Pharmacological Treatment of Substance-Abusing Schizophrenic Patients

by Samuel G. Siris

Abstract

This article reviews special clinical dilemmas inherent in the differential pharmacotherapy of patients with the dual diagnoses of schizophrenia and substance abuse. The author discusses the role of neuroleptic medications in treating the psychotic diathesis, preventing recurrences of schizophrenic symptomatology, counteracting psychotic exacerbations engendered by abused substances, and potentially generating side effects such as akinesia and akathisia that patients may attempt to "self-medicate" with substances of abuse. Also addressed are the potential adjunctive roles of antiparkinsonian medications, tricyclic antidepressants, and benzodiazepines in appropriately selected cases, as well as pharmacokinetic and pharmacodynamic interactions of psychotropic medications and substances of abuse. Throughout the course of these psychopharmacological strategies, the value of psychosocial interventions geared to recognizing and compensating for specific schizophrenic vulnerabilities should be emphasized, as substance abuse is addressed in the context of a complication in the course of schizophrenia.

As the epidemic of substance abuse spreads throughout the population of patients who carry the diathesis for schizophrenia, clinical problems of enormous proportions ensue. The problems of treating substance abuse, per se, are now compounded by the effects of various substances, at various doses, at various durations on the potentially vulnerable brains of schizophrenic persons. The problems of treating these patients are also compounded by the various potential interactions between substances of abuse and those medications that schizophrenic patients may already be taking and, for that matter, the effect of substance abuse itself on the medication-taking behavior. Substance abuse may also lead to potentially stressful interpersonal interactions for schizophrenic patients, as well as all the clinical sequelae that those interactions may entail.

In general, the major concerns are that substance abuse will exaggerate the difficulty of engaging patients in treatment and also lead to increased frequency or severity of psychotic exacerbations among schizophrenic patients (Galanter et al. 1988). This latter concern is reinforced by the observation that psychostimulant substances may be preferentially abused by schizophrenic patients (Breakey et al. 1974; McLellan and Druley 1977; Richard et al. 1985; Schneier and Siris 1987), and by the fact that psychostimulants have particular potential for psychotogenic effects (Snyder 1973; Angrist et al. 1974; Janowsky and Davis 1976; van Kammen et al. 1977; Gold and Bowers 1978; Angrist and van Kammen 1984; Richard et al. 1985; Lieberman et al. 1987a, 1987b), although other abused substances can certainly also have psychotogenic effects in schizophrenic patients (Schuckit 1983). The issue of treating substance abuse in schizophrenia, therefore, involves two aspects: treatments to prevent or limit the abuse of the substances themselves, and treatments for the effects of the substances once their use has occurred.

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Unfortunately, there are few properly controlled clinical studies to guide us in these treatments. There are, of course, a number of reasons for the lack of studies: (1) schizophrenia is a difficult enough disorder to treat and study on its own without the added complication of substance abuse; (2) substance abuse is a difficult enough disorder to treat and study on its own without the added complication of schizophrenia; (3) the problem of substance abuse has only recently risen to its current high prevalence level and visibility as an issue; (4) at best, studies of the treatment of substance-abusing schizophrenic patients are very difficult and require a considerable period of time to complete; and (5) the patterns of substance abuse may change more rapidly than studies of treatment can be completed. It is against this background that we must nevertheless develop sensible strategies for treatment based on the knowledge that we do have of schizophrenia and its treatment, and the understanding we possess of the pharmacology of substances of abuse.

Neuroleptic Drugs

The advantages of maintenance neuroleptic treatment in schizophrenia are well documented (Davis 1975; Kessler and Waletsky 1981; Rifkin and Siris 1983), and neuroleptic drugs will obviously figure prominently in any strategy for the pharmacotherapy of schizophrenic patients who are prone to substance abuse. While it is still possible that an intermittent neuroleptic treatment strategy may be sensible for some patients with schizophrenia (Herz et al. 1982; Carpenter et al. 1987), substance-abusing schizophrenic patients would not ordinarily be considered good candidates for that approach.

