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Adolescent depression: clinical features and therapeutic strategies

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Abstract. – BACKGROUND: Major depressive disorder (MDD) is a common disorder during adolescence and it is associated with an increased risk of suicide, poor school performance, impaired social skills, social withdrawal and substance abuse. Further, as many depressive episode in adolescents do not reach the diagnostic threshold for MDD, the disorder remains undetected.

AIM: This review aims to provide an update of clinical features of adolescent MDD and to focus on the most appropriate therapeutic strategies to adopt in clinical practice.

MATERIALS AND METHODS: We reviewed the international literature to identify studies focusing on clinical features and therapeutic options in adolescents affected by MDD. PubMed, Medline and Cochrane Library databases were searched for English language papers.

RESULTS: The clinical picture of depression is variable with sex and age. Somatic complaints, particularly headache and fatigue, are a common presentation in adolescent MDD. Irritability is present most frequently in female and it is related to the severity of MDD. Adolescent MDD is also characterized by a high rates of suicides. The therapeutic strategy in adolescent depression includes psychotropic medications, psychotherapy or a combination of both treatments, with selection of the most appropriate strategy depending on symptom severity. As first-line treatment the traditional cognitive behavioural therapy (CBT), as well as the cognitive Post-Rationalist (PR) approach, are so far considered the goal standard.

CONCLUSIONS: The therapeutic approach to the adolescent affected by MMD should respect the person in his/her psycho-physical entirety. The intervention may help the subject in seeking a more stable and adaptable identity. It is relevant to have a good knowledge of the peculiar clinical picture of adolescent MDD in order to make an early identification of the disorder and to define an appropriate personalized therapeutic program.

Key Words:

Adolescent, Major depressive disorder (MDD), Psychopatology, Psychotherapy, Antidepressants, Selective serotonin reuptake inhibitors (SSRIs).

Introduction

Major depressive disorder (MDD) is a complex disabling condition which affects all aspects of life and impairs individual's family and personal relationships, work adjustment and general health. This disorder represents a major cause of morbidity and disability worldwide and is currently considered the fourth-leading cause of disease burden[1-3]. MDD is common also during childhood and adolescence and it is associated with an increased risk of suicide, poor school performance, impaired social skills, social withdrawal, and substance abuse[4]. In particular, the physiological, psychological and social changes that characterize adolescence can increase the risk for MDD and other related depressive disorders[5]. The incidence of depression in preadolescence is between 0.5% and 2.5% and from 2.5% to 8% during adolescence, while the prevalence is estimated to be between 4% to 8%[6]. Further, as many depressed adolescents do not reach the diagnostic threshold for MDD, the disorder is often not identified. Even though the depressive episode may not meet the criteria for MDD, the symptoms may still have long-term clinical and social implications and can predispose to later development of a full blown disorder[7].

The clinical picture of MDD in adolescents is quite different from the adult, in fact it is characterized by heterogeneous and changing symptoms, sometime hidden from somatic complaints and complicated by the high comorbidity rates with anxiety disorders, substance abuse, disruptive behavior disorders, personality disorders, and medical illnesses[8-11]. In detail, in adolescents as well as in adults, although suicide has many causes, 85% to 95% of those dying by suicide have psychiatric illness (especially MDD)[12]. Further, there are significant psychosocial and educational consequences if such an episode remains undetected[13]. It should be noted that parents can both minimize or overestimate symptoms, espe-

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cially if they are emotionally distressed as often it happens when an adolescent requires psychiatric interventions. Therefore, in these subjects it is difficult to recognize depressive symptoms and make a correct diagnosis, as well as to establish an adequate therapeutic strategy. The aims of this review are a) to provide a comprehensive update of the clinical features of MDD in adolescents, and b) to indicate, on the basis of evidences so far available, the most appropriate therapeutic interventions to adopt in adolescent MMD.

Materials and Methods

We reviewed the international literature to identify studies focusing on adolescent MDD. PubMed, Medline and Cochrane Library databases were searched for English language papers by using the following key words: adolescent, major depressive disorder (MDD), clinical manifestations, psychopharmacology, antidepressants, psychotherapy.

