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Suicide in schizophrenia. What are we going to do about it?

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Summary. - Suicide is the single major cause of death among patients with schizophrenia. Follow-up studies have estimated that 10-13% of these patients die by suicide. Various studies have identified risk factors for suicide in schizophrenic patients which are of great value for prediction and prevention of self-inflicted death. Despite great efforts, both on the side of drug treatment and psychosocial strategies, the number of suicides among schizophrenic patients has remained unchanged. We focus on a number of issues that are of paramount importance for the understanding and prevention of suicide in these patients, pointing to the need of supporting programs addressed to families and to establish a valid doctor-patient relationship with these patients both during consultation with psychiatrists or general practitioners and with medical staff during inpatient treatment.

Key words: suicide, schizophrenia, risk factors, prevention.

Riassunto (*Suicidio nella schizofrenia. Che cosa abbiamo intenzione di fare?*). - Il suicidio è la principale causa di morte tra i pazienti schizofrenici. Studi di follow-up hanno stimato che il 10-13% di questi pazienti muore a causa del suicidio. Diversi autori hanno identificato fattori di rischio per il suicidio tra i pazienti schizofrenici. Questo ha una grande rilevanza per prevenire e predire il fenomeno. Nonostante i grandi sforzi sia nell'ambito della terapia farmacologica che nelle strategie psicosociali, il numero dei suicidi tra i pazienti schizofrenici è rimasto immutato. In questo articolo ci soffermiamo su varie tematiche rilevanti per la comprensione e la prevenzione del suicidio tra questi pazienti, sottolineando la necessità di programmi di supporto per la famiglia e di stabilire una efficacie relazione medico-paziente sia nell'ambito delle visite psichiatriche che in quelle con i medici di base e con il personale medico durante il ricovero ospedaliero.

Parole chiave: suicidio, schizofrenica, fattori di rischio, prevenzione.

Introduction

Suicidal behavior is identified as a major public health problem and a considerable drain on resources in both primary and secondary health care settings in many countries worldwide. Among teenagers and young adults, it is the third most frequent cause of death. According to World Health Organization [1] estimates, approximately 1 million people died from suicide, and 10 to 20 times as many attempted suicide worldwide in the year 2000. This averages out to one death every 40 seconds, and one attempt every three seconds. Youth suicide, the third leading cause of death among teenagers and young adults. Each suicide has a serious impact on at least six other people and the psychological, social and financial impact of suicide on the family and community is immeasurable. The World Health Organization [2] recognizes suicide as a complex problem for which there is no single cause, no single reason. It results from a complex interaction of biological, genetic, psychological, social, cultural and environmental factors. Shneidman [3], who is considered the father of suicidology, has proposed the following definition of suicide: "Currently in the Western world, suicide is a conscious act of self-induced annihilation, best understood as a multidimensional malaise in a needful individual who defines an issue for which the suicide is perceived as the best solution". We shall continue with another citation by Edwin Shneidman [4] who suggested "that suicide is best understood not so much as a movement toward death as it is a movement away from something and that something is always the same: intolerable emotion, unendurable pain, or unacceptable anguish. Reduce the level of suffering and the individual will choose to live". Profound psychic pain is a major part of the clinical picture, so much so that self-harming thoughts and behaviors, including self-mutilation,

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suicidal ideation, gestures and attempts, may become a way of attempting to cope with this pain and the marked social isolation. The best way to prevent suicide is to learn what is causing the distress, the tension and anguish - and the work to treat these emotions within the suicidal person. Several governments around the world have established suicide prevention programs. A major reason for this has been the very large increase in suicide in young people, especially males, seen in many countries.

