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BUSPIRONE POTENTIATION OF ANTIDEPRESSANTS IN THE TREATMENT OF PTSD†

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INTRODUCTION

Controlled trials and clinical experience suggest that antidepressants are effective in controlling many posttraumatic stress disorder (PTSD) symptoms (Friedman and Southwick, 1995). Major depression is often a comorbid diagnosis in PTSD. However, patients with either disorder often demonstrate only a partial, if any, response to antidepressant treatment.

To our knowledge, there have been no reports regarding the efficacy of potentiating agents for antidepressants in PTSD. Several open clinical series suggest that buspirone is effective in depressed patients when added to concurrent antidepressant medication (Jacobsen, 1991; Bakish, 1991; Joffe and Schuller, 1993). Buspirone may also be effective in treating some PTSD symptoms when used alone (LaPorta and Ware, 1992; Wells et al., 1991). We have reviewed the efficacy of buspirone when added to existing antidepressant treatment in the following series of PTSD patients.

METHODS

All patients were male Vietnam combat veterans meeting DSM-IV criteria for PTSD. The PTSD and comorbid diagnoses were made by a multidisciplinary treatment team and confirmed by a symptom checklist and the Clinician Administered PTSD Scale (CAPS)-diagnostic version (Blake et al., 1990). Buspirone was added to the regimen of patients judged to be unresponsive or only partially responsive to antidepressant treatment. Response to buspirone was estimated at baseline and after potentiation using a clinical global impression-change (CGI-C) scale (–3 = marked deterioration, –2 = moderate deterioration, –1 = minimal deterioration, = = no change, 1 = minimal improvement, 2 = moderate improvement, 3 = marked improvement). All CGI-Cs were estimated with the date of buspirone initiation as the baseline reference.

RESULTS

Axis I diagnosis, concurrent psychotropic medications, buspirone dose, and clinical response are shown in Table 1. The average patient age was 49.5 ± 2.76 years. All patients met DSM-IV criteria for PTSD associated with Vietnam combat. All but one (93%) met DSM-IV diagnostic criteria for major depressive disorder (MDD); four (27%) had histories of comorbid alcohol or substance abuse, currently in remission; two (13%) had psychotic features and another two (13%) had comorbid panic disorder. The one patient without comorbid depression stopped buspirone due to a side effect.

A positive response to buspirone augmentation occurred in 11 of 14 patients (73%). Buspirone was discontinued in four patients, two due to side effects and two due to lack of efficacy (symptoms unchanged). No patients experienced worsening symptoms. Of the responders, two had a mild response, four had a moderate response, and five had a marked response to buspirone potentiation. The average buspirone daily dose was 40 mg in responders (range 30–60 mg/day).

DISCUSSION

This preliminary report suggests the potential utility of buspirone as an adjunct to antidepressant medication in some PTSD patients. Since buspirone is a partial serotonin 1A receptor agonist and responding patients were taking serotonergic antidepressants, the mechanism of action is likely through facilitation of serotonin function.

Responding symptoms included all symptom clusters of PTSD and, as expected, depressive symptoms. Improvement of core reexperiencing symptoms, i.e., intrusive memories, occurred in seven of the responders. These symptoms are often the least responsive to traditional antidepressants (Friedman and Southwick,

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TABLE 1. Clinical features of subjects receiving buspirone potentiation of existing antidepressant regimens[a]

Pt. no.	Age (years)	Diagnoses (Axis I)	Concurrent psychotropic medication and dose (mg/day)	Buspirone dose (mg/day)	CGI response	PTSD symptoms responding	MDD symptoms responding
1	43	PTSD, MDD	Paroxetine (30)	45	3	Anxiety, intrusive thoughts, nightmares, avoidance	Mood, energy, motivation
2	54	PTSD, MDD	Paroxetine (40), Trazodone (100)	45	2	Intrusive memories, startle, irritability	Mood, suicidal ideation, energy level
3	54	PTSD,MDD, alcohol dependence, in remission	Paroxetine (40), Naltrexone (50) Lorazepam (4), Bupropion (450)	60	1	Nervousness, concentration, irritability	Mood
4	47	PTSD, MDD	Fluoxetine (20), Diazepam (10)	30	3	Intrusive memories, avoidance	Mood, libido, energy level
5	45	PTSD, MDD	Fluoxetine (40), Diazepam (10)	30	3	Avoidance, irritability, concentration	Mood, activity, concentration
6	55	PTSD, MDD, alcohol abuse in remission	Doxepin (200)	30	2	Anxiety, irritability, concentration	Mood, energy
7	45	PTSD, MDD with psychotic features	Paroxetine (40), Risperidone (2), Lithium (900), Trazodone (100)	60	1	Hallucinations, intrusive memories	Mood
8	48	PTSD, MDD, substance abuse in remission	Paroxetine (40)	60	2	Intrusive memories, nightmares	Mood, energy, sleep, outlook
9	50	PTSD, alcohol abuse in remission	Paroxetine (40), Clonazepam (3)	30	X	(Dizziness)	
10	52	PTSD, MDD, panic disorder-social phobia	Paroxetine (40), Diazepam (20)	30	2	Auditory hallucinations, flashbacks, intrusive thoughts	Mood, sleep quality, outlook
11	52	PTSD, MDD	Sertraline (150)	30	3	Anxiety, intrusive memories	Mood, sleep, self-esteem
12	49	PTSD, MDD	Paroxetine (10), Diazepam (30)	15	X	(Nausea)	
13	49	PTSD, MDD	Fluoxetine (40), Hydroxyzine (50), Carbamazepine (600)	30	3	Irritability, avoidance	Mood, energy level
14	50	PTSD, MDD with psychotic features	Paroxetine (20), Haloperidol (2)	30	No response		
15	50	PTSD, MDD, panic disorder	Fluoxetine (40), Diazepam (15)	10	No response		

[a] *0 = no change or worse; 1 = minimal improvement; 2 = moderate improvement; 3 = marked improvement; X = discontinued drug before therapeutic dose reached with side effects given in parentheses.*

1995). Intrusive memories are phenomenologically similar to obsessions. These phenomena may share a common biological diathesis, i.e., serotonin dysregulation, given the response to serotonergic agents noted in obsessive-compulsive disorder.

The medication was well tolerated in responding patients. A number of these patients were on relatively complicated medication regimens, reflecting the refractory nature of some of their symptoms. Buspirone has minimal sedation, psychomotor effects, or drug-interactions, which may be advantageous when the drug is added to existing medications. Although several patients had relatively high combined SSRI and buspirone doses, e.g., paroxetine 40 mg/day combined with buspirone 60 mg/day, there was no evidence of serotonin syndrome or related symptoms (Brown et al., 1996). Given the potential cost of buspirone and SSRI antidepressants (Joffe and Schuller, 1993), future work should include a longer, controlled trial to establish the efficacy of this combination in PTSD.

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