Suicide and depression

Diego De Leo and Lay San Too

Introduction

Suicide is a complex and multicausal phenomenon. It has a strong association with mental disorders, particularly major depressive disorder. Suicidal behaviors (both fatal and non-fatal) in patients with mood disorders are determined by their severity. Suicidal acts likely occur during depressive episodes, less often during mixed states, and very rarely in hypomania. However, the prevalence of suicidal behaviors in depressive disorders might be over-represented as a result of the misdiagnosis of normal sadness as a psychiatric disorder. There is a large amount of evidence showing that antidepressants are effective in preventing suicidal behaviors in mood disorders, but their effect remains controversial in young patients. The reduction in suicide is more prominent when combining pharmacotherapy and psychotherapy, rather than either therapy alone. This chapter reports on the epidemiology of suicidal behaviors in each type of mood disorder, discusses the boundaries between sadness and depressive disorders in relation to suicide, and highlights possible prevention strategies for suicide in patients with mood disorders.

Mood disorders

Mood disorders are a leading public health problem worldwide. They are not only enormously detrimental to society and the economy and have negative consequences on personal and interpersonal circumstances (Richards 2011), but are also related to the fatal outcome of suicide. A meta-analysis of psychological autopsy studies published between 1990 and 2007 indicated that mood disorders are strongly predictive of suicide risk, particularly in women (OR = 12.95, 95% CI 3.06–54.83) but also in men (OR = 6.56, 95% CI 2.65–16.28) (Yoshimasu et al. 2008). Other reviews demonstrated that mood disorders are the most life-threatening of psychiatric illnesses: approximately 90% of suicide cases are diagnosed with a psychiatric disorder, and almost half of these with a diagnosis of mood disorder (Bertolote et al. 2004; Arsenault-Lapierre et al. 2004). Nevertheless, there are still many individuals with a mood disorder who have never completed or attempted suicide. In 1970, Guze and Robins performed a review of studies on the suicide mortality of inpatients diagnosed with mood disorders, which indicated that, in general, an average of 15% of depressed patients complete suicide. However, Bostwick and Pankratz (2000) reassessed the lifetime prevalence of suicide in patients with mood disorders. They showed that the lifetime risk of suicide was 8.6% for hospitalized patients with suicidality, 4.0% for hospitalized patients without suicidality, 2.2% for mixed inpatients/outpatients, and 0.5% for non-depressed people. In terms of non-fatal outcomes, a cross-national analysis of mental disorders and suicidal behavior carried out in 21 countries with a total sample of 108 664 reported that major depressive disorder (MDD), dysthymic disorder (DD), and bipolar disorder (BD) each significantly contributed to the potential onset of a suicide attempt. The odd ratios ranged from 5.1 (DD), 5.8 (MDD) to 7.1 (BD) in developed countries and from 5.1 (MDD), 6.7 (BD) to 7.1 (DD) in developing countries (Nock et al. 2009).

Unipolar disorders

Unipolar disorders primarily include major depressive disorder and dysthymic disorder. Based on the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (Text Revision) (DSM-IV-TR) (American Psychiatric Association 2000), major depressive...
disorder is a diagnosis determined by the presence of a specified number of symptoms for a duration of at least two weeks. The individual must have experienced symptoms primarily of either depressed mood or loss of interest or pleasure, and at least three of the following symptoms: disturbance of appetite or sleep, psychomotor agitation or retardation, inability to think, feelings of worthlessness and guilt, and suicidal thoughts and ideation. Dyshymic disorder is characterized by symptoms that are less severe than those for major depressive disorder, but persist for at least two years. It includes symptoms of depressed mood and two or more of the following: problems with appetite or sleep, low energy, low self-esteem, poor concentration, and feelings of hopelessness. An individual is not diagnosed if he/she is symptom-free for at least two months. A systematic review of the literature published between 1980 and 2000 revealed a lifetime prevalence of 6.7 per 100 for major depressive disorder and 3.6 per 100 for dysthyemic disorder in the general population (Waraich et al. 2004).