Suicide is the main cause of premature death in psychiatric patients and its estimated risk in some accurate studies is generally higher than previously reported, notably in schizophrenia and personality disorder, and in former inpatients [5, 6]. Harris and Barraclough [7] investigated suicide as an outcome in mental disorders and found in their meta-analytic investigation that self-inflicted death is a more frequent phenomenon in most psychiatric disorders compared with the general population (Table 1). Also, retrospective studies indicate that the absolute majority (81-100%) of suicides occur in subjects with a psychiatric illness, depression being the most common diagnosis [8]. Hiroeh *et al*. [9] reported findings that indicated high rates of death from homicide, suicide, and accidents in people who were hospitalized in psychiatric units, stressing the high risk of death by homicide among people with severe mental disorders, such as schizophrenia and affective psychosis. Casarola *et al*. [10] have investigated suicide among Italian patients treated in public psychiatric services. These authors found that psychotic patients were the second most numerous diagnostic category among suicide victims (after depressive patients) and noted a lack of preventive measures in 25% of these cases. They also stressed the need of a proper identification of risk factors for suicide and the implementation of shared guidelines and programs for a joint effort in suicide prevention.

Table 1. - Suicide in various mental disorders combining studies as reported in the meta-analysis by Harris and Barraclough [7]

Psychiatric disorder	Suicide risk (number of times the expected in general population)
Schizophrenia	8.5
Bipolar disorder	15
Major depression	20
Personality disorder	7
Epilepsy	5
Eating disorders	23

In 1977 Miles [11] reviewed 34 studies of suicide among schizophrenics and estimated that 10% of schizophrenic patients kill themselves. Follow-up studies have estimated that 10-13% of individuals with schizophrenia die by suicide, which is the main cause of death among these patients [12]. Suicide attempts, which often result in completed suicide, are a burning issue among patients with schizophrenia; 20-40% of these patients do make suicide attempts [13-15]. The lifetime incidence of suicide in the general population is about 1% [16]. It has been estimated that the life expectancy among schizophrenic persons, as a group, is shortened by 9 to 10 years, and that the excess in mortality is chiefly accounted for by suicide and accident deaths [17, 18].

Many factors associated with suicide in schizophrenia have been identified, but attempts to identify high-risk patients have so far produced too many false positive results to be clinically useful [12]. And yet, identification of risk factors is a major contribution for prediction and prevention. Despite great efforts, both on the side of drug treatment and psychosocial strategies, the number of suicides among schizophrenic patients has remained unchanged [19]. Although Nordentoft *et al*. [20] have shown that in Denmark suicide among patients with schizophrenia has fallen, paralleling the reduction of suicide in the general population.

This paper aims at presenting a broad overview of the phenomenon of suicide among schizophrenic patients, focusing on those preventive strategies, the implementation of which may lead to reduction of suicide victims among this class of psychiatric patients.

Background analysis

We conducted careful MedLine, Excerpta Medica and PsycLit searches to identify papers and book chapters in English during the period 1966-2003. We also performed Index Medicus and Excerpta Medica searches prior to 1966. Search terms were "suicid*", (which comprises suicide, suicidal, suicidality, and other suicide-related terms), "parasuicid*", "schizophreni*", "inpatient" or "in-patient", "Follow-up". Each term was also cross-referenced with the others using the MeSH method (Medical Subjects Headings). Also, using the same databases and methods, we also crossed-referenced the above mentioned terms with key words such as "neurocognition" or "neurocognitive", neuroleptics or antipsychotics (all molecules belonging to the neuroleptics or to the antipsychotics categories were checked).

We also consulted a number of international experts in the field to determine whether studies selected were relevant for discussing suicide among

schizophrenic patients and preventive measures for suicide in schizophrenia. The authors and experts consulted performed a careful analysis of the literature data and agreed on a number of key subjects relevant to the aim of this paper.

We considered all studies published in peer-reviewed journals dealing with psychiatric patients who either committed or attempted suicide, focusing only on data related to patients with a diagnosis of schizophrenia. Studies that included data of schizophrenic patients pooled with those of other psychiatric patients without allowing for their identification, were excluded from our review. Included were all relevant studies with data on suicide among patients or with reviews of suicide and schizophrenia. We excluded from our analysis any studies vaguely reporting suicide in schizophrenia or using inadequate or unclear diagnostic criteria for schizophrenia or those inappropriately assessing suicide.

The entire literature on suicide in schizophrenia was thus carefully reviewed. By reviewing selected articles we identified some specific fields of interest which are listed below.