Neuroleptic drugs are effective in the treatment of psychotic exacerbations occasioned by substances of abuse in nonschizophrenic individuals (Dubin et al. 1986; Ellison and Jacobs 1986; Slaby and Swift 1987), as well as the idiopathic psychosis of schizophrenia. Thus, their use in patients who present with the combined problem seems a sensible choice. Studies of dose do not exist to guide us for the treatment of acute psychotic exacerbation in schizophrenia that may be occasioned by substances of abuse, but the usual antipsychotic dosage of the equivalent range of 400–1200 mg/day of chlorpromazine (Kessler and Waletzky 1981) is a logical place to start. Doses can be titrated up from that point, if necessary. It should be remembered, however, that (1) response of the psychosis in schizophrenia often requires several weeks of treatment, irrespective of neuroleptic dose; (2) larger doses or acute loading doses of neuroleptic have generally not been found to be superior to a more moderate treatment dose in managing psychosis in schizophrenia (Donlon et al. 1980; Neborsky et al. 1981; Escobar et al. 1983; Dubin et al. 1986; Coffman et al. 1987), and (3) the substance that may have triggered the psychotic exacerbation is likely to pass out of the patient’s system quickly if the patient is kept away from his source of it.

High-potency antipsychotic medications are preferable to low-potency antipsychotic medications in the treatment of acute substance-induced intoxication for several reasons (Dubin 1986; Slaby and Swift 1987). High-potency compounds are less likely to contribute to orthostatic hypotension and tachycardia, which may result from many abused substances. Also, since they have fewer anticholinergic side effects of their own, high-potency neuroleptics are less likely to potentiate the anticholinergic side effects that may result from many of the substances of abuse. Substance-abuse-prone patients, who are often sensitive to side effects, may also find the sedative properties of low-potency neuroleptics objectionable. An additional potential side effect, particularly for patients in acute cocaine psychosis, is cocaine-induced hyperthermia, which may be enhanced by neuroleptic medication (Kosten and Kleber 1988).

The rationale for the use of neuroleptic agents in chronic maintenance treatment to reduce the potential euphoric and/or psychotogenic effects of substances used, and thereby to decrease the tendency for and consequences of substance use, is speculative but inviting. It is based on what we currently know of the mode of action of such psychotogenic agents as cocaine or amphetamine being direct or indirect catecholamine agonists (Gawin and Kleber 1986b; Pollack et al. 1989), and on the capacity of neuroleptic drugs to blockade dopaminergic receptors. Indeed, in one study, monkeys given high doses of neuroleptics were found to have a reduced tendency to self-administer cocaine (Woolverton and Balster 1981). But such activity may represent a two-edged sword. The use of neuroleptics may also foster the use of such substances as cocaine, because the individual may attempt to use the abused psychostimulant to override undesired neuroleptic effects—a phenomenon that has been well-demonstrated in rats (Roberts and Vickers 1984) but not
yet tested in humans. This likely effect may well be dose-related, either with regard to the neuroleptic itself or to the abused substance. It is also possible that the “balance point” between the effects of neuroleptics and psychostimulants may vary depending on exactly which effect is under consideration. For example, one open neuroleptic study involving four nonschizophrenic cocaine abusers found that, whereas neuroleptics appeared to be useful in reducing paranoia during a binge, no effect of lessening cocaine-induced euphoria was apparent (Gawin 1986).

