., Dip.Th., Editor

The Best Medicine: Doctors, Patients, and the Covenant of Caring

by Mike Magee, M.D., and Michael D'Antonio.
St. Martin's Press, New York, N.Y., 1999, 256 pages, \$23.95.

The Best Medicine is a collection of short stories about special patient/physician relationships. These real-life stories are unique in that they are told from the perspective of both the patient and the physician. Each story begins with a synopsis of the setting and the background of the patient followed by the patient's account of how the relationship with the physician developed. Patients' perceptions of the qualities and characteristics of the physicians who calmed their fears, engendered their trust, and solidified their relationships are very insightful.

The second portion of each story begins with a description of the physician's background, training, specialty, interests, and philosophical precepts that shaped his or her approach to life and to medicine. This is followed by the physician's account of how the special relationship with the patient developed and progressed. In almost every case, the central themes of openness, honesty, humanity, connectedness, and respect for patients can be found. I was impressed with the diversity of both patients and physicians that was encompassed in these short stories.

In every story, I gained insight into the ways in which each physician encourages the building of trusting relationships with his or her patients. In addition, each physician revealed the things he/she had learned from the patient and the relationship. The book demonstrates that the patient/physician relationship transcends all specialties, genders, socioeconomic strata, and family structures. It stresses the importance of the emotional aspect of the physician, debunking the myth of the cold intellectual who only analyzes tests and prescribes

treatment. The book also underscores the concept that a strong patient/physician relationship is therapeutic and leads to better outcomes. Often, the patient/physician relationships described took in family members, who were then enlisted as members of the support team. Each patient's trust allowed the physician to have special insights into symptoms and treatment responses that helped the physician know how to better help the patient.

One of my favorite stories is under the section entitled "Lessons in Love." Ms. Alvarez is a mother of 4 children, 2 of whom are retarded and 1 of whom is autistic. She developed a strong bond with Dr. Elisa Nicholas. From this patient/physician pair, I learned that parents are frequently stronger and wiser after having gone through such suffering. It seems that these persons are more apt to understand what is important in life. Dr. Nicholas relates the story of being invited to lunch at the home of one of her patients. While most doctors wouldn't go, she went and was truly blessed. One of Dr. Nicholas' profound observations was that when you invest in relationships with families, they allow you access into their lives, which allows you in turn to gain insight into how to live your own life. These relationships help keep physicians from becoming burned out and remind us why we chose to practice medicine in the first place.

In the current health care culture, with its fetish for technology and its outright attack on autonomous patient/physician relationships, this book is both refreshing and reaffirming. What we do as physicians is important and unique. The patient/physician relationship is a privilege that we should make the central theme of our health care system. I would highly recommend this book to medical students, residents, and seasoned practitioners.

David E. Roberts, M.D.
University of Tennessee Family Practice Center
Jackson, Tennessee