As indicated by Rihmer’s review (2007), the most predictive clinical risk factors for suicide in depressive disorders are major depressive episodes, while minor depression and pure dysthyemic disorder are relatively rare among subjects who die by suicide and among attempters. A five-year prospective study examining suicidal behavior in Finnish patients with major depressive disorder showed that the prevalence of suicide attempt varied markedly depending on the state of depression, being highest during major depressive episodes (OR = 7.74, 95% CI 3.40–17.6) and four times higher during partial remission (OR = 4.20, 95% CI 1.71–10.3) than in full remission (Holma et al. 2010). Another prospective study on suicide incidence between 1947 and 2006 was conducted in the south of Sweden, revealing that depression played a major role in contributing to suicide (44%). In particular, severe depression with psychotic and/or melancholic features was diagnosed in 66% (19/29) of all cases of depression. Twenty-nine per cent (19/66) of all suicide victims had major depression with severe features, while 15% (10/66) had depression without these features (Bradvik et al. 2010).

The importance of the severity of the illness in the risk of suicide in depression was further emphasized by a study on a sample of American outpatients (Witte et al. 2009). This was the first study to distinguish between the predictive powers of the different forms of depressive illness (dysthyemic disorder, single episode of major depression, recurrent major depressive disorder, and double depression). A cluster analysis showed that only recurrent major depressive disorder exclusively contributed to an increased risk of suicide (B = 1.27, SE B = 0.27, p < 0.0001). Individuals with recurrent major depressive disorder were about three times more likely to be in the higher risk rather than lower risk cluster, even after controlling for the number of comorbid Axis I and Axis II diagnoses. By contrast, none of the other depressive diagnoses was identified as a significant risk factor for suicide (Witte et al. 2009).

Bipolar disorders

Bipolar disorder is characterized by alternating episodes of mania and depression over the course of life. A diagnosis of bipolar I disorder requires at least one manic or mixed episode, while a diagnosis of bipolar II disorder requires neither of these but at least one each of hypomanic and depressive episodes (DSM-IV-TR). A cross-sectional World Mental Health Survey was conducted in 11 countries with a sample of 61,392 adults to measure the prevalence of bipolar disorders using DSM-IV classifications (Merikangas et al. 2011). The findings demonstrated that the lifetime prevalence of bipolar I disorder, bipolar II disorder, and subthreshold bipolar disorder were 0.6%, 0.4%, and 1.4% respectively, while the 12-month prevalence was 0.4%, 0.3%, and 0.8% respectively. In total, the lifetime and 12-month prevalence of bipolar disorders was 2.4% and 1.5%, respectively (Merikangas et al. 2011).

Initial reports estimated that between 4% and 19% of patients with bipolar disorder would complete suicide, and between 25% and 60% would attempt suicide, at least once in their lifetimes (Goodwin & Jamison 1990). However, a more recent review concluded that incidence of both non-fatal and fatal suicidal behaviors in bipolar disorders (especially bipolar II disorders) is overestimated (Rihmer 2005). This was further highlighted in a 35-year (1965–99) longitudinal study on the suicide mortality of British patients with bipolar disorder (Dutta et al. 2007). The analyses showed that, compared to the general population, the standardized mortality ratio (SMR) for suicide was 9.77 (95% CI 4.22–19.24), higher than all other causes of death (SMR = 1.03, 95% CI 0.71–1.44). In particular, the suicide ratio for males was 12 times higher (SMR = 12.76, 95%
CI 5.13–26.29) and for females was four times higher (SMR = 4.27, 95% CI 0.11–23.78) than in the general population. Overall, only 2.5% of those with bipolar disorder eventually completed suicide, an incidence lower than commonly cited (Dutta et al. 2007). In 2010, Novick and colleagues performed a comprehensive meta-analytic review on suicide attempts in both bipolar I and bipolar II disorders. For bipolar II individuals, retrospective, prospective, and descriptive studies reported a lifetime history of suicide attempt in 32.4%, 19.8%, and 20.5%, of individuals, respectively. The difference in the prevalence of attempted suicide in bipolar II (32.4%) and bipolar I (36.3%) cases was not significant (OR = 1.21, 95% CI 0.98–1.48, p = 0.07).

