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Risk for Suicide during Treatment with Selective Serotonin Reuptake Inhibitors Antidepressants Medication

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ABSTRACT
Background: prolonged stress may lead to depression which also can lead to suicidal attempts. Serotonin reuptake inhibitors (SSRIs) remain the dominant class of antidepressants. Many mental health care providers have conflicts to the therapeutic role of antidepressants. Some studies found that SSRIs protect from suicide and others find no effect.
Aims: to find if there is a relationship between the use of SSRIs and suicide.
Methods: Computerized literature searches using CINAHL, Pub Med, and science direct database were undertaken, using the key words 'SSRI antidepressants', 'suicide, ' FDA black box warnings regarding SSRI antidepressants' , ' relationship between SSRIs and antidepressants', prevalence of SSRI antidepressants prescription among elderly', 'prevalence of suicide among patients treated with antidepressants'
Conclusion: Increased risk of suicide and self-harm caused by SSRIs antidepressants cannot be ruled out, but more searches with longer follow up are required to assess the balance of risks and benefits to be fully understood.

Introduction

Every person occasionally feels black and sad, but these emotions usually disappear over the time. When a person has a depressive disorder, it interrupts the quality of life, normal functioning, and causes suffering for the person with the disorder and burden for those who look after him or her. Many people with a depressive illness never seek treatment. But the vast majority, even those with the most severe depression, can get better with treatment .Intensive research into the illness has resulted in the development of medications, psychotherapies, and other methods to treat people with this disabling disorder (National Institute of Mental Health, 2008).

Depression is a common mental illness that affects more than 19 million Americans each year (U.S department of Health and Human Services [USDHHS], 2005). Most persons who experience it need treatment to get better and to restore their normal functioning.

Depression is an illness that can have a significant impact on a person's life, hindering the ability to function, interfering with relationships, and causing a loss of interest or pleasure in the activities of living (Brock et al., 2005). Depression is the fourth leading cause of disability worldwide, creating an enormous burden for society (Ustun, Ayuso-Mateos, Chatterji, Mathers, & Murray, 2004). There are several forms of depressive disorders. The most common are major depressive disorder and dysthymic disorder (U.S department of Health and Human Services [USDHHS], 2008).

Depression can complicate other diseases, causing additional health problems and potentially leading to suicide. Between 2 and 8% of depressed patients eventually die from suicide
(Bostwick & Pankratz, 2000; In skip, Harris ,& Barraclough,1998) which is two to five times the rate seen in the general U.S. population (Centers for Disease Control and Prevention , 2008), furthermore, latest studies showed that lifetime risk of suicide among patients with untreated depression ranges from 2.2% to 15% according to black box warning regarding risk for suicide during treatment of depression in 2007 .

According to the Centers for Disease Control and Prevention (CDC) (2007), more than 30,000 people in the United States died by suicide in 2001, in 2002 more than 116,000 people were treated and released from emergency rooms after suicide attempts, and more than 130,000 people were hospitalized following suicide

attempts.

Suicide is an intended decision to end one's own life. Start from non-fatal suicidal behavior appears in the form of ideation, where there are thoughts that promote the desire to end one's life, which become aggravated when they are accompanied by a suicide plan, in which a method for ending one's life is formulated. Attempted suicide involves conduct designed to cause death, which it may or may not result in (Nock, M K, 2008).

Several risk factors for suicide attempts among depressed patients have been identified and they include being unmarried, more severe depression, a co-occurring alcohol use disorder, and a history of prior suicide attempts (Sokero et al., 2005).

The drug of choice which is mainly used to treat the depressive disorders is the selective serotonin reuptake inhibitors (SSRIs) remain the dominant class of antidepressants. Their ease of use, versatility, and safety has favored the SSRIs in both psychiatric and general medical practice (Schatzberg, Cole, & DeBattista, 2007).