Many of the deleterious aspects of excessive neuroleptic doses in schizophrenic patients are already well known (Kane et al. 1983; Marder et al. 1987). Specifically, patients may feel “snowed” by the medication or they may develop obvious parkinsonian side effects, such as muscle stiffness, cogwheeling, and tremor. The motor restlessness syndrome of akathisia may be more difficult to recognize and can easily be mistaken for agitation or “acting-out” behavior (Van Putten 1975; Siris 1985). The hypokinetic neuroleptic-induced extrapyramidal syndrome of akinesia may also appear as a different kind of subtle behavioral disturbance in which the patient is deprived of initiative, spontaneity, or sense of vitality (Rifkin et al. 1975; Van Putten and May 1978; Siris 1987). Since this form of akinesia is not necessarily accompanied by motor stiffness or slowing, it can easily be missed or misinterpreted as a manifestation of depression, negative symptoms, or schizophrenic “burnout.” Whether the use of neuroleptic medications may be associated with a true “depression-like” syndrome has also been debated (Ananth and Ghadirian 1980; Hirsch 1982; Siris et al. 1988c). In any of these cases, patients may well attempt to medicate themselves out of an undesirable subjective state with “street-corner” psychopharmacology. This implication, then, is clear that excessive doses of neuroleptic medications are usefully avoided in the schizophrenic population. Nevertheless, there may be some situations among the dually diagnosed in which we are truly caught in the dilemma where the neuroleptic doses that are necessary to control psychotic symptomatology when patients are abusing psychostimulant substances may, in fact, also be doses stimulating them to abuse more substances. In the face of such a dilemma, there is no substitute for a meaningful therapeutic relationship that will allow frank discussion of what subjective states are contributing to which behaviors (Siris and Docherty, in press). In this relationship, of course, both patient and clinician must also be alert to the limitations in the extent to which the patient is able to discern correctly what his motivations truly are, and when affectively driven rationalization has begun to supervene.

Once an optimal neuroleptic effect is achieved, in many cases it is advantageous to administer medication in intramuscular depot form. This approach will assure compliance with the medication and allow the clinician to know immediately if the patient is noncompliant (i.e., misses a scheduled injection). The use of depot neuroleptics, however, is not without its own problems. Chief among these is that the long half-life of these compounds makes dose titration difficult. Since steady-state levels may not be achieved for 6 months with depot neuroleptics (Marder et al. 1986), plasma concentrations may creep up (or down) during this interval following dosage changes, without the clinician’s realizing that the patient’s true exposure to medication effects is changing despite a seemingly steady rate of administration. The use of depot neuroleptics is also complicated by the fact that conversion values between oral neuroleptics and their depot counterparts are less than perfectly worked out (Schooler et al. 1980; Yadalam and Simpson 1988). Thus, rating the dose of depot neuroleptics is a difficult enough task among schizophrenic patients who are not challenging themselves with various substances of abuse, let alone against an inconsistent background of stimulant and/or other substance abuse. Given these considerations, it is probable that adding extra oral neuroleptic, when needed, to a steady basal depot neuroleptic dose may be the optimal strategy in many cases.

Antiparkinsonian Medications

One way to reduce the potential for substance abuse is to use medications that reduce neuroleptic side effects. In particular, the syndrome of neuroleptic-induced akinesia can often be circumvented by antiparkinsonian medication (Rifkin et al. 1975, 1978; Van Putten and May 1978; Siris 1987). It is unknown to what extent neuroleptic-induced akinesia may predispose to substance abuse in vulnerable individuals; but the feelings of anergia, subtle or otherwise, which often accompany akinesia might prompt psychostimulant or other substance abuse. In fact, psychostimulants such as cocaine or amphetamine, which are dopamine agonists, would actually be a treatment, albeit misguided, for akinesia.
Therefore, a clinical trial of full therapeutic doses of anticholinergic antiparkinsonian medication (i.e., benztropine 2 mg p.o. t.i.d., or the equivalent) may be warranted in neuroleptic-treated substance abusers.

Anticholinergic antiparkinsonian medications, of course, may be potential substances of abuse in their own right (Jellinek 1977; Mac-Vicar 1977; Smith 1980; Pullen et al. 1984; Fisch 1987; Dilsaver 1988). Thus, their use in a population prone to substance abuse must be considered carefully. The clinical determination is a difficult one when a patient is truly abusing a substance, and when the patient is desperate to use an agent that he knows can make him feel normal when, without it, he feels dysphoric, anhedonic, or anergic (Fisch 1987; Tandon and Greden 1989). There may be a much needed role, in such situations, for organized individual clinical trials—to determine in a careful prospective manner if a particular patient does better on or off a particular agent. Again, the value of a functioning therapeutic alliance and a frank dialogue between patient and clinician cannot be overestimated.

