OPEN TRIAL OF CLONAZEPAM IN THE TREATMENT OF POSTTRAUMATIC STRESS SYMPTOMS IN MPD

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ABSTRACT

Few consistently helpful psychopharmacological interventions have been described in the treatment of multiple personality disorder. We report a successful open trial of clonazepam for posttraumatic stress symptoms in a group of patients with multiple personality disorder. Patients reported notable, sustained improvement in sleep, nightmares, flashbacks, panic attacks and other posttraumatic stress disorder symptoms while undergoing clonazepam treatment. The authors discuss the limitations of the current study and suggest a phenomenological framework for pharmacological interventions in multiple personality disorder.

Patients with multiple personality disorder (MPD) frequently also meet diagnostic criteria for posttraumatic stress disorder (PTSD) and patients with PTSD are often described as having dissociative symptoms (American Psychiatric Association, 1987; Braun, 1986; Kluft, 1985, 1988; Spiegel., 1984; van der Kolk , 1987). In multiple personality disorder, it is thought that dissociative defenses are used to protect the child from the full psychological impact of severe trauma — usually extreme, repetitive child abuse (Braun, 1986; Kluft, 1984a, 1985a, 1988; Putnam et al., 1986). Under the pressure of a variety of developmental factors secondary structuring and personification by the child of the traumatically induced dissociated states of consciousness leads to development of multiple "personalities" (Kluft, 1984a). Once dissociative defenses are in place, they may be used preferentially to handle subsequent traumatic experiences as well as to cope with a variety of other developmental vicissitudes (Kluft,, 1984a).

Reports of several clinical series suggest that, in many cases, the symptoms of multiple personality disorder can be dramatically alleviated by appropriate treatment with intensive, dynamically-oriented psychotherapy, with adjunctive hypnotherapy in selected cases (Kluft, 1984b; Braun, 1986; Coons , 1986). However, there is no known definitive pharmacotherapy for the "core" symptoms of multiple personality disorder (Kluft, 1984b). Adjunctive pharmacotherapy for affective, anxiety, and posttraumatic symptoms in multiple personality disorder has been tried primarily on an ad hoc basis (Barkin R., et al., 1986; Kluft, 1984b). Sporadic success has been reported in individual cases with a variety of agents, including antidepressants, lithium, carbamazepine, major and minor tranquilizers, beta-blockers and others (Barkin et al., 1986). No consistent pharmacological response pattern has been noted in MPD. There are no controlled, double-blind studies in the literature on pharmacotherapy for MPD (Barkin et al., 1986). A few MPD patients have been studied in double-blind fashion for presumed treatment refractory affective disorders in medication trials at the NIMH. Trials of lithium, antidepressants, and carbamazepine failed to ameliorate symptoms in MPD patients in these trials (Putnam, unpublished data).

Benzodiazepines frequently have been used in the treatment of MPD in an attempt to alleviate panic, anxiety and posttraumatic stress symptoms including poor concentration, hyperarousal, fragmented sleep with repetitive nightmares, anxiety and panic attacks triggered by situations which evoke traumata, and intrusive flashbacks of traumatic experiences. The authors' clinical experience with a large number of multiple personality disorder patients is that benzodiazapenes often have minimal impact on symptoms in multiple personality disorder, are often used in ever-increasing doses by the patient, and are commonly abused. Frequently, MPD patients have transient, subjective positive responses to psychopharmacological agents, only to relapse quickly to their baseline highly symptomatic state (Kluft, 1984).

This paper describes an open, non-blind, clinical trial of clonazepam for post traumatic symptoms in multiple personality disorder patients. Clonezepam is a long-acting,

high-potency, benzodiazepine with oral anticonvulsant activity, originally used to treat several types of epilepsy (Browne, 1978; Rosenbaum, 1987). It has been suggested that clonazepam may have an effect on serotonin systems in the brain, leading to a functional increase in serotonin at central sites in addition to agonist effects on benzodiazepine receptors (Chadwick et al., 1977; Chouinard G., 1987; Chouinard et al., 1983; Greenblatt et al., 1987). A series of recent reports have suggested that clonazepam has a spectrum of activity different from that of other benzodiaze-pines with specific efficacy in the treatment of acute mania, schizo-affective disorder, and panic disorder (Chouinard et al., 1983; Chouinard, 1987; Fontaine, 1985; Pollack et al., 1986; Victor et al., 1984). Carbamazapene, another orally active anticonvulsant which has efficacy in epilepsy and bipolar disorders (Ballenger & Post, 1980), has also been reported effective in an open trial for posttraumatic stress symptoms in combat veterans (Lipper et al., 1986).

