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REVIEW ARTICLE

Adolescent Depression and Antidepressant

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Abstract

Aim: To review antidepressant in litter therapeutic effect in the treatment of adolescent depression, and more side effect of switching to mania and suicide, including non-suicidal self injury(NSSI).

Methods: To re-understand the antidepressants in treatment child and adolescent depressionby retrieving the related reference and assess the therapeutic effect and side effects.

Results: The related reference show that antidepressant have litter therapeutic effect more side effect of switching to mania and suicide, NSSI.in the treatment of child and adolescent depression

Conclusion: Antidepressants are the main drugs used to treat depression, but they have not shown intreatment child and adolescent depression.However, many adolescent treatment guidelines still recommend the use of antidepressants, especially specific serotonin reuptake inhibitors(SSRI). This review discusses the serious side effects associated with antidepressant drugs. In the process of developing guidelines, drug recommendations should not only focus on improving symptoms, but also pay special attention to side effects.

Keywords: Adolescent Depression, Antidepressant, Switch, Suicide, NSSI.

1. Adolescent Depression Concept

Adolescent depression refers to a type of mental illness that occurs during adolescence and is characterized by significant and persistent low mood and lack of interest. The clinical manifestations of adolescent depression are similar to those of adult depression, but they also have their own characteristics, often with irritability and emotional reactions as the core symptoms. They may also manifest as various physical symptoms such as sleep disorders, eating disorders, fatigue, pain, as well as behavioral problems such as self harm, truancy, smoking, alcohol abuse, internet addiction, not doing homework, declining grades, and tense interpersonal relationships[1].The incidence rate of adolescent depression is 19.85% in China, with 17.8%, 23.7%, and 22.7% in the eastern, central, and western regions, respectively[2].The adolescent refer to from 14-18 years old or 10-21 years old[1,3]

2. Adolescent Depression Treatment Guideline

The systematic analysis of the 2019 Global Burden of Disease Study shows that depression is one of the 10 key diseases leading to an increase in the global burden of disease, and adolescent depression has risen from 8th place in 1990 to 4th place in the adolescent burden of disease[3].Adolescent depression treatment guideline successively be released.These part of the guidelines is intended to assist clinicians in the identification and initial management of adolescents with depression in an era of great clinical need and shortage of mental health specialists[4,5].All guidelines emphasize the importance of psychological quality. The use of medication is only appropriate when psychological therapy is not effective[1, 4, 5].During the application of drugs, the following aspects should be done excellently[5]. (1) active monitoring of mildly depressed youth, (2) treatment with evidence-

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based medication and psychotherapeutic approaches in cases of moderate and/or severe depression, (3) close monitoring of side effects, (4) consultation and comanagement of care with mental health specialists, (5) ongoing tracking of outcomes, and (6) specific steps to be taken in instances of partial or no improvement after an initial treatment has begun. The strength of each recommendation and the grade of its evidence base are summarized.Obviously, choosing which type of medication is a particularly important decision, which requires evidence from deficiency medicine.

3. The Negative Side Effects of Antidepressants in Treatment of Adolescent Depression

The use of antidepressant drugs for the treatment of depressive disorders is beyond doubt. However, adolescent depression is different from adult depression in that it is not only a clinical manifestation issue, but also more likely that the response of adolescents to antidepressant drugs is different from that of adults[1,6,7].This reaction includes both positive effects of treating depression and negative clinical side effects.

The side effects of antidepressant conclude suicide,switch to mania,serotonin syndrome,sex dysfunction, sleep disorder and other side effects in every system in body[8].Although these side effects are classified into early and late stages, suicide and relapse are still considered the most serious problems[6,7,8].These two serious side effects was considered to association with activation[6,7].

The some evidence found antidepressant exposure seems to have an increased suicidal risk among children and young adults[9]. Moreover, the use of antidepressants may increase the risk of NSSI.In those individuals with affective disorders as the primary diagnosis, periods without medication were associated with significantly lower NSSI/day compared to all four other medication conditions (benzodiazepines $p<10^{-8}$, antidepressants/SSRIs p=0.0004, high-potency antipsychotics p=0.0009, low-potency antipsychotics $p<10^{-4}$). In individuals with a primary diagnosis other than an affective disorder, NSSI was significantly lower during the period without medication compared to the treatment periods with benzodiazepines (p=0.005) and antidepressants/SSRIs (p=0.01)[10]. Suicidality was common in youth treated with SSRIs. The proportion with attempted suicide was stable in the weeks following SSRI initiation. Previous suicidality, depression, female sex and previous NSSI are important predictors for suicidality during SSRI treatment in youth[11]. And the some evidence also found antidepressant exposure seems to have an increased switching to mania risk among children and young adults[12].Prior antidepressant treatment was associated with an increased incidence of mania/bipolar disorder ranging from 13.1 to 19.1 per 1000 person-years. Multivariable analysis indicated a significant association with selective serotonin reuptake inhibitors (HR 1.34, 95% CI 1.18 to 1.52) and venlafaxine (1.35, 1.07 to 1.70)[13].The younger the age, the more likely it is to turn into mania.Patient age is an effect modifier on the risk of antidepressant-associated manic conversion. Treatment with antidepressants is associated with highest conversion hazards among children aged 10 to 14 years[14].The high probability of turning manic may be related to more manic connotations.It have four phenomenon. which refer to mania or hypomania,mixed episode, accelerating of rapid cycling and antidepressant-induced chronic irritable dysphoria[15]. It is obvious that questioning the use of antidepressants for adolescent depression is also reasonable.