Most antiparkinsonian agents are thought to exert their effects through their anticholinergic properties—cholinergic pathways being in balance with the dopaminergic pathways in the relevant basal ganglia systems. Their potential for abuse is assumed to result from these anticholinergic properties as well (Fisch 1987; Dilsaver 1988; Tandon and Greden 1989). However, not all antiparkinsonian medications have their effect on the basis of anticholinergic mechanisms. Amantadine is thought to exert an antiparkinsonian effect by virtue of being a dopamine agonist with a predilection for the nigrostriatal system, but with little affinity for the mesolimbic system which has been implicated in the pathophysiology of psychosis (Bailey and Stone 1975; Allen 1983). Thus, amantadine might be a useful antiparkinsonian medication in patients prone to abuse anticholinergic agents. That speculation, however, represents an untested hypothesis. Also untested is the safety of amantadine, or any other antiparkinsonian agents for that matter, in the face of the abuse of dopaminergic psychostimulants. Several trials among nonschizophrenic patients, however, have suggested that amantadine itself may have value as an anticing drug for stimulant abusers on the basis of its dopamine agonist properties (Kosten 1989).

Bromocriptine is another dopaminergic antiparkinsonian medication, and one which has been advocated for the treatment of cocaine abuse among nonschizophrenic patients (Dackis et al. 1985, 1987). The reasoning is that bromocriptine, as a dopamine agonist, will stimulate postsynaptic dopamine receptors leading to their downward regulation and consequent reduced affinity to such dopaminergic agents as cocaine. Bromocriptine, however, being a dopamine agonist and being thought to have the potential for exacerbating psychosis, at least in unmedicated schizophrenic patients (King 1978; Tammenga and Schaffer 1979), has been little used in schizophrenia to date, except in the treatment of neuroleptic malignant syndrome (Addonizio et al. 1987; Dhib-Jalbut et al. 1987; Roehrich et al. 1987) and possibly in the treatment of tardive dyskinesia (Roehrich et al. 1987) or neuroleptic-induced galactorrhea (Beumont et al. 1975). The parameters for its clinical use in schizophrenia for other purposes have yet to be worked out.

It may not be necessary to use bromocriptine to give stimulant-abusing schizophrenic patients the possible benefit of the dopaminergic receptor downward regulation strategy. Benztropine, one of the anticholinergic antiparkinsonian medications widely used to treat neuroleptic side effects in schizophrenia, has also been noted to have substantial dopaminergic agonist properties of its own (Coyle and Snyder 1969; Horn et al. 1971; Modell et al. 1989). Therefore, when we use benztropine in an ostensibly “conservative” maintenance antiparkinsonian medication strategy, we may also be pursuing a strategy of dopamine receptor downward regulation.

**Antidepressant Medications**

The self-medication hypothesis of substance abuse in schizophrenia (Richard et al. 1985; Millman and Sbriglio 1986; Schneier and Siris 1987) suggests that patients may be attempting to treat their own dysphoric feelings with the substances they are using. Such a psychostimulant self-medication hypothesis is well known for depression and other dysphoric states among people who are not schizophrenic (Gawin and Kleber 1984; Resnick and Resnick 1984; Khantzian 1985; Gawin and Kleber 1986a, 1986b; Mirin and Weiss 1986). This self-medication hypothesis raises the issue of the possible therapeutic use of adjunctive antidepressant medications in substance-abusing schizophrenic...
patients. The use of antidepressant drugs in this situation, of course, would parallel the postulated efficacy of antidepressant medications for reducing dysphoria and craving among substance-abusing non-schizophrenic patients. This strategy has been suggested in several preliminary reports, presumably on the basis of reductions caused in dopaminergic receptor sensitivity (Gawin and Kleber 1984, 1986b; Resnick and Resnick 1984; Giannini et al. 1986; Kosten 1989; Pollack et al. 1989).

