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Do Antipsychotic Drugs Influence Suicidal Behavior in Schizophrenia?

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ABSTRACT ~ The literature concerning the net effect of antipsychotic medication on suicidality in patients with schizophrenia is not consistent. This review assesses this problem in the light of relevant research. MEDLINE was used to search for articles written in English from 1964 to 2006. Articles were classified according to the following three orientations: positive, negative, or null effect on suicidality. Several inconsistencies among the studies and methodological difficulties appeared and a singular conclusion on this issue was not possible. Competing properties of various antipsychotic drugs may have differential effects on suicidality. Second-generation antipsychotic agents appear to have a better potential for preventing suicide in schizophrenia, but the relative profile of each drug is yet to be clarified. A good profile to treat hostility, impulsivity, and depression while not provoking extrapyramidal side effects is crucial when choosing an antipsychotic in the presence of suicide risk. The strongest and perhaps unique evidence has been shown for clozapine, which seems to have a clinically relevant advantage over both first- and second-generation antipsychotics for reducing suicidality. Although clozapine has not yet demonstrated a specific preventing effect on completed suicide in patients with schizophrenia, it should be considered when suicide risk is detected in a patient with schizophrenia. *Psychopharmacology Bulletin*. 2007;40(3):128-142.

INTRODUCTION

It is well known that suicidal behavior is a common concomitant of several psychiatric illnesses including schizophrenia. Suicide rates for this illness differ along the studies but the rate seems to be between 10%, which is the generally accepted modal rate,^{1,2} and 5%.³ Suicide-related costs include both financial losses, namely years of lost productivity and general hospital costs, and intangible costs. In this last sense, personal testimonies may do better than statistics when trying to understand this source of suffering and loss.⁴ Moreover, suicidality during life is not only a painful situation for the patient but also a powerful contributor to

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family burden.⁵ Although financial consequences are difficult to quantify in a comprehensive way, some studies have suggested a significant potentiality of second-generation antipsychotics (SGAs)⁶ and, particularly, clozapine,⁷ for ameliorating such costs. This article subjects these assertions to a critical review.

Since antipsychotic treatment is the mainstay of the treatment of schizophrenia, we should know whether and how these drugs influence suicidal behavior. Regrettably, these questions have remained elusive for almost half a century. It is a commonly held opinion that first-generation antipsychotics (FGAs)⁸ and SGAs⁹ have not reduced (or may have even increased) suicidality among schizophrenic patients. However, it is relevant to observe that the magnitude of suicidal risk is hard to establish because of the sporadic nature of the event and inconsistencies across the various studies. Therefore, attempted comparisons may not be reliable and firm conclusions may still be premature.

Soon after their introduction, some studies reported that antipsychotic medications might either have no effect¹⁰ or actually increase the risk of suicide.^{11,12} However, these early negative reports have not been replicated and several studies have not found differences in neuroleptic treatment between suicide and control groups.¹ Indeed, several controlled studies have rejected a negative influence on completed suicide¹³ and have even shown a preventing effect on suicide attempts.^{14,15} More recently, several other studies have indicated that both FGAs and SGAs probably reduce the risk of suicide and suicide attempts in schizophrenia.^{16,17}

One of the most intuitive ways of understanding this issue comes from analyzing the neuroleptic dose-suicide relationship. But again results have varied. One study did not find any association.¹⁸ Three studies have shown a relationship between lower doses and suicide,¹⁹⁻²¹ although the difference was not statistically significant in the second study.²⁰ Finally, one study found higher doses of antipsychotic medications to be associated with suicide,²² while another found this association only for those patients taking depot fluphenazine, probably through extrapyramidal side effects.²³ Therefore, we can conclude that there is not a linear relationship between suicide and neuroleptic dose (or blood level). An explanation for these findings has been suggested by Palmer et al.¹⁶ According to these authors, it would follow an inverted "U" in which very low doses would be ineffective and higher doses might also be associated with higher suicide rates through side effects or by an artifact of the studies, namely, more severe (and suicidal) schizophrenic patients being treated with higher doses of neuroleptics.

Literature suggests that SGAs might have a different effect on schizophrenic suicide than FGAs. Although this is probably true, this article

will not make an a priori assumption that there is a difference, but rather discuss this issue objectively as it has unfolded in the literature to date.