One of us (RJL) has had favorable experiences with clonazepam in the treatment of mania, schizo-affective disorder, atypical psychosis, and anxiety disorders. As will be described below, clonazepam was initially prescribed serendipitously to a patient with multiple personality disorder with markedly prominent posttraumatic stress symptoms. After a significant alleviation of symptoms occurred in this patient, additional patients with multiple personality disorder were treated with clonazepam.

METHODS

We describe open clinical trials of clonazepam for post traumatic symptoms in a consecutive series of multiple personality disorder patients. Systematic use of clonazepam was started in these patients after notable success in one case (Case 1, below). Patients met all three DSM-III and both DSM-III-R criteria for multiple personality disorder and DSM-III- R criteria for PTSD (American Psychiatric Association, 1980, 1987). In addition, all patients had psychogenic amnesia. In each of these cases, clinicians had witnessed switching to clear-cut alter personalities demonstrating different overt characteristics from one another and reporting relatively separate memory subsystems. Clonazepam treatment was administered to the patients in a non-blind fashion, titrating the medication dosage to optimal therapeutic effect balanced against development of side effects, typically sedation.

All patients gave informed consent for use of clonazepam for post traumatic and dissociative symptoms.

For each patient included in the study, clinicians completed a 21-item questionnaire retrospectively rating 1) changes in post-traumatic symptoms (based on DSM-III-R criteria) rated on a 4-point scale; 2) global improvement of the "total human being" on medication; 3) global improvement in utilization of psychotherapy on medication; 4) medication side effects and the development of tolerance to clonazepam; and 5) differential effects reported by the alters to clonazepam, if any. Demographic data and history of prior medication trials were also reported on the questionnaire. The questionnaire was devised for this study and has not been used in any prior investigation.

CASE REPORTS

Case 1: Ms. A is a woman in her late thirties who had been treated for approximately two years in intensive psychotherapy and hypnotherapy for multiple personality disorder secondary to reported severe, repetitive sadistic sexual, physical, and emotional abuse perpetrated by both parents from about age five until late adolescence. She had been in treatment for years before the diagnosis of multiple personality disorder was made, receiving a variety of other diagnoses including major depressive disorder and schizo-affective disorder. Over the years, depressive, anxious, and "psychotic" symptoms had not been ameliorated despite generally adequate trials of imipramine, amitriptyline, trimipramine, nortriptyline, desyrel, doxepin, fluphenazine, alprazolam, diazepam, and triazolam. Many of these medications were tried before the diagnosis of multiple personality disorder was made, although others were initiated in an attempt to control depressive and anxiety symptoms which continued after the correct diagnosis was determined.

The patient's psychotherapy was focused on intensive uncovering of memories of traumatic experiences. As she recalled more and more traumatic memories, she suffered increasingly from crippling posttraumatic panic attacks, hyperarousal, intrusive flashbacks, and nightmares completely disrupting normal sleep. Hypnotherapeutic methods were not helpful in relieving these symptoms or the patient's intense dysphoria.

Due to multiple somatic complaints, the patient had had a very complicated medical history leading to chronic abuse of narcotic analgesics, barbiturates, and minor tranquilizers necessitating that her husband control access to all medications. This patient was effectively disabled much of the time due to somatoform, MPD, and PTSD symptoms.

At that time of the initial consultation, the patient was taking imipramine 125 mg per day (with an adequate blood level), alprazolam 0.25 mg t.i.d. and q.h.s., and triazolam 0.25 mg q.h.s. Dosages of minor tranquilizers were stable at this time since the patient's husband controlled access to the medication. The patient reported feeling "better" on these medications, but outside observers detected little objective change or decrease in reports of symptoms on the medications.

Initially, through the consultation, attempts were made to slow down the pace of uncovering of traumatic memories, increase cooperation among the alters, stabilize the therapeutic alliance, and to help the therapist work more directly with dependency conflicts and masochistic character problems presented by the patient. At first, no attempt was made to change the patient's medications since the patient professed to be reasonably satisfied with her regimen. However, as time went on, the patient began to ask if there were a medication which might help her more with her chronic sleep disorder. Clonazepam was selected because it was a long-acting benzodiazapene with known sedating properties. It was hoped that there might be an additional anti-anxiety effect, but the consultant did not anticipate any

other major change in symptoms with the drug.

After clonazepam 0.5 mg b.i.d. and q.h.s. was substituted for the other benzodiazepenes, the patient immediately began to be able to sleep five to six hours a night with marked decrease in nightmares. With gradual titration upwards the patient was eventually stabilized on clonazepam 1 mg b.i.d. and 3 mg q.h.s. If the patient awakened in the early morning, she took an extra 1 mg of clonazepam and generally was able to return to sleep even if a nightmare had occurred. The patient stated that for the first time in years she was able to return to sleep after awakening. She described significant improvement in anxiety symptoms and intensity of flashbacks. She reported being able to modulate her reaction to triggering stimuli which she had previously found overwhelming. On clonazepam, she felt able to "bounce back" from flashbacks allowing her to function more effectively in daily living tasks.