Findings

Risk factors

There is evidence that those affected by schizophrenia who are more likely to commit suicide are young, male, white, unmarried, have good pre-morbid function, have post-psychotic depression, have a history of substance abuse and suicide attempts. Hopelessness, social isolation, awareness of illness and hospitalization are also very important risk factors in schizophrenics who commit suicide. Deteriorating health with high level of premorbid functioning, recent loss or rejection, limited external support and family stress or instability are other risk factors traceable in patients with schizophrenia who commit suicide. These patients usually fear further mental deterioration and experience excessive treatment dependence or loss of faith in treatment (Fig. 1, Table 2). Suicides as a result of command hallucinations are rare and lack of statistical evidence, but reported as having a role in certain cases of suicidal behavior [22, 23]. Delusions have also been considered as a risk factor for suicidal behavior. However, a study focusing on this issue did not find evidence that the presence of delusions distinguished persons with or without a history of suicide attempt [24]. Schwartz and Cohen [25] studied 267 patients with schizophrenia and identified certain symptoms of illness, psychosocial impairment, and demographic characteristics significantly correlated with current suicidal intent. They found that depression had a strong correlation with suicidality whereas they found an incerse correlation between positive symptoms and suicide intent. These authors suggested that severe psychosis may distract the patient and impair executive functioning to such a degree that plans and means of engaging in self-harm behaviors are not feasible. Other factors associated with suicide intent in this study were traumatic stress, young age and

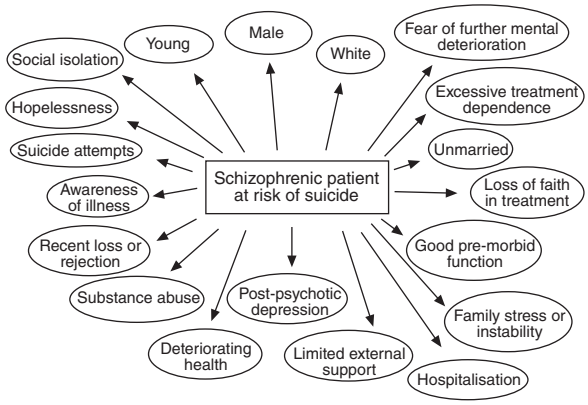

Fig. 1. - Risk factors for suicide in schizophrenia.

Table 2. - Risk factors for suicide in depressive illness [8] and substance abuse [21]; in bold risk factors common to schizophrenia

Disorder	Risk factors
Depressive disorder	**Hopelessness**, feeling of guilt, **loss of interest** and loss of self-esteem, **post-discharge period**, previous episodes of depression not treated by a psychiatrist, insomnia, impaired memory, self-neglect, **male sex**, older age in female, **single status, living alone, history of suicide attempts, undertreatment, comorbid substance abuse** and/or personality disorders (especially borderline)
Substance abuse	**Experience of a loss** within six week or less of their death [marital separation, divorce, widowhood, bereavement of a close family member], current heavy drinking, **talk or threat of suicide, major depression, little social support**, serious medical problem, **unemployment, living alone**

female gender. It is noteworthy that younger female schizophrenic patients may be at greater risk of suicidal intent, although males show an increased risk of completing suicide. This leads to the hypothesis that underdeveloped coping strategies in younger patients or increased sensitivity and emotionality among patients who are female may pave the way for suicide.

Among the numerous risk factors for suicide in schizophrenia, awareness of illness has been reported as a major problem in treating suicidality, an almost necessary prerequisite for actually committing suicide. Although general awareness seems not to predict suicide, there seems to exist an awareness spectrum, whose elements may or may not lead to suicide [26]. According to Drake *et al*. [27], a patient may be aware of current disability and remain confident of improvement in the future. Nevertheless, when patients fear further mental deterioration, suicide becomes more likely [28]. Schwartz and Petersen [29] and Schwartz [30] underlined the role of hopelessness in patients with awareness of illness. They observed that if treatment does not diminish emotional symptoms and does not improve psychosocial skills, hopelessness may result. This is the pathway which eventually leads to depression and suicide. Drake and Cotton [31] described a demoralization syndrome in which schizophrenic patients become aware of their illness and its consequences. Patients then may compare their fair premorbid adjustment with the current one and become hopeless and depressed and eventually become suicidal. At the moment we still do not know if improved awareness of illness, which can predict a more favorable outcome, may also expose patients to suicidal tendencies.