Suicidal thoughts are a symptom of depression, and completed suicide is a tragic complication of depressive illness (Howland, 2007). Despite the relative effectiveness of antidepressant medications, there has been some concern that these drugs might have a paradoxical effect in inducing suicidal states, at least in a minority of treated patients (Teicher, Glood, & Cole, 1990). Besides, the contributions of other studies lead major authorities like Food and Drug Administration (FDA) to issue warning regarding use of antidepressants.

In October 2004, the U.S. FDA ordered that all antidepressant medications carry a warning indicating that they are associated with an increased risk of suicidal thinking, feeling, and behavior in children and adolescents. In May 2007, the FDA expanded this warning to include information about an increased risk of suicidal symptoms in young adult's ages between 18 to 24.

Does anti-depressant drug treatment increase or decrease the risk of completed suicide?

Since major depression is a leading risk factor for suicide, and because antidepressant drugs are generally effective in treating depression [Goldsmith et al., 2002], it might be expected that Increasing use of antidepressants would reduce suicide. However a number of recent studies Suggest that the most commonly used class of antidepressant drugs – selective serotonin reuptake Inhibitors (SSRIs) – might actually increase the risk of suicidal behavior [FDA, 2006, Hammad et al., 2006].

Observational studies have found varied results: some signify that SSRIs protect from suicide-related events (Gibbons RD et al, 2007) and others find no effect (Schneeweiss S, et al , 2010 & Jick H, Kaye JA, Jick SS, 2004) or an increase in risk of suicide-related events (Olfson M, Marcus SC, Shaffer D, 2006 & Gibbons RD et al, 2012) . These studies, however, have methodological limitations including small sample size and high attrition rates.

One candidate explanation is heterogeneity in psychopharmacological effects: some patients might experience a worsening of mood from SSRI treatment. Another candidate explanation comes from the possible behavioral responses of patients and medical practitioners to the improved safety and reduced side effects of SSRIs relative to older tri-cyclic antidepressants (TCAs), a version of what Viscusi [1984, 1985] terms the "lulling effect." In response to these recent studies, regulatory agencies in both the US and UK have issued warnings about the use of SSRIs first for people under 18 years of age [U.K. Department of Health, 2003; FDA 2003, 2004; Goode 2003] and more recently for adults as well [FDA, 2005].

Significance of the Literature Review

The significance of this study lies in its goal to find if there is a relationship between the use of selective serotonin reuptake inhibitors (SSRIs) antidepressants and suicide. In addition, the prevalence causes, and consequences in order to raise awareness and provide some recommendations about this problem for best practice in mental health field in future.

Also the benefits of these pieces of information can be helpful for psychiatric setting administration, education of mental health staffs, and progression of evidenced-based clinical practice.

In 2000, SSRIs were the second most commonly prescribed drug class in the U.S., and the third best-selling drug class in the world [IMS Health, 2006]. Understanding how SSRIs affect suicide is relevant for policy decisions about whether to restrict or encourage access to these drugs, and about how to regulate their use.

Literature Review

Methodology

The objective of this literature review was to examine the existing body of

Knowledge concerning prevalence of antidepressants among adolescents and elderly, the correlation between SSRI with suicide, and the effects of FDA on prescribing antidepressants and suicide rates. This literature review

provided a clear picture about the mentioned concepts. Moreover, it has manifested guidance and organization for the ideas and theories pertaining to suicide among depressed patients whom treated with SSRI antidepressants.

A number of papers in the international journal reporting that suicide are prevalent among patients whom treated with SSRIs antidepressants. The review of literature will look at this topic in multiple approaches in order to facilitate comprehensive understanding.

Computerized literature searches using CINAHL, Pub Med, and science direct database were undertaken, using the key words 'SSRI antidepressants', 'suicide, ' FDA black box warnings regarding SSRI antidepressants' , ' relationship between SSRIs and antidepressants', prevalence of SSRI antidepressants prescription among elderly', 'prevalence of suicide among patients treated with antidepressants' . As articles were retrieved their references' were reviewed for potential studies to be included in the review. Selected for inclusion within the review were research studies written in English language that were related to the prevalence, causes and effects of FDA warning.