A course-related depression-like syndrome is well known to occur in a substantial proportion of schizophrenic patients—usually reported to be in the range of 25 percent or more (McGlashan and Carpenter 1976; Knights and Hirsch 1981; Siris et al. 1981; Roy et al. 1983; Summers et al. 1983; Martin et al. 1985; Bartels and Drake 1988; Barnes et al. 1989). Though not all reports agree about the usefulness of adjunctive antidepressants in dysphoric schizophrenic patients (Waehrens and Gerlach 1980; Johnson 1981; Becker 1983, 1988), the addition of adjunctive tricyclic antidepressants to an ongoing neuroleptic regimen has been found to be useful for at least some "depressed"-appearing schizophrenic patients (Singh et al. 1978; Prusoff et al. 1979; Siris et al. 1987, 1988a). This has particularly been found to be the case when the patients have manifested a syndromal, rather than merely symptomatic, expression of depression (Siris et al. 1981) that is stable over time (Siris et al. 1986) and unresponsive to anticholinergic antiparkinsonian medication used to treat neuroleptic-induced akinesia (Siris 1987; Siris et al. 1987, 1988a). The most positive of these reports have initiated adjunctive tricyclic antidepressant treatment very gradually, in addition to depot neuroleptic and antiparkinsonian treatment, but eventually increased the tricyclic antidepressant drug up to doses equivalent to those used in primary depression (Siris et al. 1987, 1988a). Histories of substance abuse have not been found to contraindicate this course of treatment (Siris et al. 1988b), but no prospective trial in active substance abusers has yet been reported. Prospective controlled trials need to be conducted, both to document the potential efficacy of adjunctive antidepressants in this patient cohort (since it is unknown if substance-abusing schizophrenic patients will respond as positively as nonsubstance-abusing schizophrenic patients), and to document the safety of adjunctive antidepressants in schizophrenic patients prone to substance abuse (both in terms of medical and psychiatric adverse interactions). These trials are necessary because substance-abusing dysphoric schizophrenic patients might be different from nonsubstance-abusing dysphoric schizophrenic patients for several reasons: (1) there may be something fundamentally different about these two groups of patients that predisposes one group to substance abuse and not the other group, (2) the use of substances may lead to various biological sequelae within the central nervous system that may result in different etiologies of dysphoria in this patient group and different reactions to antidepressant medications when these are used, and (3) continued use of substances of abuse during an antidepressant trial could potentially lead to a whole host of pharmacokinetic or pharmacodynamic drug interactions among the substance-abusing patients that do not pertain to nonsubstance-abusing patients.

Antidepressant trials among substance-abusing patients should exclude monoamine oxidase (MAO) inhibitors. The presence of an MAO inhibitor could present a particular medical danger, principally hypertensive crisis, for any individual who abused a substance while under treatment with the MAO inhibitor. Probably not much is lost by this limitation, though, since the positive reports to date of the usefulness of adjunctive antidepressants in schizophrenia have tended not to be the ones that used MAO inhibitor antidepressants (Siris et al. 1978; Brenner and Shopsin 1980). However, hypertensive reactions to abused psychostimulants may also occur with tricyclic antidepressants—particularly at the start of treatment, because catecholamine uptake blockade occurs quickly in response to tricyclic antidepressants, whereas downward regulation of receptor sensitivity takes several weeks (Kosten 1989).

Lithium is another agent that may warrant trial in selected schizophrenic individuals who abuse substances. Lithium is not contraindicated in the face of possible abuse of other substances. In fact, it may possibly counteract euphoric effects of psychostimulants which patients may self-administer, although this is by no means certain (Rosenblatt et al. 1979; Gawin and Kleber 1986b; Pollack et al. 1989). Particular candidates for a trial of adjunctive lithium would be those patients who had a clinical picture suggestive of bipolar mood swings. Nonschizophrenic cocaine abusers with cyclothymia have also been reported to respond favorably to lithium (Gawin and Kleber 1984;
Kleber and Gawin 1986). This bipolar-type diathesis could be represented by episodes of grandiosity as a component of the illness or simply periods of extreme excitement. Unfortunately, however, there are no available controlled studies of adjunctive lithium in either dysphoric schizophrenic patients or substance-abusing schizophrenic patients to provide further guidance. The use of lithium in substance-abusing schizophrenic patients would therefore need to be empirical and on a case-by-case basis.