Fenton *et al*. [32] suggested that negative symptoms, when present as a prominent component of illness, are associated with a significantly lower long-term risk of suicide among patients with schizophrenia. They found that nondeficit schizophrenia, where enduring negative symptoms are lacking, defines a group of patients whose risk for suicide is six times greater than that of deficit schizophrenic patients. Conversely, two positive symptoms (suspiciousness and delusions) appear to be associated with elevated long-term risk for suicide. The paranoid subtype of schizophrenia, where positive symptoms prevail and negative symptoms are few, is associated with a suicide risk that is three-fold than the one associated with nonparanoid subtypes and eight times greater than the risk associated with the deficit subtype. Paranoid delusions and command hallucinations may nonspecifically increase violent behavior and account for increased risk. In the Achté *et al*. study [33], paranoid traits were found to occur in 58% of the cases.

Suicide among inpatients with schizophrenia

Prevention of suicide of inpatients with schizophrenia is a daily-based challenge, which has to be performed with various modalities. Suicide rate in psychiatric hospitals is higher than in the general population [34-38]. Risk factors for suicide in inpatients with schizophrenia [39] are:

- deliberate self-harm;
- pre-admission and intra-admission suicidal attempts;
- fluctuating suicidal ideation;
- prescription of a greater number of neuroleptic and antidepressants;
- increased length of stay and increased number of ward changes;
- period of approved leave;
- apparent improvement;
- past and present history of depression;
- frequent relapses and rehospitalization;
- longer hospitalization periods than other psychiatric inpatients;
- negative attitudes towards medication;
- reduced compliance with therapy;
- undertreatment or non compliance with therapy and negative attitude towards medication;
- living alone before the past admission;
- discharge planning;
- charged feelings about their illness and hospital admission;
- early signs of a disturbed psychosocial adjustment;
- dependence and incapability of working;
- age under 30 years;
- high number of hospital admissions;
- period following discharge;
- difficult relationship with staff and difficult acclimation in ward environment;
- good premorbid functioning;
- hospitalization close to crucial sites (big roads, railway stations, rivers, etc.).

Small *et al*. [40] reported that nine patients leaped from a height between 1974 and 1980 while inpatients at the Erich Lindemann Mental Health Center Adult Inpatient Unit. They were young, diagnosed with schizophrenia, unmarried, socially isolated, and chronically psychotic, despite neuroleptic therapy. All had prolonged psychiatric hospitalizations or multiple admissions and discharges. A history of addictive, assaultive, or suicidal behavior was common.

Barner-Rasmussen [41] found that schizophrenic patient suicides had multiple and lengthy hospitalizations and that their suicide frequency seemed remarkably constant as compared with other psychiatric patients. Schizophrenic suicides (n=337) had an average length of hospitalization between 400 and 550 days.

Modestin [42] reported that schizophrenic inpatient suicides were of a young age, mostly single and childless. They frequently presented signs of a disturbed social adjustment before age 25 in terms of delinquency, vocational difficulties, and difficulties in initiating and maintaining reliable, lasting relationships.

Zmitek and Acoviæ [43] found longer hospitalization periods in patients with schizophrenia who committed suicide after hospital discharge.

Modestin [42], Pokorny [44], Temoche *et al*. [45], Roy [46] and Allebeck *et al*. [47] found a strong relation between suicide risk, age, and duration of follow-up. Patients younger than 30 years continued to be 50 times more at risk of suicide even after five years of follow-up, differently from other age groups, where suicide risk, although constantly higher than in the general population, dropped markedly after the first year of follow-up [48].

Drake *et al*. [27] and Allebeck *et al*. [49] have estimated that the highest suicide risk in schizophrenia occurs during the first 10 years of illness. Steblaj *et al*. [50], Tsuang and Woolson [51] and Heilä *et al*. [52] stated that suicide may occur at any point during the course of illness, especially where the course is severe with frequent relapses and rehospitalizations [53]. Roy [46] found that suicide often occurs early on during hospitalization or soon after discharge from the hospital.