At this point, we can already realize we are facing a complex relationship. It seems that antipsychotic drugs influence suicidal behavior but do not have a net positive effect. Several possibilities can be mentioned:

- (a) Antipsychotic drugs might induce suicidal behavior but:
 - Each antipsychotic agent has a different profile in regard to this negative effect.
 - Other variables mitigate this consequence.
 - The relationship between antipsychotic drugs and suicidality depends on diagnosis.
- (b) Antipsychotic medication can prevent suicidal behavior but:
 - Not all antipsychotic drugs have the same potential for preventing suicide.
 - Other “external” factors interact with their effect.
 - The effect varies among different diagnoses.

As the result of possible combinations of these effects, a noninfluence status may appear as a net effect.

The aim of this review is to analyze whether and how antipsychotic drugs influence suicidal behavior in schizophrenia in the light of relevant research. A better knowledge on this issue is necessary to prevent suicidal risk in patients with schizophrenia.

FIRST HYPOTHESIS: NEGATIVE INFLUENCE

Healy et al.⁹ compared suicide and suicide attempt rates from a pre-neuroleptic period (1875–1924) in the North Wales Asylum with rates from antipsychotic trials submitted to the Food and Drug Administration (FDA). Their results point to an increase in suicide rates after the introduction of antipsychotics and the authors defend a possible contribution to that increase from antipsychotic agents. This study provides the biggest database from the preantipsychotic era for lifetime suicide rates in psychoses in terms of number of patients and of deaths and has several external and internal validators. On the other hand, one could question whether these two types of data are comparable. For example, since the introduction of antipsychotic medications, there has been a massive discharge of patients out of hospitals and into the community where stimuli, structure, continuing treatment, and protections are all different than what they had been in the in-patient environment.

FGAs might have different profiles in regard with suicide risk potentiation but this has not sufficiently been proved and contradictory data appear in the few studies that have assessed this issue.¹⁷

Neuroleptic-related potential for suicide can be mediated for several mechanisms that usually involve a worsening of depressive symptoms. These drugs can cause depressive symptoms either through their side effects (mainly “akinetic depression” and antipsychotic-induced dysphoria) or by inducing depression.

DEPRESSIVE SYMPTOMS RELATED TO EXTRAPYRAMIDAL SIDE EFFECTS

Akinesia

This side effect consists of a diminished ability to initiate or sustain motor behaviors that can mimic depression.²⁴ The term “akinetic depression” was coined by Van Putten and May²⁵ to define a separate clinical entity that includes a reduced level of activity as well as anhedonia and responds to anticholinergic medication.

Severity of parkinsonism seems to predict more suicidal behaviors as it has been confirmed in a recent international study where both the severity of depression and the severity of parkinsonism were among the most predictive variables for suicidal behaviors.²⁶ However, the term parkinsonism includes symptoms such as tremor and rigidity besides akinesia. To our knowledge, no study has specifically studied a possible relationship between akinesia and suicide, and it could be that this particular symptom may even protect against suicidal behavior, although not against suicidal thinking, because behaviors of all sorts tend to be attenuated in the state of akinesia.²

Akathisia

This common side effect is characterized by subjective and motor restlessness. It is hard to differentiate from neuroleptic-induced dysphoria, which is extremely unpleasant for patients.^{27,28}

Akathisia was soon linked to suicidal behavior with antipsychotics²⁹ and also with antidepressants.³⁰ Shear and Ehrlich³¹ were the first to report two cases of completed suicide occurring impulsively in the context of akathisia. Other case reports came after them to describe an association between both completed and attempted or suicidal ideation with akathisia. Moreover, Shaw et al.³² reported both suicidal and homicidal ideation associated with akathisia in a double-blind crossover study. A good review by Hansen³³ concluded that, at this stage, akathisia could neither be excluded as an etiological factor for suicidal behaviors nor unequivocally be linked to it. However, this author has recently failed to

find any association between either akathisia or parkinsonism with suicidality in a study of patients with treatment-resistant schizophrenia.³⁴

If they are associated, both depression and treatment noncompliance can be the links between akathisia and suicide. A study by Atbasoglu et al.³⁵ gives support to the first mechanism. The second possible link should not be forgotten and implies the possibility of poor compliance because of this unpleasant side effect as some authors soon recognized.³⁶

Tardive Dyskinesia

It has also been identified as a potential risk factor for suicidality in schizophrenia patients³⁷ although there is not enough evidence to confirm it.