Moreover, a prospective 18-month study examined the incidence of suicide attempts in different phases of bipolar disorder in Finnish inpatients and outpatients (Valtonen et al. 2008). In comparing the phases of the illness, the findings indicated that the incidence of suicide attempt was 37 times higher (95% CI 11.8–120.3) during combined mixed and depressive mixed states, and 18 times higher (95% CI 6.5–50.8) during major depressive phases. Both phases were independent predictors of suicide attempt. It was suggested that the overall risk for suicide attempt among bipolar disorder patients is likely to be determined by the amount of time in high-risk illness phases (Valtonen et al. 2008).

**Sadness and suicidal behaviors**

While suicidal behaviors are convincingly predicted by clinical depression, as indicated above, their association with “normal” sadness has been neglected and never properly examined. This is likely the result of the confusion between normal sadness and depressive disorders among contemporary psychiatrists and researchers. In 2007, Horwitz and Wakefield discussed this issue extensively and stressed that the increasing occurrence of major depressive disorder is not the consequence of a genuine rise in the prevalence of mental illnesses, but the result of a process of the medicalization of sadness in recent decades. This means that individuals with fluctuations in mood due to sadness as a physiological reaction to a life event would easily fulfill the symptomatic requirements for major depressive disorder in the DSM, and would then be misdiagnosed as mental disorder sufferers. Other consequences of this phenomenon include a dramatic increase in the number of patients receiving treatment for depression, an increase in the prescription and sale of antidepressants, and an inflated estimate of the social and economic costs of depression (Horwitz & Wakefield 2007).

Horwitz and Wakefield (2007) hypothesize that normality and abnormality exist along a continuum: it is difficult to distinguish between them without knowing the internal mechanisms of response to loss. Nonetheless, normal sadness is mainly different from depression by the existence of a cause or context, such as negative life events. That is, normal sadness is context-specific, and reasonably proportional to the nature of the loss, and it either ends when the circumstances become better or when the individual adjusts to the new circumstances, or endures if the circumstances persist. On the other hand, clinical depression tends to be unnatural, dysfunctional, recurrent, chronic, and disproportionate to the loss, rather than context-specific and time-restricted.

The DSM excludes the bereavement of a loved one from the diagnosis of a major depressive disorder. However, apart from this type of loss, individuals encountering other life stressors (e.g., the ending of a romantic relationship, losing a valued job, or being diagnosed with a severe physical illness) similarly tend to experience symptoms such as depressed mood, sleep problems, a lack of interest in usual activities, an inability to concentrate, and reduced appetite that might naturally persist for a period of at least two weeks (American Psychiatric Association 2000). These symptoms easily meet the DSM criteria for a diagnosis of major depressive disorder, but they are neither abnormal nor inappropriate in light of the situation. Horwitz and Wakefield (2007, p. 14) highlighted that the fundamental flaw of the DSM concept of MDD is that it “fails to take into account the context of the symptoms and thus fails to exclude from the disorder category intense sadness, other than in reaction to the death of a loved one, that arises from the way human beings naturally respond to major losses.”

Recently, a study investigated whether individuals were able to distinguish between normal sadness and clinical depression (Holzinger et al. 2011). People in Vienna were presented a vignette depicting a case of depression fulfilling the DSM-IV criteria. The vignette was provided either with or without information about preceding life stressors. It was found that, as opposed to the conceptualization in the DSM,
people were less likely to perceive depressive symptoms caused from losses as an indication of a major depressive disorder, and less likely to recommend professional help in such circumstances. This seems to confirm that the DSM has mistakenly considered normal responses to loss as a mental disorder.