Results and Discussion

Clinical Features

During adolescence, medically unexplained symptoms, such as headache and abdominal pain, fatigue or loss of energy, and irritability are particularly common in subjects with MDD[14,15]. In fact, a common early presentation of depression in primary care is characterized by somatic complaints in the absence of an organic disease[6]. Somatic complaints are the most frequent symptoms in both gender and are strictly related to the presence of depressive symptoms.[4] In a population-based study, it was demonstrated that duration and severity of depression were related to the number of somatic symptoms[16]. Further, a strong correlation between the presence of somatic symptoms and suicidal ideation, suicidal attempts, disruptive behavior and stressful relationships has been reported[17,18].

Irritability is another common symptom of adolescent MDD. In fact, the Diagnostic and Statistical Manual for Mental Disorders IV-Text Revised[19]s pecifies that depression in children and adolescents may be characterized as an irritable mood. Irritability is more common in female and it appears to be age related, becoming more frequent during mid-adolescence (13-15 years) with a rate of 75.5% while decrease in adulthood (19-21 years) till to 51.5%[20]. The presence of irritability is also strongly related to severity of MDD[21].

Concerning gender differences, it has been reported that in female feelings of sadness, lonely, irritability, pessimism, hating themselves, crying, and eating disorders are more frequent; in male are more present somatic complaints, reduced ability to think or concentrate, decision making, feelings restless and anhedonia. In addition, irritability in males is very often associated to the presence of conduct disorders and substance use[15,20-22]. Furthermore, in female, negative body image is frequently present. In fact, because appearance is a relevant concern for girls in western culture, feelings of displeasure with their body may have a consequent impact on their mood[23]. Negative body image becomes less likely as symptom of depression as subjects were reaching young adulthood with a rate of 23.5% versus 45.4% in mid-adolescence[20].

In particular, 20%-24% of MDD adolescents attempt suicide, while 25%-66% show suicidal ideation, especially from 16 to 19 years and in presence of irritability[20,24-28].

The clinical picture of depression is extremely variable with age. Overall, while children and younger adolescents have more symptoms of somatic complaints, anxiety and irritability, older adolescents and youth adults have more affective and cognitive symptoms, closely resembling those of adults[20].

Treatment Options

The treatment strategy for adolescent MDD includes psychotropic medications, psychotherapy or a combination of both treatments, with selection of the most appropriate strategy depending on symptom severity[29,30]. The guidelines of the National Institute for Health and Clinical Excellence (NICE)[31] recommend that "...when assessing a young person with MDD, healthcare professionals should routinely consider, and record in the patient's notes, potential comorbidities, and the social, educational and family context for the patient and family members, including the quality of interpersonal relationships...". As first-line treatment, the NICE guidelines suggest a specific psychological therapy cognitive behavoiural therapy: CBT, interpersonal psychotherapy (IPT) or shorter-term family therapy for at least 3 months. If there is no response to a specific psychotherapy within four to six ses-

sions, it is suggested to review and consider alternative or additional psychological therapies. According to the NICE guidelines, antidepressants should not be used except that in combination with a concurrent psychological therapy. In fact, in adolescents all antidepressants were found to significantly increase the risk of suicide[32-34]. Fluoxetine (FLX) is the most studied Selective Serotonin Reuptake Inhibitor (SSRI) and recent reviews indicated that FLX should be considered the first-line drug treatment of adolescent MDD[35-37]. If treatment with FLX is unsuccessful or is not tolerated because of side effects, consideration should be given to the use of another antidepressant[31]. In this case sertraline or citalopram are the recommended second-line treatments. The Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) as well as old generation antidepressants should not be used for the treatment of young people with MDD[31,38,39]. In fact, the evidence that antidepressants may induce a worsening of depressive symptoms and increase the risk of suicide led the Food and Drug Administration (FDA) to publish a warning regarding such a risk in patients up to age 24[40,41]. In the recent years, the use of antidepressants in adolescence has decreased as a result of the above-mentioned concerns regarding the suicide during antidepressant treatment. On the contrary, according to other Authors, the use of SSRIs in adolescent MDD is not related to any increase of the risk of suicide[36,42,43]. In any case, a close drug monitoring of antidepressant drugs should be considered if such drugs must be utilized in the treatment of adolescents with moderate to severe MDD.