Prevalence of Antidepressant Use among Elderly People

The proportion of antidepressant users increased from 9.3% of the elderly population in 1993 to 11.5% in 1997. Prescriptions for SSRIs accounted for 9.6% of antidepressant prescriptions dispensed in the first 30 days of 1993 and 45.1% of those dispensed by the last 30 days of 1997 and were projected to increase to approximately 56% by the end of 2000. Prescriptions for tricyclic antidepressants fell from 79.0% in the first 30 days of 1993 to 43.1% by the last 30 days of 1997 and were projected to decline to approximately 28% by the end of 2000. Annual antidepressant costs (in Canadian dollars) increased by 150%, from $10.8 million in 1993 to $27.0 million in 1997. Population shifts and an increase in the prevalence of antidepressant users accounted for at least 20% of this increase, whereas the prescribing transition from tricyclic antidepressants to SSRIs accounted for at least 61% of the increase (Mamdani et al., 2000).

Blazer et al., (2000) conducted a study its sample 4,162 elders equally distributed between African American and white community-dwelling subjects in the Piedmont region of North Carolina during four in-person interviews spanning 10 years. The authors found that a total of 4.6% of whites and 2.3% of African Americans used antidepressants in 1986. Approximately 14.3% of whites and 5.0% of African Americans used antidepressants in 1996. In controlled analyses, the prevalence odds ratio for antidepressant use in whites, compared to African Americans, was 1.76 in 1986 and 3.77 in 1996. According to study, it could be concluded that African American elders are much less likely to take antidepressants, and the difference in use increased over the 10 years of the survey.

In elderly people with depression, 24% received no antidepressant treatment, 26.3% received old antidepressants (tricyclics and monoamine oxidase inhibitors) alone or in combination with psychotherapy, 64.3% received new antidepressants (selective serotonin reuptake inhibitors) alone or in combination with psychotherapy, 14.8% received both new and old, and 75.8% were treated with any antidepressant (old, new, or both) in the same calendar year. Thirty seven per cent of black people, 22.4% of white people, 13.8% of Asian people and 23.6% of Hispanic people received no drug treatment for depression.

African Americans with a primary diagnosis of depression were almost twice as likely as whites not to receive an antidepressant within the study period (odds ratio=1.91, 95% confidence interval=1.62-2.24). Significantly more black, non- Hispanics were receiving no treatment than whites (p, 0.001). Other risk factors for no pharmacotherapy were being male, aged 65–74 years and being in long term care (Strothers et al, 2005).

Prevalence of Antidepressant Use among Adolescents

Rushton, and Whitmire, (2001) conducted a retrospective study in North Carolina Medicaid recipients, 1992 through 1998, aged 1 to 19 years. The population ranged from 342333 children in 1992 to 581088 in 1998. The study revealed that the number of children and adolescents who received stimulants increased from 6407 (24584 claims) in 1992 to 27951 (135057 claims) in 1998. The number of SSRI recipients increased from 510 children (1326 claims) in 1992 to 6984 children (25392 claims) in 1998.

Prescription prevalence in school-aged children 6 to 14 years increased from 4.4% to 9.5% for stimulants during the study period, and from 0.2% to 1.5% for SSRIs antidepressants. In 1998, stimulant prescription prevalence was highest for white school-aged males (18.3%) versus black females (3.4%) and SSRI prescription prevalence was highest for white school-aged males (2.8%) versus black females (0.6%). Combination pharmacotherapy also increased during 1992 through 1998.