Crammer [54] highlighted the importance of taking environmental factors into account when thinking proactively about suicide among inpatients. He pointed to the potentially disruptive effects of transitions - for example, initial acclimation to ward life or plans for discharge or rehabilitation. He also emphasized the environmental impact of staff variables, such as low morale or the absence of key personnel, as well as the need for effective communication among relevant staff about patients judged at increase risk of suicide. Yarden [55] drew attention to the importance of suitable discharge plans and aftercare programs. Supportive, supervised living arrangements are ideal. With chronic, incapacitated patients, surveillance should be increased in times of personal crisis and impeding environmental change, including staff, therapist, or contact person changes, hospitalization, discharge, or rehospitalization [56].

Patients who attempt suicide or are at risk for suicide are the ones that most benefit from empathic relationships with nurses and doctors [57].

Taboos in staff impair professional judgment and communications about patients identified as suicidal. Because of these blocks, professional staff are often hampered in applying what they already know, and they may even avoid eliciting or reporting information about the suicidal behavior of their patients, whether is attempted or committed. Pompili *et al*. [58, 59] recently reviewed the international literature that dealt with the nursing of schizophrenic patients who are at risk of suicide These authors outlined key elements in the nursing of these individuals, such as the unpredictability of suicide due to fluctuating suicide ideation, staff's "countertransference" reactions to these patients and the apparent improvement that precedes suicides. Nursing a schizophrenic patient who is at risk of suicide involves the establishment of very uncommon relationship. An interesting topic is the concept of "terminal malignant alienation" [60, 61]. Some patients, particularly those with recurrent relapses and resistance to treatment, may be perceived by staff as manipulative, provocative, unreasonable, over-dependent and feigning disability [60, 61]. Patients with fluctuating suicidal ideation are particularly likely to fall into these categories and may lead to under-reporting of suicidal ideation by nursing staff. This may result in criticism and a lower level of support leading to alienation. The combination of such alienation and fluctuating suicidal ideation can lead to failure in the recognition of seriousness of suicidal risk [60-62].

Suicide attempts

Compared with suicide attempts among persons without schizophrenia, attempts among those with schizophrenia are serious and typically require medical attention [63]. Intent is generally strong, and the majority of those who attempt suicide have made multiple attempts. In addition, the methods used to attempt suicide are considered more lethal than those used by suicidal persons in the general population. Suicide attempt is one of the most important risk factors for prediction of a completed suicide.

Gupta *et al*. [64] reported that in their sample of patients with schizophrenia, suicide attempts were associated with the number of lifetime depressive episodes. Depression has been recognized as a major risk factor among persons with schizophrenia who have attempted suicide. Also, Roy *et al*. [65] found that significantly more of their sample of patients with schizophrenia who had attempted suicide had suffered from a major depressive episode at some time during their illness.

Great caution is required in the period after hospital discharge, because patients with schizophrenia usually experience hopelessness and demoralization. For these patients, discharge often means losing the hospital environment and the people who in some way have become central in their life. The number of psychiatric admissions, which are usually higher among patients who have attempted suicide, may be indicative of a severe relapsing illness [65].

Nevertheless, Drake *et al.* [66] found in their sample of patients with schizophrenia that those who had attempted suicide were trying to manipulate others, consolidate support, or gain entrance to the hospital. Attempts frequently occurred in the context of interpersonal conflict, such as arguments with family or housemates, rather than isolation. These authors suggested that impulsive attempts were associated with dysphoric side effects of medication, such as akathisia.

More recently, an investigation devoted to suicidal behavior in schizophrenia found that those schizophrenic patients who had attempted suicide had suffered from major depressive episodes, had comorbid diagnosis of substance abuse or dependence, were more likely to have a duration of untreated psychosis >1 year and were more frequently prescribed typical antipsychoatics [67].