Depressiogenic Effect

This effect seems to apply more to FGAs and is very relevant here since depression is probably the most common reason for suicide in chronic schizophrenics.³⁸ Both a direct “pharmacogenic” depression and a depression due to the experience of side effects can occur.

Relevant literature is not completely concordant about this issue. Casey et al.³⁹ were pioneers in associating neuroleptic treatment and depression. De Alarcon and Carney⁴⁰ proposed that antipsychotics acted directly causing “pharmacogenic depression.” These authors and others^{23,31,41} have linked suicide with depot antipsychotics.

Johnson⁴² argued that a significant part of depression is not drug related, but that neuroleptics could play a role (~10%) in the etiology of depression. In contrast, Hogarty and Munetz⁴³ as well as Hirsch et al.⁴⁴ did not find evidence of a potential depressiogenic effect of antipsychotics. Harrow et al.⁴⁵ found a strong relationship between neuroleptic treatment and depressive-like symptoms, particularly anhedonia, in their prospective study. More recently, a study has reported a positive relationship between haloperidol plasma levels and depressive symptoms.⁴⁶ Voruganti and Awad⁴⁷ reviewed the relationship between neuroleptics and dysphoria to conclude, among other things, that dysphoric responses typically manifest as a dislike toward medication and may lead to increased suicidality when persisting over time. These authors emphasize the interference with the physiological processes of hedonic capacity by these drugs through their ability to block dopaminergic receptors in the prefrontal cortex and the shell of nucleus accumbens.⁴⁷ Moreover, higher D2 receptor occupancy in striatal, temporal, and insular regions was associated with negative subjective experience in patients taking risperidone or olanzapine in a very recent study.⁴⁸ Dynamic interactions between the state of the dopamine receptor and the pharmacological properties of neuroleptics may be responsible for individual variability in dysphoric responses.⁴⁹

We tend to think that an association between antipsychotic drugs and depression is not the general rule. Two sets of data give the strongest evidence against the hypothesis of a depressiogenic effect for these drugs. First, depressive symptoms are frequently present before the initiation of neuroleptic treatment and often subside during this treatment.² Second, both FGAs⁵⁰ and second-generation antipsychotics (SGAs)⁵¹ have been found to have antidepressant properties.

It has been established that SGAs have a better although heterogeneous profile of extrapyramidal side effects. However, it is yet to be demonstrated whether or not they have better antidepressant properties, and what would be the specific profile of each one. Limited evidence exists, but clozapine could be superior to olanzapine⁵²; olanzapine⁵³ and amisulpride⁵⁴ could be better than risperidone; and finally, risperidone⁵⁵⁻⁵⁷ and quetiapine⁵⁸ would be preferable to haloperidol in regard with antidepressive effect. One caveat should be mentioned. Haloperidol may not be the gold standard among FGAs as far as antidepressant efficacy is concerned. Future studies, preferably independent ones, and including ones involving prospective use of antiparkinsonian agents in the case of FGAs, will help to clarify these issues.

SECOND HYPOTHESIS: POSITIVE INFLUENCE

Evidence suggests that not all antipsychotics have the same potential for preventing suicide. Altamura et al.⁵⁹ found that SGAs (clozapine and risperidone) were associated with a lower rate of suicide attempts than FGAs in their retrospective study. This is concordant with other reports for olanzapine^{60,61} and quetiapine.⁶² Moreover, an international, prospective, double-blind, but nonindependent study showed that several events, including suicide attempts, occurred more often among risperidone- than olanzapine-treated patients.⁶³ However, a recent study by Barak et al.⁶⁴ has shown a protective effect for both drugs with a larger but not statistically significant effect-size for risperidone (3.16) than olanzapine (1.76). Although a case report has recently suggested a potentiating effect on suicidality for aripiprazole,⁶⁵ there is a lack of published information for this drug and ziprasidone.