The partially flawed understanding of depression in the DSM and its use by contemporary clinicians deserves further attention, as it has important social, clinical, and scientific implications. Importantly, given that clinicians and scientists might fail to differentiate sadness from depression, the available literature on the prevalence of suicidal behaviors associated with depression may depict the relationship in a biased manner. While stressful life events may place an individual at risk of suicide (Logan et al. 2011), the normal response of sadness that can be "physiologically" tied to these stressors is likely associated with suicide. Therefore, it is possible that suicide rates attributed to depression are in fact inflated by the inclusion of non-pathological sadness in the diagnosis of depressive disorder. This highlights the significance of the need to distinguish between normal and abnormal human behavior in order to capture a more accurate picture and enable relevant organizations to develop effective suicide prevention initiatives. Similarly, particular attention should also be paid to the recent controversy over the pathologizing of "suicidal behavior," as there is insufficient scientific evidence available to support this, as discussed by De Leo (2011).

**Suicide prevention for patients with mood disorders**

It is challenging to prevent suicide in individuals diagnosed with mood disorders. As suicide is strongly associated with mood disorders, particularly major depressive episodes, the hypothesis that suicide could be prevented by the treatment of depression is certainly not implausible. In recent years, a growing amount of research has examined the risk of suicidal behaviors associated with antidepressants. As presented by Isacsson et al. (2010), ecological studies showed that the use of antidepressants was inversely associated with suicide rates in 40 countries (Australia, Sweden, Denmark, Finland, Great Britain, Hungary, Israel, Italy, Japan, New Zealand, Norway, Slovenia, the USA, and 27 other countries, with the exception of Iceland). Similarly, a 27-year observational study conducted at five US academic medical centers found that the risk of suicidal behaviors was reduced by 20% among depressed patients who were prescribed antidepressants (OR = 0.80, 95% CI 0.68–0.95, z = −2.54, p = 0.01) (Leon et al. 2011). Other long-term observational studies revealed the degree of risk reduction to be more than 50% (Baldessarini et al. 2006, Guzetta et al. 2007).

Nevertheless, a systematic review of 702 randomized controlled trials showed that, compared to other active treatments or a placebo, individuals prescribed with antidepressants were at double the risk of both fatal and non-fatal suicidal behaviors (Fergusson et al. 2005). This was particularly prominent in depressed adolescents. The opposite effect was found in depressed adults, especially those aged 65 or above (Barbui et al. 2009). The adverse effect of antidepressants in young people was further evidenced by a meta-analytic review indicating that the use of antidepressants such as paroxetine, sertraline, citalopram, and venlafaxine, but not fluoxetine, increased the risk of suicidal behaviors in children and adolescents with depression (Whittington et al. 2004). Further, selective serotonin reuptake inhibitors (SSRIs) were found not to significantly increase suicidality in individuals under 19 years of age (Isacsson et al. 2005). Similarly, a non-significant increase in the rate of suicide associated with SSRIs was found among Danish youths (Søndergaard et al. 2006). Recently, a comprehensive review analyzed 130 studies (including ecological, cohort, case–control, and randomized controlled) on antidepressants and suicide risk published during the period 1965–2010 (Pompili et al. 2010). It emphasized that antidepressants generally contributed to a decrease in the risk of suicide in adults with major affective disorders, but that the controversy surrounding the potential suicidal risk caused by antidepressants in younger patients remains. Pompili et al. (2010) further explained that the latter phenomenon might be due to the possible presence of many unrecognized "pseudo-unipolar mixed states" in younger patients that could contribute to suicidality.