After initiation of clonazepam the patient was also able to do significant work in psychotherapy for the first time in months, working more directly on the issues of identifying additional alters and attempting to decrease the level of internal warfare among them.

She has remained on the same dose of clonazepam for 21 months without development of apparent tolerance or abuse of clonazepam. Despite a high level of on-going difficulties in many areas, the patient has consistently identified the clonazepam as significantly helpful in controlling her sleep disturbance, anxiety, flashbacks, and hyperarousal symptoms. Her husband and psychotherapist both have concurred enthusiastically in this assessment.

Case 2: Ms. B is a 44 year old divorced female who reported an extensive childhood history of neglect and sexual, physical, and emotional abuse from age two until adolescence. She was a highly complex patient with over 180 reported alters. She had made major improvements in all aspects of her life during five years of intensive out-patient psychotherapy for multiple personality disorder. However, she could only bring traumatic memories into treatment very slowly since this was accompanied by frighteningly intense revivification experiences which lasted for several days after a therapy session. At these times, sleep was markedly disturbed by nightmares and she had overwhelming daytime flashback experiences and increased dissociative symptoms which were disruptive at work and at home. Despite an extensive drug abuse history in adolescence and early adulthood, she generally resisted medication treatment, only requesting it when overwhelmed by posttraumatic nightmares, hyperarousal, anxiety and frighteningly intense flashbacks and imagery. Prior attempts to ameliorate these symptoms with hypnotherapy and modifications in the pace of psychotherapy did little to change the intensity of these symptoms. Intermittent trials of oxazepam, lorazepam and alprazolam in varying doses had been ineffective and the patient had frequently used more than the prescribed amount of medication due to severity of symptoms, often rapidly ingesting her entire modest prescription without symptom improvement.

Prior to diagnosis and treatment of MPD, the patient had been treated with little clear-cut results for what were thought to be schizo-affective and/or epileptic disorders with adequate trials of neuroleptics, lithium, and carbamazepine. Multiple EEGs and extensive neurobehavioral and neuropsychological investigations at that time had all been within normal limits.

Clonazepam 1 mg q.h.s. was started during a harrowing period of recalling traumatic memories at a time when the patient needed to function at a particularly high level of efficacy at work. On clonazepam, there was immediate improvement in sleep with decrease in nightmares and diminution in intensity of flashbacks and anxiety symptoms during the day. Difficulties with work also eased as the patient could attend to here-and-now issues without being bombarded by flashbacks and bizarre dissociative symptoms. The patient found the 1 mg of clonazepam mildly sedating which was unusual since she could usually consume excessive dosages of other minor tranquilizers almost without noticeable effect. This patient declined on-going clonazepam treatment. She used clonazepam 1 mg q.h.s. p.r.n. successfully for brief periods when overwhelmed by posttraumatic stress symptoms. No tolerance, abuse, or other side-effects have been noted during six months of use of clonazepam. She stated: "This stuff really *works*!"

Case 3: Ms. C is a woman in her thirties with a reported history of extreme physical, emotional, and sexual abuse throughout childhood. She had a demanding job which she performed well despite extraordinarily high levels of symptoms outside of work. She suffered from overwhelming anxiety and panic symptoms, nightmares, and flashbacks during which she would mutilate herself and bang her head severely. She reported marked disorientation upon awakening from nightmares, including finding herself running out of her house or down the street. She described high levels of internal arousal, "like a motor." Trials of alprazolam and lorazepam had failed to alleviate these symptoms. The patient described taking more and more alprazolam in an unsuccessful attempt to dampen her symptoms.

Her psychotherapy for multiple personality disorder had been disrupted due to the unanticipated loss of her therapist. Transition to a new therapist was quite stormy. Despite the lack of stability in therapy, which the patient experienced with anxiety and distress, initiation of clonazepam 0.5 mg q.h.s. led to an immediate improvement in sleep and significant diminution in nightmares, nighttime disorientation and fugues. Self-mutilation and head banging were also decreased, at least intermittently, apparently due to the decrease in panic and anxiety at night. The patient also reported improvement in daytime anxiety symptoms with p.r.n. doses of clonazepam. Despite this, the patient continued to report periods of flashbacks, anxiety, panic symptoms, and self-mutilation which did not respond to up to 4 to 5 mg of p.r.n. clonazepam. At this dose, the patient noted oversedation and dysfunction in performing her daily tasks.