Benzodiazepines

Benzodiazepines could have a useful role to play in the treatment of certain substance-abusing schizophrenic patients. Since the combination of schizophrenia and substance abuse can have devastating consequences in the lives of the individuals involved, it is reasonable to leave no stone unturned in an attempt to find a treatment for them.

In addition to a well-defined role in treating many forms of acute substance-induced toxic states (Dubin et al. 1986; Ellison and Jacobs 1986; Slaby and Swift 1987), benzodiazepines might be used in patients who are attempting to self-medicate a subjective state of anxiety. This issue of anxiety, per se, has been relatively little studied in schizophrenic patients. However, the one study that specifically examined anxious schizophrenic patients in a double-blind paradigm found that patients treated with adjunctive chlordiazepoxide, in addition to their neuroleptic, were less anxious than they were when they were treated with adjunctive placebo (Kellner et al. 1975). It is also possible that some patients who had been attempting to self-medicate negative symptoms of schizophrenia could benefit from benzodiazepines, since some studies have suggested that adjunctive benzodiazepine treatment may reduce negative symptoms (Csérmansky et al. 1984; Wolkowitz et al. 1986; Finkel 1987). This finding, however, is controversial (Csérmansky et al. 1988; Adan and Siris 1989). Therefore, at best, it may only be a subgroup of negative symptom patients who would benefit from benzodiazepines.

Another group of schizophrenic patients who might attempt to self-medicate would be those schizophrenic patients who suffer a phenocopy of panic attacks as a component of their clinical state (Sandberg and Siris 1987; Kahn et al. 1988). These patients might benefit from the addition of adjunctive alprazolam to their neuroleptic regimen (Sandberg and Siris 1987; Kahn et al. 1988), or perhaps even an adjunctive tricyclic antidepressant (Siris et al. 1989), although both of these treatment possibilities have yet to be tested in proper prospective, randomized, placebo-controlled, double-blind trials.

Although neuroleptic drugs themselves have antianxiety properties, it may be unwise to increase neuroleptic dosage in an attempt to treat anxiety. Since excessive neuroleptic dosing could contribute to side effects that might stimulate patients to abuse substances, as outlined earlier (as well as predisposing to the risk of tardive dyskinesia), neuroleptics are best used to treat psychosis, not anxiety. In a number of patients, this may leave a role for an adjunctive benzodiazepine—at least until a proper clinical trial indicates a lack of usefulness in individual cases. In fact, some evidence exists that an adjunctive benzodiazepine may actually reduce the necessary dose of neuroleptic required to treat an exacerbation of psychosis (Kellner et al. 1975; Arana et al. 1986; Salzman et al. 1986; Cohen and Rosenbaum 1987; Wolkowitz et al. 1986; Douyon et al. 1989), but further work is required to determine the exact indications for benzodiazepines in this circumstance.

The use of benzodiazepine, of course, is not without its own risk in substance-abuse prone patients. Benzodiazepines have at times been associated with syndromes of behavioral dyscontrol (Gardos 1980; Hall and Zisook 1981; Rosenbaum et al. 1984; Dietch and Jennings 1988) and can be habit forming (Schopf 1983; Noyes et al. 1988). Therefore, although a therapeutic trial of an adjunctive benzodiazepine may be a sensible undertaking in schizophrenic patients prone to substance abuse who also have features of anxiety, it is not a trial to be undertaken trivially or continued without the sense that a therapeutic gain is being realized.