Zito et al., (2002) found that, in 1994, antidepressants (ATD) prevalence per 1000 youths was 19.10 Midwestern Medicaid (MWM), 17.78 mid-Atlantic Medicaid (MAM), and 12.85 health maintenance organization (HMO), which represented a consistent increase in prevalence from 1988–1994: 2.9-fold (MWM), 4.6-fold (MAM), and 3.6-fold (HMO). TCAs were the most commonly used ATD subclass in 1988, but by 1994 SSRIs nearly equaled the prevalence of TCAs.

Despite the rapidly expanding use of selective serotonin reuptake inhibitors prescribed mainly for depression, more than half of ATD use in 1994 was still attributable to tricyclic antidepressants prescribed mainly for attention-deficit/hyperactivity disorder. ATD prevalence was generally predominant among 10 to 14 year-old boys and among 15 to 19 year-old girls. In the Medicaid populations, 42% (MAM) and 72% (MWM) of ATD-treated youths had primary care services, whereas the bulk of the remainder had psychiatric services. Obviously, ATD treatments among youths substantially increased in the 1990s.

Rational for why SSRI antidepressants induce suicide

Juurlink and his colleagues in 2006 studied the risk of suicide with selective serotonin reuptake inhibitors in the elderly and concluded that the initiation of SSRI therapy is associated with an increased risk of suicide during the first month of therapy compared with other antidepressants. The absolute risk is low, suggesting that an idiosyncratic response to these agents may provoke suicide in a vulnerable subgroup of patients.

Breggin (2004) proposed another rational for suicidality in adult and children through SSRI treatment that caused by the adverse drug reactions that lead to the following overlapping clinical phenomena: a stimulant profile that ranges from mild agitation to manic psychoses, agitated depression, obsessive preoccupations that are alien or uncharacteristic of the individual, and akathisia. Each of these reactions can worsen the individual's mental condition and can result in suicidality, violence, and other forms of extreme abnormal behavior.

Evidence for these reactions is found in clinical reports, controlled clinical trials, and epidemiological studies in children and adults. Recognition of these adverse drug reactions and withdrawal from the offending drugs can prevent misdiagnosis and the worsening of potentially severe iatrogenic disorders. These findings also have forensic application in criminal, malpractice, and product liability cases.

The Effects of FDA Warning and Prescribing Antidepressants

One of the interesting studies regarding FDA warnings effects is the one which was conducted by Olfson, Marcus, and Druss in 2008. It showed during the pre-warning study period, there was a 36.0% per year (P<.001) increase in total youth (aged 6-17 years) of all antidepressants use. Specific significant increases were evident for paroxetine, other SSRIs, and “other antidepressants” but not tricyclic antidepressants. It was followed by decreases of −0.8% per year (P=.85) and −9.6% per year (P=.21) during the paroxetine and black box warning study periods, respectively. The difference in trends between the pre-warning and paroxetine warning periods was significant (P<.001).

Youth paroxetine use also significantly increased during the pre-warning study period (30.0% per year; P<.001) before significantly declining during the paroxetine warning study period (−44.2% per year; P<.001), which was also a significant between-period difference in trends (P<.001). Changes in antidepressant use were less pronounced in adults than in youth. For adults 65 years and older, overall antidepressant use significantly increased (8.1% per year; P<.001) during the black box study period. Changes in the pattern of antidepressant use varied little by patient sex.

Conclusively, the paroxetine and black box warnings had modest and relatively targeted effects on the intended populations. These changes, which were greatest for youth, were broadly consistent with the FDA warnings and the scientific literature.

Libby et al., (2007) conducted a cohort study its sample (N=65,349) from 1998 to 2005. Time-series models were used to compare diagnosing and prescribing trends during the 2 years after the FDA advisory and the expected trends based on data from the 5-year period preceding the advisory. The authors found that from 1999 to 2004, the rate of diagnosed new episodes of pediatric depression increased steadily, in 2005, the rate decreased sharply.