This patient was reluctant to take medications on an ongoing basis and resisted seeing the medical consultant for medication reassessments. Nonetheless, she found herself unable to discontinue clonazepam because she found it "a

necessity in keeping things under control". She made efforts to not overuse the medication, realizing that at times her symptoms would simply exceed the beneficial effects of the drug. After six months on clonazepam, the patient identified the medication as consistently helpful in controlling her sleep problems and intermittently helpful with other posttraumatic symptoms. The therapist described a notable decrease in head-banging and self-mutilation episodes. These effects persisted even though the patient has remained only tenuously connected to her new therapist.

Case 4: A 25 year old female had been receiving intensive outpatient psychotherapy for multiple personality disorder for two years. The patient reported a history of neglect as well as emotional, sexual and profound physical abuse perpetrated by her highly disturbed mother who also met criteria for multiple personality disorder based on the patient's report and several pieces of objective evidence such as multiple handwriting styles, wardrobes, bank accounts, etc. Incest with the father was suspected but never confirmed. The patient's psychiatric treatment history which began eight years before the dissociative disorder was suspected included a plethora of psychiatric diagnoses, medication trials, six psychiatric hospitalizations and a history of episodic oral substance abuse including alcohol, codeine, benzodiazepenes, and amphetamines. Results of multiple EEGs and a CT scan had been within normal limits. Since childhood, the patient had complained of symptoms of severe anxiety, panic attacks, intrusive thoughts and imagery, confusion, "time-loss", and nightmares. In addition, she described chronic symptoms of decreased appetite, sadness, feelings of worthlessness and hopelessness, suicidal ideation, and sleep disturbances including increased sleep latency, frequent mid-cycle awakening and early morning awakening. She experienced recurrent stress-related exacerbations of all these symptoms. Symptom worsening characteristically lasted several months, followed by a gradual return to baseline. Previous medication trials occurred during symptom exacerbations and included adequate unsuccessful trials of five different heterocyclic antidepressants, an MAOI, and a brief unsuccessful trial of low dose neuroleptics. Trials with diazepam, oxazepam, alprazolam, and temezepam brought variable results. The patient would report initial reduction in anxiety and panic attacks and a slight improvement in sleep. The beneficial effects were short-lived, however, and the patient began abusing the medications with escalating doses in an attempt to control symptoms. On one occasion, hospitalization became necessary to withdraw the patient from dangerously high doses of alprazolam.

At the outset of the clonazepam trial, the patient was experiencing a particularly severe symptom exacerbation. Despite marked storminess in her psychotherapy, she had been an out-patient and drug-free for over three months. Treatment with clonazepam was initiated with a dose of 0.5 mg q.i.d. and then gradually increased over a week until reduction in symptomatology occurred at a dose of 1.0 mg q.i.d. The patient reported little if any response to clonazepam before a total dose of 3 mg per day and she was unable to tolerate doses above 4 mg per day because of drowsiness. At 4 mg per day, the patient noted an immediate and substantial decrease in anxiety; the frequency and severity of panic attacks; a dramatic reduction in frequency of intrusive thoughts and imagery; decreased "time-loss;" also less confusion, and improvement in all reported sleep disturbances, including nightmares. Her other symptoms of decreased appetite, suicidality, and dysphoria remained unchanged, however. The patient reported two side-effects: feeling emotionally "dulled" and slightly "slowed down" motorically.

Symptom improvement was steady and enduring over six months on 1.0 mg q.i.d. of clonazepam. The patient did not increase dosage or abuse this medication during this period. In fact, she complained of its inability to get her "high". After six months, the patient discontinued clonazepam because she found new employment requiring a maximal level of precise motor coordination. Improved functioning and a decrease in symptoms were sustained despite the discontinuation of clonazepam. Recently, however, the patient again became acutely symptomatic due to several life stresses. Reinstitution of clonazepam 4.0 mg per day induced the same improvement as before, permitting more focused work in psychotherapy to deal with the life stresses.

Case 5: Ms. F is a woman in her forties who had been hospitalized on an in-patient psychiatric unit after an acute suicidal crisis. She had been in out-patient treatment for multiple personality disorder and an apparent major depression for about seven years. The patient reported a history of sexual, physical, emotional, and confinement abuse at the hands of several family members. Abuse had frequently occurred at night. The patient stated that she had "always" had fragmented and fitful sleep with recurrent nightmares, middle and early morning awakening, and total sleep reportedly averaging 4 to 5 hours a night. Her depressive symptoms had been treated for long periods of time with little clear-cut response to trazadone 450 mg daily. Also, she had had little response to alprazolam up to 3 to 4 mg a day for symptoms of anxiety, panic, hyperarousal, sleeplessness, and nightmares. Treatment with clonazepam was initiated and the dosage gradually increased to 3 to 4 mg at bedtime. At this dose range, the patient reported a disappearance of the recurrent nightmares. She denied having a complete normalization of sleep on the drug, but she did note less sleep fragmentation with longer total sleep time. Clonazepam was also used on an as needed basis for anxiety and flashback symptoms during the day. The patient found 0.5 to 1.0 mg every four to six hours helpful when overwhelmed by panic symptoms. No sedation or other side effects were described. Total daily dosage rarely exceeded 6 mg per day. The patient gradually decreased her nighttime clonazepam dosage as her overall symptom status improved during a two month hospitalization. On discharge, she was taking 2 mg at bedtime and 0.5 mg as needed during the day. This regimen has continued for a total of 10 additional months of outpatient treatment. Dosage has remained stable except for times of severe crisis when she has transiently used additional p.r.n. clonazepam during the day and for sleep.