According to the Treatment for Adolescents with Depression Study (TADS)[44,45] an appropriate treatment for moderately to severely depressed adolescents has been established. The combination of FLX and CBT was significantly superior to CBT or FLX alone as allowed to minimize the risk of suicidality that could be related to the use of FLX alone[46]. A recent meta-analysis on combined treatment with newer-generation antidepressants and CBT confirmed an advantage (even if limited) for the treatment of an episode of depression in adolescents[47]. However, patients and providers may wish to begin treatment with CBT alone in order to avoid the risk of antidepressant-induced suicidality. Moreover, as recently demonstrated in the naturalistic 1-year follow-up phase of the TADS, patients treated with the combination of FLX and CBT maintain the improvement in both depressive and suicidality scores.

The CBT is the most effective psychotherapeutic intervention, besides to the interpersonal psychotherapy for depressed adolescents (IPT-A)[28,48,49]. In particular, although CBT has been mainly studied in adults, there is a growing evidence that it can be useful both in children and adolescents[50-52]. Further, adding continuation CBT sessions after acute improvement may decrease the risk of relapse[53-56].

Among cognitive psychotherapies, the Post-Rationalist (PR) approach constitutes one of the most innovative strategy, proposing a useful epistemological theory of mental functioning with successful application in clinical practice[57-60].

According to the PR theory, different significant factors are involved in the development of a Personal Meaning Organization (PMO), such as constitutional factors, attachment relationships, and a subjective manner of managing life experiences. Knowledge of the "self system" is central, as it deeply influences the attitude of the therapist, the assessment procedures and the dynamics of the therapeutic change. Furthermore, the PR approach allows a subject-centred reconstruction of immediate experiencing, thus modifying dysfunctional patterns of self-perception and achieving more adaptive and lasting changes[61]. Using this approach, feelings of self-negativity, perceived as objective and unchanging aspects of the self, are focused as subjective patterns in organizing experience, giving them a new significant. A specific early intervention on adolescent turmoil, which causes a negative view of the self and the world, can be useful to cope such problems and to prevent chronicity[62].

Conclusions

MDD is common during childhood and adolescence and it is characterized by a high incidence of somatic complaints, loss of energy, irritability, and by disruptive consequences, including increased risk of suicide and behavior disorders, poor school performance, impaired social skills, and substance abuse. The lack of recognition and appropriate treatment of depressive symptoms can be consequently at risk of serious long-term psychological and educational consequences.

The treatment options of MDD during adolescence, however, is still controversial. A warning on the possible negative consequences of the use of antidepressants, in particular the increased risk

of suicide, has been indicated by the FDA, while a CBT approach is considered the first line treatment. On the contrary, there is a numbers of clinical evidences suggesting the efficacy of CBT in combination with antidepressants. In any case, it is clear that the best therapeutic intervention in the adolescent with MDD should be always personalized. The intervention may help the subject in seeking a more stable and adaptable identity. Helping the adolescent to cope the turmoil related to growth can give to the subject adequate tools to become a well-balanced adult.

Conclusions

It is relevant to have a good knowledge of the clinical features of adolescent MDD in order to make an early diagnosis and to define an appropriate personalized therapeutic program.

Conflict of Interest

None to declare.