For both male and female patients, the observed 2005 rate was significantly lower than the rate predicted from the regression line ($p<0.0001$), indicating that the observed rate in 2005 was significantly lower than would have been expected on the basis of the historical trend.

For male pediatric patients, the observed rate of diagnosed new episodes in 2005 was 2.3 per 1,000 enrollees, while the trend predicted a rate of 3.8 (65% higher than observed). For females, the observed rate in 2005 was 3.5 per 1,000 enrollees, whereas the trend predicted a rate of 6.0 (71% higher than observed).

Among patients with depression, the proportion receiving no antidepressant increased to three times the rate predicted by the pre-advisory trend, and SSRI prescription fills were 58% lower than predicted by the trend. There was no evidence of a significant increase in use of treatment alternatives (psychotherapy, atypical antipsychotics, and anxiolytics). It could be concluded that the FDA advisory was associated with significant reductions in aggregate rates of diagnosis and treatment of pediatric depression and the diagnosis rates among enrollees were not explained by changes in the base population.

The Effects of FDA Warning and Suicide

Gibbons et al., (2007) conducted a study by examining U.S. and Dutch data on prescription rates for SSRIs antidepressants from 2003 to 2005 in children and adolescents (patients up to age 19), as well as suicide rates for children and adolescents, using available data (through 2004 in the United States and through 2005 in the Netherlands).

Surprisingly, the findings were that SSRI prescriptions for youths decreased by approximately 22% in both the United States and the Netherlands after the warnings were issued. In the Netherlands, the youth suicide rate increased by 49% between 2003 and 2005 and shows a significant inverse association with SSRI prescriptions. In the United States, youth suicide rates increased by 14% between 2003 and 2004, which is the largest year-to-year change in suicide rates in this population since the Centers for Disease Control and Prevention began systematically collecting suicide data in 1979.

Risk of Suicide and SSRIs Antidepressants

A major technological innovation in the treatment of depression occurred in 1984 with the introduction of the selective serotonin reuptake inhibitors (SSRIs). SSRIs are described as "selective" because they affect only the reuptake pumps responsible for serotonin, a small molecule that serves as a neurotransmitter, or "chemical messenger," in the brain. SSRIs increase the amount of the neurotransmitter serotonin that is active in the synapses between cells, thereby enhancing neuronal activity and improving mood.

In contrast to SSRIs, the TCAs affect multiple neurotransmitters. While the SSRIs seem to be similar to the older TCAs in their ability to reduce depression (e.g., Ryan [2003], Vaswani et al. [2003]), they are more selective in their operation and therefore have fewer physical side effects (such as dry mouth, drowsiness, or cardiac arrhythmia) and are less toxic in overdose.

The question of whether SSRIs antidepressant drugs might actually increase suicide risk first came to national attention in 1990, with the publication of a report describing six adult patients who apparently became suicidal as a result of being treated with fluoxetine (Prozac). The ensuing debate led the FDA to review the issue, with hearings in 1991. A review of all of the clinical trials conducted by the manufacturer revealed no sign of increased suicidality associated with the use of Prozac [Beasley et al, 1991].

Over the next several years, as newer drugs came to market, pooled analyses of Individual clinical trials were updated in order to search for possible signs of risk. In May of2003, GlaxoSmithKline Company reported an increased risk of suicide-related adverse events in a pediatric trial of paroxetine (Paxil).

This led to an analysis of all available pediatric trials, and finally to an FDA "black box" warning of increased risk of suicidal behavior associated with SSRIs antidepressant use in pediatric patients. Since then, the FDA has commissioned several large pooled studies, the first covering pediatric clinical trials of new antidepressants, and the most recent covering adult trials. Taken together, these studies have found a plausible and statistically significant association between assignment to SSRI (versus placebo) and non-lethal suicidal behavior in adolescents [Hammad et al 2006] and in young adults, as well as a statistically significant decrease in suicidal ideation and behavior from drug treatment in older adults [FDA 2006].