GROUP DATA

The length of clonazepam treatment for this group of patients was 6 to 21 months (mean: 11.8 mos.). Standing doses of clonazepam ranged from 1.0 mg to 6.0 mg q.d. with use of additional p.r.n. doses by several patients at times of increased stress.

Quantification of the data from the PTSD symptom inventory (Table 1) should be regarded very cautiously due to the open, non-blind nature of the trial and the lack of validation of the symptom questionnaire. Nonetheless, taking the median improvement scores on each item, those showing the most improvement on clonazepam were, in order: 1) nightmares; 2) global improvement of the total human being, difficulty falling asleep, intrusive recollections, panic/severe anxiety (all equal); and 3) intensity of flashbacks. (See Table I).

OTHER CASES

In addition to these cases, the authors have successfully treated a number of additional MPD patients with clonazepam for posttraumatic stress symptoms. Improvement in nightmares and insomnia has been the most striking finding in these patients, but amelioration of other PTSD symptoms such as flashbacks, anxiety, hyperarousal, and panic has occurred as well.

On the other hand, other patients have not had a good outcome with clonazepam. Several patients responded to clonazepam in a manner more typical of MPD patients taking other benzodiazepenes. They reported an initial brief decrease in symptoms followed by a rapid recrudesence of complaints without response to increases in dosage of medication.

DISCUSSION

Our data suggests that clonazepam may be particularly effective in the treatment of refractory posttraumatic stress symptoms in some patients with multiple personality disorder. Reduction in nightmares and amelioration of disturbed sleep were the most prominent finding in these patients. Improvement also occurred in other posttraumatic stress symptoms as well as in clinicians' ratings of global improvement. Primarily, clonazepam ameliorated the "intrusive," "paroxysmal" symptoms of PTSD such as flashbacks, nightmares, intrusive imagery, panic attacks, hyperarousal, confusion, and irritability. As with other pharmacologic interventions in PTSD, clonazepam had relatively little effect on avoidant symptoms such as numbing, alienation, and withdrawal from people (Friedman, 1988, van der Kolk, 1987).

One must be cautious in evaluating the results of an open, uncontrolled, non-blind clinical trial about which the authors had become enthusiastic after the surprising success in case 1. On the other hand, all patients had failed trials of other medications and modifications of psychotherapy for their symptoms. The same clinicians involved in the clonazepam trials had attempted many of these unsuccessful interventions. If only placebo factors were at work, one would not expect much difference between the effects of clonazepam and these other interventions.

It could be argued that the favorable response in these MPD patients is not due to any specific effect of clonazepam. Instead, the high binding affinity of clonazepam may permit better benzodiazepine receptor saturation accounting for the apparent specificity of response to clonazepam (Skolnik, personal communication; see also Greenblatt et al., 1987). On the other hand, the authors observed that even very high doses of other benzodiazepines had been ineffective in several of the same patients who responded to clonazepam.

Clonazepam is not a curative intervention for PTSD symptoms in MPD. In several patients, sufficient additional life stress led to symptoms which "broke through" the beneficial effect of the medication. On the other hand, *any* sustained symptom reduction was welcomed by most of these patients. In addition, successful treatment with clonazepam generally allowed more productive psychotherapeutic work to go forward.

Little abuse of clonazepam was encountered in this group of patients, although a number of them had substantially misused benzodiazepines and other medications in the past. Patients were generally maintained on stable doses of clonazepam for months with little pressure to increase the standing dose of medication.

Somewhat surprisingly, patients tolerated relatively high doses of clonazepam with few side effects. This may be due to the high baseline levels of hyperarousal in MPD patients. The latter might also be a factor in most patients' requirement for more than a single daily dose regimen of clonazepam, despite the medication's long half-life. Placebo factors may be at work here in part, however.