Role of pharmacotherapy

The impact of atypical antypsychotics on suicidality in patients with schizophrenia has been reviewed [68]. Clozapine, olanzapine, risperidone and quetiapine have shown some power in reducing suicidality among schizophrenic patients [68, 69] Clozapine was shown to reduce suicide in schizophrenia [70, 71]. According to these authors, the potential decrease in suicide mortality with clozapine treatment is estimated to be as high as 85%. In terms of benefit versus risk, while 1.5 of every 10 000 patients with schizophrenia who were treated with clozapine would be expected to die from agranulocytosis (evidence suggests an even lower percentage), 1000 to 1300 would be expected to complete suicide with standard treatment [72]. In fact, the U.S. Food and Drug Administration recently approved clozapine for the treatment of suicidal behavior in patients with schizophrenia or schizoaffective disorder [19]. Yet, according to Sernyak *et al.* [73], clozapine treatment was not associated with significantly fewer deaths due to suicide. These authors used for the first time a matched control group to examine the effect of clozapine on the rate of suicide in patients with schizophrenia. In their sample, they did not observe a significant reduction of suicides due to clozapine. However, one third of the sample received clozapine for less than six months, even though the follow-up period was five to six years.

There is anecdotal evidence that increased insight associated with clozapine treatment may lead to suicide [74]. Various studies [75-77] reported that insight/symptom awareness is positively related to cognitive functioning, but on the other hand, it appears that schizophrenic patients at high-risk for suicide and nonsuicidal patients have similar cognitive functioning; this would suggest that suicidality may be a separate domain with a distinct pathophysiology [78]. Clozapine enhances neurocognition and clinical recovery more than standard neuroleptics [79] and appears to have effects on some aspects of attention, memory, response speed and fluency. This pattern of improvement may be likewise present in patients with insight into illness. Aguglia *et al*. [80] found that switching from conventional neuroleptics to atypical antipsychotics, such as clozapine, olanzapine and risperidone, improved patients' insight.

Summarizing, drug treatment of schizophrenia is generally associated with lower suicidality. However, since the administration of newer, atypical antipsychotics may be accompanied by increased insight and illness awareness, and since sudden increases in insight by more than 25% may lead to increased suicidality in schizophrenic patients [81], caution is needed and the patient should be followed-up closely to contain such abrupt insight increases within an appropriate therapeutic relationship.

Psychosocial interventions and the role of stigma

The literature abounds with descriptions of various psychosocial interventions for schizophrenic patients whose treatment often requires integration of pharmacological and rehabilitative strategies (Fig. 2). Nevertheless, the impact of these strategies on suicide has only rarely been investigated (Fig. 3). Drake *et al*. [83] pointed to the need for empathic support for reducing suicide risk. These authors suggested that clinicians should acknowledge the patient's despair, discuss losses and daily difficulties and help to establish new and accessible goals. Social isolation and work impairment are frequently reported as risk factors for suicide in individuals with schizophrenia. A broad overview of the role of these strategies has recently been investigated [84].

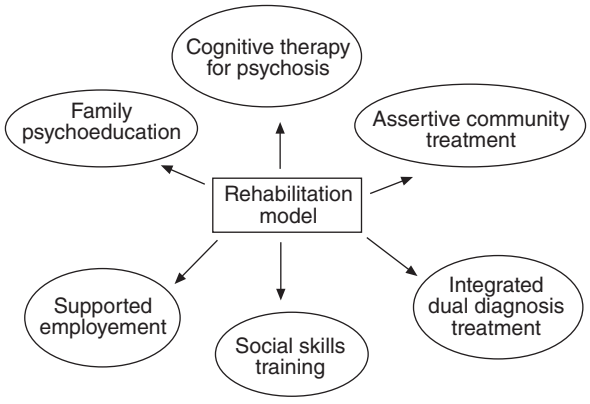

Fig. 2. - Psychosocial strategies for schizophrenia which received the most empirical support [82].

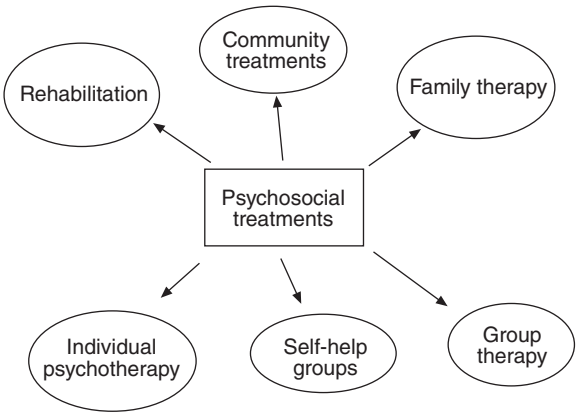

Fig. 3. - Psychosocial treatments for patients with schizophrenia that might reduce suicidality (Modified from [84]).