In term of age, the relationship between suicide and use of SSRIs antidepressants is miscellaneous. In 2009, Barbui and his colleagues conducted a systematic review of eight observational studies (involving more than 200,000 patients with moderate to severe depression) that reported completed or attempted suicide in depressed individuals who were exposed to SSRIs compared with those who were not exposed to antidepressants. The analysis of findings suggested that use of SSRIs may be associated with a reduced risk of suicide in adults with depression, while among adolescents; use of SSRIs may increase suicidality. Furthermore, Christiansen et al (2015) conclude that the risk of suicide attempt is higher for young patient in the first months after initiation their first prescription for SSRIs, compared to non-users.

In addition, Kauffman. J (2009) reveled that there was no causal connection between SSRIs and suicide after conducting a meta analysis regarding correlation between SSRI and suicide.

Comparison between the Different Antidepressants and suicide

Khan et al., (2003) analyzed reports from randomized controlled trials to compare suicide rates among depressed patients assigned to an SSRI, other antidepressants, or placebo. There was no statistical difference in crude suicide rates among patients assigned to SSRIs, other antidepressants, or placebo ($\chi 2=2.83$, df= 2, $p>0.05$). In addition, when groups were compared on the basis of patient exposure years, there was no statistical difference

in suicide rate among patients assigned to SSRIs, other antidepressants, or placebo ($\chi 2=1.39$, df=2, $p>0.05$). Methods of suicide were available for 39 of the 77 completed suicides. Of the 38 suicides of patients assigned to an SSRI, three were by hanging, two were by overdose, and one was by drowning. Of the 34 suicides of patients

assigned to other antidepressants, nine were by hanging, six were by overdose, six were by drowning, five were by gunshot, three were by jumping, and three were by carbon monoxide poisoning. Of the five suicides of patients assigned to placebo, the one completed suicide for which the method was known was by hanging. No clear differences were observed for patients treated with SSRIs compared with patients given other antidepressants.

Juurlink et al., (2006) revealed that during the first month of therapy, SSRIs antidepressants were associated with a nearly fivefold higher risk of completed suicide than other antidepressants (adjusted odds ratio: 4.8, 95% confidence interval= 1.9–12.2). The risk was independent of a recent diagnosis of depression or the receipt of psychiatric care, and suicides of a violent nature were distinctly more common during SSRI therapy. No disproportionate suicide risk was seen during the second and subsequent months of treatment with SSRI antidepressants, and the absolute risk of suicide with all antidepressants was low.

Relative to other antidepressants, SSRIs were more strongly associated with suicides of a violent nature (hanging, gunshot, jumping, stabbing, vehicle collision, blunt trauma, explosion, electrocution, and self-immolation) than other antidepressants. A tendency toward violent suicide was apparent only during early therapy with SSRIs, whereas nonviolent suicide was equally common among patients treated with SSRIs and other antidepressants.

Surprisingly, meta-analyses of Randomized Control Trials (RCT) suggest that SSRIs increase suicide ideation compared with placebo but the observational studies suggest that SSRIs do not increase suicide risk more than older antidepressants (Hall, & Lucke, 2006).

On the other hand, it was found that Suicide attempt rates were lower among patients who were treated with antidepressants than among those who were not, with a statistically significant odds ratio for SSRIs and tricycles. For SSRIs versus no antidepressant, this effect was significant in all adult age groups. Suicide attempt rates were also higher prior to treatment than after the start of treatment, with a significant relative risk for SSRIs and for non-SSRIs. For SSRIs, this effect was seen in all adult age groups and was significant in all but the 18–25 groups (Gibbons et al., 2007). Furthermore, in comparison between selective serotonin reuptake inhibitors (SSRI) and tricyclic antidepressant (TCA) prescriptions and suicide-related events in children and adolescents, it had been found that no systematic differences between the association of TCAs and SSRIs and the incidence risk ratios for attempted suicide, and the rates of suicide did not exceed pre-exposure levels for antidepressant (Linda P M et al., 2013).