These data also suggest that clonazepam might be working in a manner different from that of the other benzodiazepenes in these patients. Carbamazepine, another orally active anticonvulsant with beneficial effects on mania and schizo-affective disorder, has also been reported efficacious in a recent open trial for PTSD symptoms in combat veterans (Lipper et al., 1986). As in the present study, carbamazepine was noted to preferentially alleviate the intrusive rather than the avoidant symptoms of PTSD (Lipper et al., 1986). Thus, it could be argued that the limbic kindling model suggested to explain the effects of carbamazepine in bipolar disorder and PTSD may be applicable to the effects of clonazepam on PTSD symptoms in MPD (Friedman, 1988; van der Kolk, 1987). However, in most case reports, carbamazepine has not been described as effective in MPD (Barkin et al., 1986; Kluft, 1984b; Putnam, unpublished data). Further controlled studies are warranted on different sub-populations of PTSD and dissociative disorder patients to delineate more precisely the relative efficacy of carbamazepine and clonazepam in ameliorating PTSD symptoms. Such studies could also help clarify the relevance of the limbic kindling model of PTSD for theorizing about the neurobiology of MPD.

In the practical pharmacologic management of MPD patients, clonazepam may have advantages over carbamazepine and other agents such as clonidine, propranolol and lithium which have been previously described as beneficial

in the treatment of PTSD (Friedman, 1988; van der Kolk, 1987). The use of the latter medications requires a high level of consistent patient cooperation. Clonazepam is a relatively safe medication, especially for acting out MPD patients who are prone to misuse medications or for patients who require varying doses of medication because of fluctuations in level of symptoms.

OVERVIEW OF PHARMACOLOGIC APPROACHES TO MPD

Prior discussions of the pharmacological treatment of MPD have focused on the importance in medication trials of apparent state-dependent medication responses described by the different alter personalities (Barkin et al., 1986). Although intriguing clinical anecdotes exist about this phenomenon, little rigorous, scientifically acceptable data can be found to document it. Until the *objective* clinical significance of this phenomenon is documented in a wide range of MPD patients, it seems reasonable to try to target symptoms for pharmacological intervention in MPD which cut across the whole human being, not those apparently localized in separate alter personality states (Kluft, 1984b).

In devising psychopharacological strategies for MPD, it is important to think systematically about the phenomenology of the disorder to acquire a list of potential target symptoms. Table II heuristically organizes symptoms in MPD into six core groups, several of which overlap to some extent. These groups are: 1) Process symptoms — including characteristics of alters, interference phenomena between alters (e.g., passive influence symptoms), and switching; 2) amnesia symptoms; 3) autohypnotic symptoms; 4) somatoform symptoms; 5) PTSD symptoms; and 6) affective symptoms (American Psychiatric Association, 1980, 1987; Bernstein and Putnam, 1986; Bliss, 1980, 1984, 1986; Braun, 1986; Brown and Fromm, 1986; Feighner, 1984; Greaves, 1980; Horowitz, 1986; Kluft, 1984a; 1985a; 1985b, 1987, 1988; Putnam, 1986; Putnam et al., 1984; Putnam et al., 1986; Spiegel, 1984; 1986; Spiegel and Rosenfeld, 1984; van der Kolk, 1986).

This classification of MPD symptoms was originally devised by the senior author in an attempting to operationalize his approach to the differential diagnosis of MPD and dissociative disorders. Initially he used this framework as an aid in teaching, supervision and in clinical research projects (Loewenstein et al., 1986). A somewhat similar typology of symptom sub-groups in MPD was independently developed by Putnam (unpublished data). Eventually it became clear that organizing symptoms in this way could be helpful in conceptualizing more systematic approaches to psychopharmacologic interventions in MPD.

SYMPTOM CLUSTERS

Process, amnesia, and autohypnotic symptoms in MPD (Groups 1-3) are primarily made up of phenomena which can be viewed as either manifestations of intrapsychic defense (attributes and interaction of alters, switching, psychogenic amnesia, etc.) and/or of autohypnotic capacity (spontaneous age-regression, self-induced anaesthesia, intense enthrallment experiences, etc.). Of course, from a different theoretical vantage point, most of the process and amnesia symptoms can also be understood as manifestations of spontaneously occurring autohypnotic phenomena (Bliss, 1980, 1984, 1986; Brown & Fromm, 1986).

A frequent problem in the management of MPD is the attempt to suppressively "treat" dissociation pharmacologically with the goal of diminishing symptoms such as amnesia, switching, and auto-hypnotic phenomena. This approach fails to appreciate the adaptiveness of these processes and the impossibility, if not the inadvisability, of attempts at their permanent suppression at least with our known repertoire of psychopharmacologic agents. Since the current literature on the psychotherapy of MPD emphasizes that suppressive psychological treatments are usually inefficacious and counterproductive (Braun, 1986; Kluft, 1984b, 1985a, 1988), it seems unlikely that suppressive psychopharmacological approaches would prove to be a useful alternative.