Many illness, not only mental, suffer from stigma. Stigma can be viewed as a powerful factor influencing the course of psychiatric disorders. The family moment has had an extraordinary effect in reducing stigma. Openness has contributed to the reduction. Treating mental illness in the family as a secret makes the illness appear shameful and deserving of stigma. Stigma is a product of fear, ignorance and prejudice [85]. Nevertheless, Phelan [86] highlighted a comparison of two studies published twenty years apart which showed that family members of psychiatric patients were twice as likely to report concealing in 1981 as in 1961 [87, 88], and a currently ongoing study of families of persons treated for psychosis indicates that half the family members concealed the hospitalization from others to at least some degree [89].

We recently supported the speculation that stigma may be a cause of suicide [90 18]. Stigmatization towards these patients is often unrecognized, as schizophrenic individuals are only rarely clearly rejected. In most instances, people behave ambiguously and not overtly. Saarinen and colleagues [91] have recognized various elements that impair the staff's ability to identify markers of suicide in patients with schizophrenia. They indicated difficulties in dealing with suicide and personal problems as major elements of the disturbance; this might be linked to stigma.

Unfortunately, family members are also stigmatized for dealing with schizophrenia. This psychiatric disorder often results in impairment of daily activities, relapses and chronicity. Family members are seen with suspicion for dealing with their sick relative and may be subjected to lack of socialization and reduced job opportunities. Pompili *et al* [92] recently proposed a pattern of behavior in patient's relatives that might somehow communicate to the schizophrenic patient that suicide is the best solution for the overall system. This speculation should not be viewed as further blaming the family; instead it should be the milestone for the implementation of family psycho-education and for preventing the burn-out phenomenon. Family members may consider the sick member as a threat to their freedom and desire for normality, and inevitably patients are excluded from normal social activities. Patients may feel alone even inside the family environment as members may be affected by discriminatory behavior. Stigma is the main cause of hostility developed by the family toward the sick member. Sometimes these negative feelings may be part of a much worse scenario, especially when family members experience hopelessness and helplessness in dealing with the member with schizophrenia. Members may unconsciously wish the suicide or accept the suicidal ideation of the sick member as a valid method to get rid of an unsustainable situation. Members may build up a network of subtle and unconscious messages that lead the patient to infer that suicide may be the best solution to the disease. This may be the result of an everincreasing pressure on the family to look after a chronic patient that interferes with the everyday life of each member. Unconscious communication has been described as a powerful tool in everyday life, which characterizes virtually all kind of interpersonal interaction, and it may contain a number of messages that convey a certain line of thought [93].

This behaviour is even recognizable among psychiatrists and mental health professionals. Also, very often schizophrenic patients meet general practitioners for drug prescription or for request of psychiatric consultation. General practitioners often do not take into consideration their role in the prevention of suicidality in schizophrenia [94, 95]. In fact, not only do people who are considering suicide often contact their doctors for general consultation prior to the suicidal action, but those who are at risk should be promptly recognized.

Biological predictors

Low concentrations of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) in cerebrospinal fluid (CSF) are associated with suicidal behaviour in patients with depressive illness and schizophrenia. In a prospective study, Cooper *et al*. [96] measured 5-HIAA in CSF taken from 30 schizophrenic patients in a drug-free state, and followed these patients for 11 years. 10 patients made suicide attempts during follow-up. Suicide attempters had significantly lower concentrations of CSF 5-HIAA at initial evaluation than non-attempters. These findings provided further

evidence of the relation between serotoninergic dysfunction and suicide, and suggested a role for drugs with serotoninergic effects in schizophrenia. Although, low CSF 5-HIAA relates to suicidal behavior irrespective of diagnostic category. Hormones known to be under serotoninergic control like prolactin (PRL) are measured in peripheral blood after stimulation or inhibition of the serotonirgic (5-HT) receptors. Fenfluramine (FEN) is a widely used serotonin probe. In humans, D-fenfluramine (D-FEN) given orally promotes a clear cut increase in plasma PRL level, which is considered to be a higly specific test of serotonergic function [97]. It has been demonstrated that a blunted PRL secretion in response to D-FEN is associated with suicidal behavior in schizophrenic patients [98]. This is an important tool as this technique give a specific indication of serotonergic function and it can be further combined with new neuroimaging paradigms such as PET and SPECT, providing images of seronergic function *in vivo* [98-101].