Different types of antidepressants/mood stabilizers seem to have different effects on suicidal behaviors in depressed patients (Pompili et al. 2010). In 2011, Moncrieff and Goldsmith investigated the psychoactive and physical effects of two commonly used antidepressants: fluoxetine and venlafaxine. They indicated that these antidepressants were rarely associated with suicidal thoughts, but that they were
correlated with unpleasant emotional effects, which may account for increased suicidal impulses in some users. Another study comparing suicidal risk in adults taking venlafaxine, citalopram, fluoxetine, and dothiepin showed that patients taking venlafaxine were prone to a higher risk of suicide compared to those taking citalopram, fluoxetine, and dothiepin. However, adjustment for possible confounders substantially minimized the excess risks of venlafaxine (Rubino et al. 2007). Further, a review article on the effect of lithium treatment among patients with major affective disorders found an approximately 80% lower risk of suicidal behaviors during lithium treatment (for an average of 18 months), in both randomized and open clinical trials (Baldessarini et al. 2006). The favorable impact of lithium on suicide has also been observed in the general population, as found in an epidemiologic study that revealed a significant negative relationship between lithium levels in tap water in 18 Japanese municipalities and the suicide rate in each municipality for 2002–06 (Ohgami et al. 2009). A similar finding was found in a study across 99 Austrian districts, further demonstrating an inverse association between suicide and lithium levels in drinking water (Kapusta et al. 2011).

In 2001, O'Leary et al. reviewed 75 follow-up studies concerning the impacts of electroconvulsive therapy (ECT) and antidepressants on the rates of suicide in patients with mood disorders. It was found that the average suicide rate was 6.3 per 1000 for the pre-treatment era, 5.7 per 1000 for the ECT treatment era (1940–59), and 3.3 per 1000 for the antidepressant treatment era (from 1960 onward). This implies that the utilization of treatment – particularly antidepressants – helps in preventing suicide in depressed patients. Further, a review of controlled studies on the enhancement of treatment adherence among bipolar patients showed that interpersonal group therapy, cognitive behavioral therapy, group sessions for partners of bipolar patients, and psycho-education were effective in improving the compliance of patients and may indirectly reduce the rates of suicides (Sajatovic et al. 2004). This suggests that the decline in suicide rates in depressed patients was likely also the result of psychological interventions, rather than the increased use of antidepressants alone.

The advantages of combined pharmacotherapy and psychotherapy appear to be greater than those offered from either therapy alone. This was supported by an investigation on the impact of psychotherapies on suicide mortality between 1991 and 2005 in Austria, revealing an association between a fivefold increase in antidepressant sales and a twofold increase in the density of psychotherapists on the one hand and a decrease in overall suicide rates on the other (Kapusta et al. 2009). Rucci et al. (2002) examined the effects of adjunctive psychotherapy and long-term lithium therapy on suicidal behavior in bipolar patients, showing that bipolar patients who received both lithium and psychotherapy had a 17.5-fold decline in lifetime suicidal rate compared to the average rate for bipolar sufferers. However, no difference between specific psychotherapy and intensive clinical management (involving regular visits with empathetic clinicians) on patients receiving lithium was found, which may indicate that any of the psychosocial interventions is beneficial in reducing suicide rates.

**Conclusions**

Although mood disorders are a strong predictor of suicidal behaviors, most individuals diagnosed with these disorders have never attempted or completed suicide. Studies show that suicidal behaviors in patients with mood disorders are state-severity dependent, and are most likely to occur during major depressive episodes. However, the rate of suicidal behaviors in depressive disorders is possibly inflated by the misdiagnosis of normal sadness as a psychiatric disorder. This counters the suggestion that mood disorders are likely underdiagnosed and undertreated in the general population. It is important to clearly distinguish normal sadness and clinical depressive disorders, because inaccurate identification, and thus wrongly prescribed antidepressants, may bring short- or long-term undesired effects, including increased suicidal risk. The DSM needs to take into account cause and context in the criteria used to diagnose major depressive disorder.

There is ample evidence that antidepressants are generally effective in reducing suicidal behaviors in adults with major affective disorders, but the question of the risk of suicide caused by antidepressants in younger patients remains. This indicates that high-quality mental health care is of paramount importance in monitoring suicidality in young individuals prescribed with antidepressants. Nevertheless, the decline in suicide rates in recent years is not the result of pharmacotherapy alone, but likely also an indirect
effect of psychotherapy. The effect is more evident in the combination of these therapies, as medicines may ease distress, making patients more receptive and compliant to psychosocial therapies in the long term.

Continued efforts to improve early detection and assessment, as well as pharmacotherapy and psychotherapy, are required to sustain the decline in self-destructive behaviors.

References