Additionally, true manifestations of intrapsychic defense per se (e.g., repression, dissociation, reaction formation, projection, etc.) and autohypnosis are generally unresponsive to attempts at direct psychopharmacological modification at least by currently available drugs. The authors are well aware, however, that appropriate pharmacological interventions can improve the overall level of ego-functioning in many patients with a wide variety of disorders (Group for the Advancement of Psychiatry, 1975). The point of this discussion is to clarify the way that this might occur in MPD patients.

Similarly, in MPD, antipsychotic medications are often initiated in an attempt to "treat" the auditory and visual hallucinations and passive-influence symptoms. Passive influence symptoms, hallucinations, and pseudohallucinations (voices, images or sensations experienced within the mind, not outside it) in MPD are generally best understood as manifestations of the alter personalities and their interactions or of posttraumatic flashbacks and imagery (Putnam et al., 1984). In addition, the MPD patient's posttraumatic mistrustfulness and sensitivity are frequently misinterpreted as representing a true paranoid process. The patient's temporary diminution in reality testing during severe flashbacks is also interpreted as "psychotic". Thus, symptoms related to traumatization and dissociation, reflections of relatively high-level ego defenses and of autohypnosis, are incorrectly conceptualized as representing a core psychotic process or vulnerability (Bliss, 1984; Putnam et al., 1984). A few MPD patients do report beneficial effects from neuroleptics. In most cases, however, careful questioning reveals that the improvement is primarily due to diminution in anxiety and hyperarousal symptoms, and only secondarily to an effect on the apparent psychotic symptoms.

Somatoform symptoms in MPD (Group 4) also are often targeted pharmacologically. Somatoform pain symptoms and pseudoseizures are most frequently treated in this way with analgesics and anticonvulsants, respectively. Use of narcotic analgesics for somatoform pain symptoms in MPD is almost invariably inefficacious in the long run and frequently leads to abuse of the medications. It is usually preferable to approach somatoform symptoms in MPD

psychotherapeutically or hypnotherapeutically as manifestations of somatic memory phenomena or of internal conflict among alters. Pseudoseizures are conversion symptoms for which no known pharmacologic treatment exists. The non-MPD literature on somatoform disorders also generally supports non-pharmacological interventions for these conditions, except to treat other intercurrent psychiatric disorders such as affective or anxiety disorders (see for example, Ford, 1983).

Only PTSD and affective symptoms (Groups 5-6) appear to be valid psychopharmacological targets in MPD. Affective symptoms are often targeted for treatment but the literature and clinical experience strongly suggest that antidepressants are rarely efficacious in MPD (Barkin et al., 1986; Kluft, 1984b; Putnam, unpublished data). There are several explanations for this. In MPD, the human being as a whole generally does not meet true criteria for affective disorder since usually only a few alters will report depressive symptoms while others describe euthymia or even apparent hypomania (Putnam et al., 1984). Clinicians frequently mistake the state of one or more alters for that of the whole human being (Loewenstein et al., 1987). In general, even when all alters report a depressive syndrome, this is a transient phenomenon related to an acute crisis. Thus, the time-course criteria for major depression by DSM-III/DSM-III-R criteria is also rarely met in MPD patients (Putnam et al., 1984).

Although an early report hypothesized that MPD was an "epiphenoma" of primary affective disorder (Coryell, 1983), it is probably more correct to conceptualize depression in

TABLE I

PTSD Symptom Improvement with Clonazepam in FIVE Consecutive MPD Cases
(In rank order of improvement based on median change score)*

CASE	1	2	3	4	5	Median Change Score
Nightmares	3+	2+	3+	2+	3+	3+
Global Improvement of Total Human Being	2+	2+	2+	2+	1+	2+
Difficulty Falling Asleep	3+	2+	2+	1+	1+	2+
Panic/Severe Anxiety	2+	1+	2+	3+	1+	2+
Intrusive Recollections	2+	2+	1+	2+	1+	2+
Flashbacks	2+	2+	1+	N/A	1+	1.5+
Reactivity to Triggers	1+	1+	1+	2+	1+	1+
Irritability/Anger	1+	1+	1+	2+	N/A	1+
Difficulty Concentrating/ Confusion	1+	2+	1+	3+	1+	1+
Exaggerated Startle	1+	1+	1+	N/A	0	1+
Physiologic React to Triggers	2+	1+	2+	1+	1+	1+
Hypervigilance	1+	0	1+	N/A	0	0.5+
Psychogenic Amnesia	0	0	0	2+	0	0
Avoidance Symptoms	1+	0	0	0	1+	0

* (Key: No change=0; Mild Improvement=1+; Moderate Improvement=2+; Marked Improvement=3+)

MPD as a *secondary* affective disorder; that is, an affective disorder co-existing with another primary Axis I DSM-III/DSM-III-R disorder (Goodwin & Guze, 1979). Therefore, even without the problem of the apparent state dependency of the affective symptoms in MPD, one would predict a more heterogeneous, less robust, response to antidepressant medication in MPD than in primary affective disorder. In addition, many of the apparent vegetative symptoms in MPD, such as sleep disturbance, poor concentration, and irritability, may be better conceptualized as manifestations of PTSD, not of an affective disorder.