Plocka *et al*. [102] investigated dexamethasone suppression test and suicide attempts in schizophrenic patients. Their results may suggest a possible association between hyperactive HPA axis and suicidal behavior in schizophrenic patients.

Reports of an association between both dexamethasone suppression test (DST) and REM sleep abnormalities and suicidal behavior in schizophrenia have been reported [103, 104]. Keshavan *et al*. [103] found that those schizophrenic patients that exhibited suicidal behavior had increased overall REM activity and REM time. Jones *et al*. [104] found that non-suppression of DST could be related to suicidal behavior in a sample of schizophrenic patients; in fact, non-suppression of the DST differentiated suicide attempters from non-attempters. Lewis *et al*. [105] contradicted these latter findings and reported that in their sample of schizophrenic patients total REM sleep time was associated with suicidal behavior. These authors suggested that since serotonergic neurons act to suppress REM sleep, reduced serotonergic function in schizophrenia could explain the association between suicidal behavior and REM time/activity observed by these authors reduced central nervous system serotonergic function, as measured by 5-HIAA level in CFS, is associated. Hinse-Selch *et al*. [106] investigated the effects of clozapine on sleep in a sample of schizophrenic patients and found a significant clozapine-induced increased of NREM sleep in patients who do not experience clozapine-induced fever; while the amounts of stage 4 and slow-wave sleep decreased significantly. These findings might add further explanations on the anti-suicidal role of clozapine as increasing REM sleep has been correlated with increased suicide risk.

Discussion

Despite a considerable number of studies and the many indications how to reduce suicide in schizophrenia, this event remains a major health problem. In Italy, suicidal behavior among schizophrenic is underestimated and official data are still lacking. Suicide is the major cause of death among patients with schizophrenia; and despite efforts both on the side of drug treatment and psychosocial interventions the number of those who die by a self-killing action has not dropped. Atypical antipsychotics, especially clozapine, have shown some power in the reduction of suicides among schizophrenic patients. Pompili *et al*. [83] have recently reviewed the international literature and identified evidence-based treatments for the suicidal schizophrenic patient, although e definite validation for some of them is still lacking. The feeling of these authors is that only a joint struggle between various mental health workers may help the reduction of the phenomenon. They also emphasized the need to work upon the establishment of shared guidelines for the prevention of suicide among these patients.

A new prevention of suicide in schizophrenia should include proper information. Information should be addressed to family and hopefully hostility toward the patient should be investigated. But information should constitute a key element for promoting changes in people's attitude toward these patients. Mass media's portray of violent schizophrenic patients should be counterbalance by delivering reality-based messages of their struggle for socialization and acceptance. Proper information should also be directed to medical staff working in psychiatric wards as they play a central role in preventing "terminal malignant alienation". Proper information should be the guide for a joint prevention between psychiatrists and GPs. Rejection from these figures may be the ultimate insult to the patients' very weak self-esteem; and although general practitioners may have an ancillary role in the treatment of schizophrenic patients, they may be in a strategic position to detect early risk factors or to contribute to the changing of state-dependent risk factors. Recently, Ponizovsky *et al*. [107] in a study of suicidality in schizophrenia, found that dissatisfaction with social relationships was only the quality of life common feature for single attempters and multiple attempters; this finding shows that the quality of life measure that these authors used can tap the quality of social relationships as a crucial element in suicidal behavior. On the other hand, suicidal thoughts are frequent among inpatients with acute schizophrenia [108]. Suicide risk continues throughout the lifespan of the individual with schizophrenia. Mental health professionals should join forces for a better definition

of guidelines specifically designed to prevent suicide among patients with schizophrenia. A body of knowledge on suicide should be part of the education of every individual involved in taking care of a schizophrenic patient.

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