A study by Herings and Erkens⁶⁶ has demonstrated a fourfold increase in suicide attempts for patients who interrupt or stop treatment with olanzapine or risperidone. Their findings are in concordance with previous studies reporting an increased sevenfold suicide attempt risk due to noncompliance with antipsychotics among schizophrenic patients.⁶⁷

On the other hand, several retrospective⁶⁸⁻⁷² and prospective⁷³⁻⁷⁶ studies seem to firmly support a specific effect of clozapine in preventing suicidal behavior (Table 1). A recent meta-analysis has shown a lower

ANTIPSYCHOTIC DRUGS AND SUICIDE

TABLE 1

STUDIES ON CLOZAPINE AND SUICIDE

STUDY	N	PATIENTS' DIAGNOSIS	TYPE OF STUDY	OUTCOME
Meltzer and Okayli ⁷³	237 neuroleptic-responsive and 184 neuroleptic-resistant	DSM-III-R schizophrenia or schizoaffective disorder	Prospective (6 months to 7 years)	Less suicidality (ideation and attempts) in neuroleptic-resistant patients with clozapine.
Walker et al. ⁶⁸	67,072 current and former clozapine users	Unspecified	Retrospective (2 years)	Mortality from suicide was decreased in current clozapine users.
Reid et al. ⁶²	More than 30,000	schizophrenia or schizoaffective disorder	Retrospective (2 yrs and 6 years in clozapine group)	Lower annual suicide rates in patients treated with clozapine.
Spivak et al. ⁷⁴	30 neuroleptic-resistant and 30 controls with FGAs	DSM-IV schizophrenia	Prospective (1 year)	Lower suicidality, aggression, and impulsivity compared with control group.
Munro et al. ⁷⁰	12,760 patients with clozapine from Clozaril patient monitoring service (CPMS)	Unspecified	Retrospective (7 years)	Lower than expected suicide rates.
Spivak et al. ⁷¹	70 neuroleptic-resistant and 30 controls with FGAs	DSM-IV schizophrenia	Retrospective (6 months)	Reduction in aggressive and suicidal behavior in clozapine group.
Ciapparelli et al. ⁷⁵	91 treatment-resistant	DSM-III-R schizophrenia, schizoaffective disorder or psychotic bipolar disorder	Prospective, naturalistic (2 years)	Clozapine was effective to reduce suicidal ideation both in schizophrenia and affective disorders.
Modai et al. ⁷⁷	561 clozapine vs 4,918 with other drugs	ICD 9 and 10 schizophrenia in clozapine group. Unspecified for control group.	Retrospective (6 years)	The rate of suicide in clozapine group was 3.6 times higher than among control group.
Sernyak et al. ⁷⁸	1,415 with clozapine and 2,830 as controls	schizophrenia	Retrospective (4 years)	No significant differences in rates of suicide.

*(continued on next page)*Aguilar and Siris *Psychopharmacology Bulletin*. Vol. 40. No. 3. 2007.

TABLE 1 (continued)

STUDIES ON CLOZAPINE AND SUICIDE

STUDY	N	PATIENTS' DIAGNOSIS	TYPE OF STUDY	OUTCOME
Altamura et al. ⁵⁹	103 patients	DSM-III-R schizophrenia or schizoaffective disorder	Retrospective (5 years)	Attempters were more frequently prescribed FGAs and less clozapine and risperidone.
Spivak et al. ⁷⁶	44 patients (18 with clozapine vs haloperidol decanoate)	DSM-IV schizophrenia	Prospective (6 months)	Reduction in aggressive and suicidal behavior in clozapine group.
InterSePT Study Group (Meltzer et al. ⁵² ; Potkin et al. ²⁶)	980 patients at high risk for suicide	DSM-III-R schizophrenia or schizoaffective disorder	Prospective (2 years) and randomized	Clozapine superior to olanzapine in preventing suicide attempts.
Modestin et al. ⁷⁹	94 patients with clozapine	Schizophrenia (N = 75), schizo-affective and affective dis.	Retrospective (mirror design) (30 months mean duration)	Clozapine diminishes the frequency of suicidal behaviors.
Kuo et al. ⁸⁰	4,237 (78 suicides were compared to 78 controls)	DSM-III, DSM-III or DSM-IV schizophrenia	Prospective (1 year)	Lifetime use of clozapine was nonsignificantly different.