References

1) Andrade L, Caraveo-Anduaga JJ, Berglund P. The epidemiology of major depressive episodes: Results from the International Consortium of Psychiatric Epidemiology (ICPE) Surveys. Int J Methods Psychiatr Res 2003; 12: 3-21.
2) Kessler R-C, Berglund P, Demler O. The epidemiology of major depressive disorder: Results from the National Comorbidity Survey Replication (NCS-R). JAMA 2003; 289: 3095-3105.
3) Weich S, Lewis G. Poverty, unemployment, and common mental disorders: Population based cohort study. Br Med J 1998; 8: 317-315.
4) Weller EB, Kloos AD, Kang J, Weller RA. Depression in children and adolescents: Does gender make a difference? Curr Psychiatr Rep 2006; 8: 108-114.
5) Hauenstein EJ. Depression in adolescence. J Obstet Gynecol Neonatal Nurs 2003; 32: 239-248.
6) Richardson LP, Katzenellenbogen R. Childhood and adolescent depression: The role of primary care providers in diagnosis and treatment. Curr Probl Pediatr Adolesc Health Care 2005; 35: 1-24.
7) Sihvola E, Keski-Rahkonen A, Dick DM, Pulkkinen L, Rose RG, Martunnen M, Kaprio J. Minor depression in adolescence: Phenomenology and clinical correlates. J Affect Disord 2007; 97: 211-218.
8) Renouf AG, Kovacs M, Mukerji P. Relationship of depressive, conduct, and comorbid disorders and social functioning in childhood. J Am Acad Child Adolesc Psychiatr 1997; 36: 998-1004.
9) Angold A, Costello EJ, Erkanli A. Comorbidity. J Child Psychol Psychiatr 1999; 40: 57-87.
10) Angold A, Erkanli A, Farmer EM, Fairbank JA, Burns BJ, Keeler G, Costello EJ. Psychiatric disorder, impairment, and service use in rural African American and white youth. Arch Gen Psychiatr 2002; 59: 893-901.
11) Paris J. Recent research in personality disorders. Preface. Psychiatr Clin North Am 2008; 31: 21-22.
12) Oquendo MA, Mann JJ. Suicidal behavior: a developmental perspective. Psychiatr Clin North Am 2008; 31: 23-26.
13) Sepede G, Gambi F, De Berardis D, Brocco C, Nacci M, Campanella D, et al. Somatic complaints and depressive symptoms in adolescence. Ital J Psychopathol 2004; 10: 343-348.
14) Carlson G-A, Kashani J-H. Phenomenology of major depression from childhood through adulthood: Analysis of three studies. Am J Psychiatr 1988; 145: 1222-1225.
15) Toros F, Gamsiz Bilgin N, Bugdayci R, Sasmaz T, Kurt O, Camdeviren H. Prevalence of depression as measured by the CBDI in a predominantly adolescent school population in Turkey. Eur Psychiatr 2004; 19: 264-271.
16) Patton G-C, Coffey C, Posterino M, Carlin J-B, Wolfe R. Adolescent depressive disorder: A population based study of ICD-10 symptoms. Aust N Z J Psychiatr 2000; 34: 741-747.
17) Buckner JD, Joiner TEJ, Pettit JW, Lewinsohn PM, Schmidt NB. Implications of the DSM's emphasis on sadness and anhedonia in major depressive disorder. J Psychiatr Res 2008; 159: 25-30.
18) Bohman H, Jonsson U, Von Knorring AL, Von Knorring L, Paaren A, Olsson G. Somatic symptoms as a marker for severity in adolescent depression. Acta Paediatr 2010; 99: 1724-1730.
19) Diagnostic and Statistical Manual of Mental Disorders, Fourth edition, Text Revision. Washington, DC, American Psychiatric Association; 2000.
20) Kovacs M, Obrosky DS, Sherrill J. Developmental changes in the phenomenology of depression in girls compared to boys from childhood onward. J Affect Disord 2003; 74: 33-48.
21) Crowe M, Ward N, Dunnachie B, Roberts M. Characteristics of adolescent depression. Int J Ment Health Nurs 2006; 15: 10-18.
22) Bennett DS, Ambrosini P-J, Kudes D, Metz C, Rabinovich H. Gender differences in adolescent depression: Do symptoms differ for boys and girls? J Affect Disord 2005; 89: 35-44.
23) Bearman SK, Stice E. Testing a gender additive model: The role of body image in adolescent depression. J Abnorm Child Psychol 2008; 36: 1251-1263.

24) Kovacs M, Goldston D, Gatsonis C. Suicidal behaviors and childhood-onset depressive disorders: A longitudinal investigation. J Am Acad Child Adolesc Psychiatr 1993; 32: 8-20.

25) Pelkonen M, Marttunen M, Pulkkinen E, Laippala P, Aro H. Characteristics of out-patients adolescents with suicidal tendencies. Acta Psychiatr Scand 1997; 95: 100-107.

26) Essau CA, Conradt J, Petermann F. Frequency, comorbidity and psychosocial impairment of depressive disorders in adolescents. J Adolesc Res 2000; 15: 470-481.