Another question is that antidepressants are ineffective in treating depression in adolescents[16].Twenty-six studies were included in a study of new generation antidepressants for depression in children and adolescents by a network meta-analysis. There were no data for the two primary outcomes (depressive disorder established via clinical diagnostic interview and suicide), therefore, the results comprise only secondary outcomes. Most antidepressants may be associated with a "small and unimportant" reduction in depression symptoms on the CDRS-R scale[16].And it also was found that venlafaxine probably results in increased odds of suicide-related outcomes.Findings suggest that most newer antidepressants may reduce depression symptoms in a small and unimportant way compared with placebo. Furthermore, there are likely to be small and unimportant differences in the reduction of depression symptoms between the majority of antidepressants.

4. The Controversy of Antidepressants in Guideline for Adolescent Depression

The last guideline for adolescent depression in prevention and treatment with integrated Chinese and western medicine in China was published in Journal of Beijing Chinese Medical University. In this guideline,it was suggested that moderate to severe adolescent depression can be treated with antidepressant, fluoxetine and sertraline is the first choices[1].It come from the meta-analysis about fluoxetine in the management of major depressive disorder in children and adolescents[17].It also come from Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents With Major

and Persistent Depressive Disorders in 2023[18].In last guideline,it was said that if antidepressant medication is ineffective, another antidepressant medication can be substituted, which involves almost all SSRIs[1,18]. From this perspective, antidepressants including SSRIs are still the preferred treatment options.Not only that, many guideline of the references listed in the Chinese guidelines suggest that if medication is needed, antidepressant is first line[1].

Guidelines are an important basis for clinical treatment decisions. In the development of guidelines, drug selection is not only about improving symptoms, but also about paying attention to side effects.When considering the risk-benefit profile of antidepressants in the acute treatment of major depressive disorder, these drugs do not seem to offer a clear advantage for children and adolescents[19]. In adults, psychological interventions, clomipramine, SSRIs or combinations of these are all effective, whereas in children and adolescents, psychological interventions, either as monotherapy or combined with specific SSRIs, were more likely to be effective[20]. This indicates that effective antidepressant drugs for adult depression may not be effective in adolescent depression, and may even have significant negative effects.

In clinical practice, we have encountered the occurrence or aggravation of self injurious behavior caused by the use of antidepressants, and there are countless similar cases. Here are some particularly typical examples illustrated with pictures.See Figure1, 2, 3, 4These typical cases all appear NSSI during therapy with antidepressant. However, our findings reflect the average effects of the antidepressants, and given depression is a heterogeneous condition, some individuals may experience a greater response. Guideline developers and others making recommendations might therefore consider whether a recommendation for the use of newer generation antidepressants is warranted for some individuals in some circumstances[16]. Future RCTs should improve their design, in particular for psychotherapy or combined interventions[20].

Figure1. *Miss A,16 years old.Diagnosed as adolescent depression.NSSI(Cutting the forearm) appear during treatment with Vortioxetine 20mg/d*

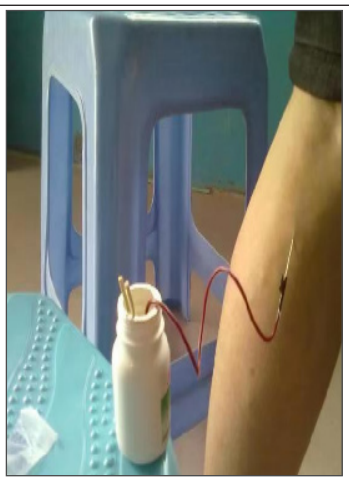

Figure 3. *Miss C,15 years old.Diagnosed as adolescent depression. NSSI bleeding appear during treatment with Sertraline 100mg/d*

Figure 2. *Mr B,18 years old.Diagnosed as adolescent depression.NSSI(burning the back of the hand with a cigarette butt.appear during treatment with Venlafaxine,225mg/d*

Figure 4. *Miss D,16 years old.Diagnosed as adolescent depression.NSSI.cutting the wrist.appear during treatment with Toludesvenlafaxine 1 pill/d*

Declaration

Ethics Approval and Consent to Participate

N/A

Consent to Publication

All authors agree to publish the manuscript.

Availability of Data and Material

N/A

Competing Interests

There were not any financial and non-financial competing interests.

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Authors' Contribution

Prof.SFL and prof.JWD participated in design and final review of article.

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