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overall risk of suicidal behaviors with clozapine vs other treatments (Risk Ratio = 3.3) with a Risk Ratio of 2.9 for completed suicide.⁸¹

The study that has provided the strongest evidence for a clozapine-specific antisuicidal effect is the InterSePT (International Suicide Prevention Trial Study).⁵² This was a multicenter, international, prospective, and randomized, 2-year, parallel-group study, comparing the effects of treatment with clozapine versus olanzapine in 980 patients with schizophrenia or schizoaffective disorder who were considered at high risk for suicide. Fewer clozapine-treated patients attempted suicide, required hospitalizations or rescue interventions to prevent suicide, or required concomitant treatment with antidepressants or anxiolytics. In our opinion, conclusions from this study should only apply to the relative effect of clozapine vs olanzapine on suicidal behavior not including complete suicides. We should also remember that both risperidone and olanzapine have been reported to be safer in overdose than clozapine,⁸² and that medication overdose is a very frequent

method of suicide in schizophrenic patients in both sexes.⁸³ Although the authors suggest that both drugs probably reduced suicidal behavior, the study design did not permit a proper test of this hypothesis.

The mode of action of clozapine in preventing suicide is not known. Data from the study by Meltzer et al.⁵² suggest that the effect of clozapine may not relate to its superior efficacy for treatment-resistant psychotic symptoms. Meltzer⁸⁴ has suggested several reasons such as a direct antidepressant action or an indirect effect through the improving of cognitive functioning, compliance, insight, negative symptoms, and substance abuse. Other hypotheses involved are its effects on neurotransmitters and serum lipid levels, and its lower rates of akathisia and tardive dyskinesia.⁸⁵ Additionally, there is also the possibility of a strictly psychological benefit for clozapine in the domain of suicidality in that patients may adopt an attitude that life and death are "out of my hands now" in response to the concept of "playing Russian roulette" with the potentially fatal complication of agranulocytosis.

It has been suggested that clozapine exerts its action through normalizing serotonergic function whose relationship with suicidality is well-established.⁸⁶ Both its antidepressive effect and its specificity on suicidal behavior can be mediated by a increased central availability of norepinephrine and dopamine, along with a normalization of central 5-HT activity, especially in the prefrontal cortex, through down-regulation of central 5-HT_{2A} and increased availability of central 5-HT.⁷⁶ This "paradoxical" down-regulation of 5-HT₂ receptors is common to antipsychotics and antidepressants.⁸⁷

Some factors other than depression or dysphoria may be involved with suicidal behavior in schizophrenia and we know little about how antipsychotic drugs may influence them. For example, psychotic decompensation, with resulting distortions of reality or faulty judgment, can result in ill-conceived and/or risky behaviors, and panic symptoms have been associated with suicidal behavior in schizophrenia.⁸⁸ The treatment of anxiety/agitation⁸⁹ and impulsivity⁹⁰ are crucial for suicide prevention. Two recent studies supply information on clozapine in regard with these symptoms. In a prospective, double-blind, randomized clinical trial, clozapine had a relative advantage over other antipsychotics (at least haloperidol and risperidone) as a specific anti-hostility agent.⁹¹ The 6-month prospective study by Spivak et al.⁷⁶ with 44 schizophrenic patients seem to indicate that the reduction in suicidality following long-term clozapine treatment may be related to a reduction in impulsiveness and aggression.

Considering all these data and the fact that the most influential antipsychotic for suicidality (clozapine) is underused all over the world, one could think that the more we use certain antipsychotics, and

particularly clozapine, the stronger the effect on suicide prevention will be.⁷ We may soon have a chance to test this hypothesis now that clozapine is approved in the United States to reduce recurrent suicidal behavior in patients with schizophrenia or schizoaffective disorder.

Some other explanations can be given for a net noneffect on suicide after the start of the neuroleptic era, despite a putative protective influence of antipsychotic medications.^{12,13} Specifically, short duration hospitalizations⁹² and the lack of follow-up community care⁹³ have often resulted in woefully inadequate out-patient care situations which could have contributed to suicide as an outcome.

Finally, there could be a specificity of effects according to the psychiatric diagnosis. We still do not know whether the advantage of clozapine therapy for reducing suicidal behavior also applies for patients with other disorders with high suicidal risk. The positive effect of clozapine, but not yet other antipsychotics,¹⁸ can probably be extended to bipolar disorders.^{75,94,95} On the other hand, several antipsychotics have also showed a beneficial effect on nonpsychotic populations, particularly borderline personality disorder, where it has been demonstrated by studies involving the effect of depot fluphenazine,⁹⁶ flupenthixol,⁹⁷ or low-dose clozapine⁹⁸ on suicide attempts.