Posttraumtic stress symptoms remain as the most promising psychopharmacological target in MPD patients. To be sure, there are MPD patients who report state dependency of certain PTSD symptoms such as panic, irritability, awareness or flashbacks, nightmares, etc. On the other hand, in clinical practice, at least some PTSD symptoms seem to manifest themselves in many if not all alters. Even alters who claim invulnerability to dysphoria of any kind will often show at least indirect evidence of posttraumatic reactivity. Not all MPD patients will meet full criteria for PTSD. Most MPD patients will, however, report at least some PTSD symptoms such as nightmares, reactivity to triggers or hyperarousal. It may be difficult to identify specific posttraumatic triggers in MPD, however. In child-abuse related PTSD syndromes, the triggers are often mundane objects or situations which evoke abuse experiences or locations where abuse actually occurred (van der Kolk, 1986). Phobic avoidance of these panic-inducing triggers may occur leading to a misdiagnosis of agoraphobia with panic attacks.

CONCLUSIONS

Our study suggests that clonazepam has potential as an adjunctive treatment for the amelioration of PTSD symptoms in MPD. Clonazepam is safe, easy to use, and not associated with significant problematic side effects or abuse in this sample. Our findings need to be replicated in well-constructed double-blind studies of MPD patients taking clonazepam. In addition, longer term efficacy, side-effects, and development of tolerance to clonazepam in MPD patients with PTSD need to be evaluated longitudinally. No double-blind trials have yet been published to document the utility of any medication treatment in PTSD, although several are currently in progress (Friedman, 1988). Clonazepam has been shown to be safe and effective in the treatment

TABLE II

Symptom Clusters in MPD

Process Symptoms
1. Alter Attributes (e.g. different stated age, gender, self-presentation/forms of self-expression, memory subsystems, etc.)
2. Passive Influence Symptoms/Interference Phenomena
3. Hallucinations/Pseudo-hallucinations
5. Linguistic usage (e.g. use of 1st person plural, 3rd person singular when referring to self; use of different names for self)
6. Switching Phenomena

Autohypnotic symptoms
(manifested by high hypnotizability)
1. Enthrallment
2. Spontaneous Age Regression
3. Negative Hallucinations
4. Voluntary anaesthesia
5. Out of body Experiences
6. Trance Logic
7. Eye-roll with switching

Amnesia Symptoms
1. Blackouts/Time loss
2. Fugues
3. Perplexing Possessions
4. Inexplicable Changes in Relationships
5. Fluctuations in Skills/Habits/Knowledge
6. Fragmentary Recall of Entire Life History
7. Chronic Mistaken Identity Experiences
8. "Micro"-Dissociations

Somatoform Symptoms
1. Conversion symptoms
2. Pseudoseizures
3. Somatization disorder/Briquet's Syndrome
4. Somatoform Pain Symptoms (e.g. headache, abdominal pain)
5. Somatic memory

PTSD Symptoms
1. Psychological Trauma
2. Flashbacks/Revivifications/Intrusions (Hyperamnesia)
3. Nightmares
4. Reactivity to Triggers
5. Hyperarousal/Startle Response
6. Panic/Anxiety
7. Numbing/Avoidance/Detachment

Affective Symptoms
1. Depressed mood (differentiate between mood disorder localized in specific alter(s) versus across "total human being")
2. Hypomania/Mood swings (differentiate between mood disorder localized in specific alter(s) versus across "total human being"; mood swings not due to interference phenomena between alters)
3. Vegetative symptoms (must be differentiated from PTSD symptoms; e.g., middle of night awakening due to nightmares, etc.)
4. Suicidal thoughts/attempts/self-mutilation
5. Guilt
6. Helpless/Hopeless

of mania and panic attacks (Rosenbaum , 1987). We feel that it is important to study further the efficacy of clonazepam in populations with severe, disabling chronic post traumatic symptoms such as MPD patients, non-MPD child abuse survivors, and combat veterans with PTSD.

In addition, targeting of PTSD symptoms readily lends itself to a general strategy for evaluating psychopharmacologic interventions in MPD. As the neuropharmacology of PTSD is clarified in various populations such as combat veterans, incest-survivors, MPD patients, and other trauma victims, we may discover similarities as well as the possibility of underlying differences between these groups. Additionally, there are likely to be subpopulations of PTSD and MPD patients who have differing response patterns to medications. This may help to explain the preliminary observation of lack of efficacy of carbamazepine in most MPD patients but its utility in treating PTSD symptoms in some combat veterans. Controlled, systematic studies are now clearly warranted to begin to address these questions. ■

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