Discussion

Many mental health care providers are faced with uncertainty on the therapeutic role of antidepressants due to conflicting data and interpretations of the effects of antidepressants
on the spectrum of suicidality. The clinician finds it difficult to distinguish between the background suicidal ideation, intent and behavior related to the underlying depressive disorder and treatment-emergent events. It is essential that clinicians develop skills in eliciting suicidality and assessing the risk. This is a topic that is often avoided on the basis of the long-discredited canard that talking about suicide increases the risk. If anything, sympathetic questioning
Lessens the risk.

Experienced clinicians have long known that the suicidal risk may be increased early on in the treatment of patients, whether that treatment is pharmacological, electro-convulsive therapy or some form of psychotherapy. Pattern of improvements vary from patient to patient, some becoming less suicidal early on, others being more delayed. Accordingly, the clinician must exercise especial caution in the first four weeks or so of treatment, particularly if response is poor, delayed or patchy. Persistence of such symptoms as insomnia, poor appetite and anxiety are particularly upsetting.

The patient should be warned that response may initially be unsatisfactory and health care providers should be asked for their observations. Frequent (3–7 days) contact is a wise precaution in the first weeks, and the clinician should be readily available in emergency. As with all such therapeutic dilemmas, the risk/benefit ratio should be set against the severity of the condition being treated. Moderate to severe depression causes much suffering and is usually accompanied by some elements of suicidality. The more severe the depression the greater is the justification to prescribe an antidepressant. In mildly ill patients such prescription is not usually justifiable as patients do better with some form of psychological intervention.

There is no strong evidence that SSRIs antidepressant prescribing lie behind suicides. Furthermore, data from pediatric trials suggest that SSRIs could be associated with an increased risk of suicidal behavior and most SSRIs seem to be ineffective for childhood depression while another studies showed that SSRIs antidepressants could be effective in reducing the risk of suicide among adult. Understanding that SSRI antidepressants may have an effect on suicide should be taken in consideration for government regulators as well as for doctors,

nurses, patients, and the family and friends of those suffering from severe depression.

However, current concerns about the safety of SSRIs come from clinical trials both of too short duration to identify longer term beneficial effects and are carried out in children and adolescents, among whom suicide is rare. So the relationship between SSRIs antidepressants and suicide is debatable issue according to our literature review because of it is age dependent and suicide per se is a complex issue ranging from ideation to intent and plan. Furthermore, not all patients with ideation attempt suicide.

From the population perspective, the balance sheet of risks and benefits of SSRIs is unclear. Any antidepressant induced suicides may be offset by the beneficial effects of antidepressants on depression and long term suicide risk associated with untreated depression. The low toxicity of SSRIs in overdose will have prevented some suicides. The balance of risks and benefits may vary depending on an individual's underlying suicide risk. For patients with conditions that have a high risk of suicide, such as severe depression, the risk-benefit balance may be more favorable than for patients with conditions such as anxiety and mild depression, in which suicide is rare. It is in these lower risk conditions, however, that much of the recent rise in prescribing has probably occurred.

Finally, depression is a common and disabling condition, and so the safety of drugs used in its management is crucial. Future trials of SSRI antidepressants should be of sufficient duration to detect longer term benefits of this class of drug and balance these against possible risks. They should also systematically collect data on suicidal thoughts and behavior. Long term studies are required to assess the effect on population health of recent rises in antidepressant prescribing.

Conclusion

Increased risk of suicide and self-harm caused by SSRIs antidepressants can not be ruled out, but larger trials with longer follow up are required to assess the balance of risks and benefits fully. Any such risks should be balanced against the effectiveness of the SSRIs in treating depression. When describing SSRIs, health care providers should warn patients of the possible risks of suicidal behavior and monitor patients closely in the early stages of treatment.

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