THIRD HYPOTHESIS: NO INFLUENCE

Two recent studies pose a doubt on the efficacy of antipsychotics in preventing suicidality in schizophrenic patients.^{99,100} A review of phase III data submitted to the US Food and Drug Administration (FDA) did not find significant differences in the rates of suicide and suicide attempts between SGAs (not including clozapine) and either FGAs or placebo.⁹⁹ Stosorum et al.¹⁰⁰ reviewed all double-blind, placebo-controlled studies that were part of a registration dossier for the indication schizophrenia and that were submitted to the Medicines Evaluation Board of the Netherlands during the years 1992 through 2002. There were not significant differences in the incidence of suicides and suicide attempts between placebo- and active compounds-treated patients.

As noted above, clozapine presents the strongest evidence of being effective against suicidal behaviors. Two studies are not in concordance with this. Sernyak et al.,⁷⁸ using national databases, concluded that clozapine did not have a significant effect on the suicide rate, although it did demonstrate a trend toward lowering it. This study had several limitations. First, they did not match for two critical suicidality factors: previous suicide attempts and depressive symptoms. Second, since the study was not randomized, the clozapine-treated group might have had a greater suicide risk at the outset. Finally, as Meltzer⁸⁴ pointed out, they included drug-free intervals in the risk period for the clozapine-treated

patients. The second study which is not in concordance was that of Modai et al.⁷⁷ This study reviewed sudden deaths that occurred in a hospital and found that the rate of suicide among patients currently receiving clozapine was 3.6 times higher than among nonclozapine-treated patients. Again, of course, these patients had not been randomly assigned to treatment medications.

An additional type of data comes from autopsy studies. In a toxicological study of 5,281 suicides in Sweden (1992–1994), Isacson et al.¹⁰¹ detected neuroleptics in 7.1% of cases, apparently in the same order of magnitude as the diagnoses of nonaffective psychoses found in suicides (2–13%). Therefore, their data provided no evidence suggesting that suicidal psychotic patients were undertreated with neuroleptics. However, this study also has limitations since actual diagnoses and treatment received were not investigated. Moreover, their results are in discordance with other comparable studies. A nationwide psychological autopsy study in Finland showed that most of suicide victims with schizophrenia are receiving inadequate neuroleptic medication, are noncompliant, or do not respond to adequate typical antipsychotic medication.¹⁰²

Finally, it could be that antipsychotics do not help to prevent suicidal behavior because suicide may be a partially independent illness. Lindenmayer et al.¹⁰³ suggest that suicidality may represent a separate symptom domain that is related to, but independent of, depression or psychosis. The same argument could be made for hostility, which also appears to be independent of the antipsychotic effect of clozapine.⁹¹ If this is the case, suicidal behaviors in schizophrenia should not be related to positive symptoms. Although relevant studies show contradictory findings, some interesting data seem to give support to this hypothesis. Some studies indicate that classifying patients with schizophrenia in regard with neuroleptic treatment response does not differentiate them with regard to suicidality.⁷⁹ Moreover, even the presence of command auditory hallucinations for suicide did not directly predict suicide attempts in a recent study.¹⁰⁴

CONCLUSIONS

Inconsistencies among studies and methodological difficulties make it difficult to compare data and come to clear conclusions if or when antipsychotic drugs have a net effect on suicide in schizophrenia. In general terms, SGAs seem to have a better potential to prevent suicidal behavior but the relative profile of each drug is yet to be clarified. The key might be to treat hostility and impulsivity while not provoking extrapyramidal side effects and depression. A greater antidepressant effect, which has been attributed to SGAs, would be a definitive advantage as well.

It is now quite well established that clozapine has a clinically relevant advantage over both FGAs and SGAs in reducing suicidality, although it is not yet completely clear to what extent it may be efficacious for this purpose. Other conditions such as affective psychoses and borderline personality disorder may also benefit from this medication. It merits mention that, except for clozapine, no pharmacologic treatment has been established to be useful in reducing suicidality in patients with schizophrenia. Clozapine should therefore be considered for those patients with suicidal risk. A more extensive use of this antipsychotic agent, together with improved outpatient supports, might contribute to a net positive effect on suicidality in the future. ❖

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