Other Treatments

This article has focused on current treatments to diminish the likelihood of patients with schizophrenia abusing substances. In the acute throes of substance toxicity following ingestion, schizophrenic patients would be handled similarly to other acutely toxic nonschizophrenic individuals. This topic has been well reviewed elsewhere (Dubin et al. 1986; Ellison and Jacobs 1986; Slaby and Swift 1987). The first priority in this situation is conservative medical support until the drug can be eliminated and the acute effects have time to abate. Behavioral toxicity
may also need to be managed, as indicated, by antipsychotic or anxiolytic agents, sedation, or interpersonal means. Recognition must be made of whatever maintenance neuroleptic or other medication the patient has been receiving, including the possibilities of additive or interactive pharmacological effects. As with the treatment of nonschizophrenic patients, clinicians must also be alert to the possibility of withdrawal syndromes from various substances which patients may have been using chronically and which may have been abruptly stopped (i.e., alcohol, narcotics, barbiturates, and benzodiazepines). Again, from a medical standpoint, these withdrawal states would be handled similarly to how they would be handled in nonschizophrenic patients. The main difference with schizophrenic patients, of course, is that care must be taken not to misattribute the organic psychosis which may accompany acute intoxication or acute withdrawal for a schizophrenic psychosis and thereby neglect to monitor vital signs appropriately or institute the proper medical support or detoxification techniques.

For long-term management of patients there are specific pharmacological preventive therapies for certain substances of abuse. For example, disulfiram is often used in patients who abuse alcohol, and methadone maintenance is used for narcotics abusers. These treatments can be used as well for schizophrenic patients being maintained on neuroleptics. In general, their parameters are the same as for nonschizophrenic patients. Particularly at the time of initiation of these treatments, however, patients need to be followed closely. Some patients have been reported to have schizophrenic-like psychoses initiated or exacerbated by disulfiram (Ban 1977; Rainey 1977; Wedington et al. 1980), although this has not been a universal finding (Kofoed et al. 1986; Galanter et al. 1988). As for methadone, its use may alter patients’ neuroleptic requirements (Gold et al. 1978; Vereby et al. 1978; McKenna 1982). This possibility is best assessed on a case-by-case basis. It is also conceivable that methadone treatment may facilitate cocaine abuse among patients prone to abuse both cocaine and narcotics because the steady presence of methadone can “cushion” the dysphoric postcocaine crash (Kleber and Gawin 1986; Kosten 1989).

The pharmacological approaches to substance abuse in schizophrenia discussed here are not to be taken as a substitute for appropriate psychosocial interventions, which need to be undertaken in addition to well-informed pharmacotherapy (Siris and Docherty, in press). Appropriate individual, group, family, behavioral, and rehabilitative therapies are indicated for these dually diagnosed patients from the perspective of substance abuse being a complication of schizophrenia for these individuals. The modes of interaction best adapted to dealing with schizophrenia should be employed, and the highly stimulating, highly confrontative, or other interventions which are typically used with primary substance-abusing patients and which are highly charged with “expressed emotion” are best avoided. Psychoeducational techniques, however, may be highly valuable. Hospitalization, of course, will need to be used for detoxification and management of acute psychosis, and may be useful for separating the patient from sources of and cues for abused substances. The hospital can provide useful external “structure” for a patient who is “out of control” until he or she can reintegrate and achieve adequate executive capacity to be responsible for the conduct of his or her life. In all of this, the appropriate therapeutic stance is fundamentally adaptational, not judgmental, and constant effort must go into building a working therapeutic alliance (Siris and Docherty, in press).

Summary and Conclusions

The comorbidity of substance abuse creates a number of complicated considerations in the psychopharmacological management of patients with schizophrenia. Extra attention needs to be devoted to determining the optimal dosage of neuroleptic medication, since substances of abuse may alter neuroleptic requirements on both an acute and chronic basis, and since either underdosing or excessive dosing with neuroleptics may lead patients to attempt to “self-medicate” with street substances. Careful attention therefore needs to be paid to assessing and treating neuroleptic side effects—although many of the antiparkinsonian neuroleptic side effect medications may themselves have abuse potential. It is possible that tricyclic antidepressants, lithium, benzodiazepines, disulfiram, and methadone may be valuable therapeutic adjuncts in appropriately chosen cases. However, with all medications used, consideration needs to be given to the various potential pharmacokinetic and pharmacodynamic interactions among the medications themselves, and between the medications and possible substances which the particular
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