27) Pantusa MF, Berardi M, Paparo S, Scornaienchi C. Differenze di genere e sintomatologia depressiva in adolescenza. Relazioni tra autostima, sintomi depressivi e ideazione suicidarla. It J Psychopatol 2006; 12: 407-414.

28) Tuisku V, Pelkonen M, Karlsson L, Kiviruusu O, Holi M, Ruuttu T, Punamäki RL, Marttunen M. Suicidal ideation, deliberate self-harm behaviour and suicide attempts among adolescent outpatients with depressive mood disorders and comorbid axis I disorders. Eur Child Adolesc Psychiatr 2006; 15: 199-206.

29) Vitiello B. Prevention and treatment of child and adolescent depression: Challenges and opportunities. EPS 2011; 20: 37-43.

30) Hendren R, McCarthly M. Child and adolescent psychiatry for the general psychiatrist. Psychiatr Clin North Am 2009; 32: 13-15.

31) National Institute for Health and Clinical Excellence, NICE (2005). Depression in children and young people: Identification and management in primary, community and secondary care. Clin Guidel 28. http://guidance.nice.org.uk/CG28/niceguidance/pdf/English

32) Emislie G, Kratochvil C, Vitiello B, Silva S, Mayes T, McNulty S, Weller E, Waslick B, Casat C, Walkup J, Pathak S, Rohde P, Posner K, March J. Treatment for adolescent with depression study (TADS): safety results. J Am Acad Child Adolesc Psychiatr 2006; 45: 1440-1455.

33) Barbui C, Esposito E, Cipriani A. Selective serotonin reuptake inhibitors and risk of suicide: A systematic review of observational studies. CMAJ 2009; 180: 291-297.

34) American Academy of Child and Adolescent Psychiatry. Practice parameter on the use of psychotropic medication in children and adolescents. J Am Acad Child Adolesc Psychiatr 2009; 8: 961-973.

35) Goodyer I, Dubicka B, Wilkinson P Kelvin R, Roberts C, Byford S, Breen S, Ford C, Barrett B, Leech A, Roth¬well J, White L, Harrington R. Selective serotonin reuptake inhibitors (SSRIs) and routine specialist care with and without cognitive behavior therapy in adolescents with major depression: Randomized controlled trial. Br Med J 2007; 335: 142.

36) Gentile S. Antidepressant use in children and adolescents diagnosed with major depressive disorder: What can we learn from published data? Rev Recent Clin Trials 2010; 5: 63-75.

37) Masi G, Liboni F, Brovedani P. Pharmacotherapy of major depressive disorder in adolescents. Expert Opin Pharmacother 2010; 11: 375-386.

38) Berard R, Fong R, Carpenter DJ, Thomason C, Wilkinson C. An international, multicenter, placebo-controlled trial of paroxetine treatment in adolescents with major depressive disorder. J Child Adolesc Psychopharmacol 2006; 16: 59-75.

39) Emslie GJ, Findling RL, Yeung PP, Kunz NR, Li Y. Venlafaxine ER for treatment of pediatric subjects with depression: Results of two placebo-controlled trials. J Am Acad Child Adolesc Psychiatr 2007; 46: 479-488.

40) Reeves RR, Ladner ME. Antidepressant-induced suicidality: An update. CNS Neurosci Ther 2010; 16: 227-234.

41) Sceeweiss S, Patrick AR, Solomon DH, Dormuth CR, Miller M, Metha J, Lee JC, Wang PS. Comparative safety of antidepressant agents for children and adolescents regarding suicidal acts. Pediatrics 2010; 125: 876-888.

42) Dudley M, Goldney R, Hadzi-Pavlovic D. Are adolescents dying by suicide taking SSRI antidepressants? A review of observational studies. Austral Psychiatr 2010; 18: 242-245.

43) Kuba T, Yakushi T, Fukuhara H, Nakamoto Y, Singeo STJ, Tanaka O, Kondo T. Suicide-related events among child and adolescent patients during short-term antidepressant therapy. Psychiatr Clin Neurosci 2011; 65: 239-245.

44) March J, Silva S, Petrycki S, Curry J, Wells K, Fairbank J, Burns B, Domino M, McNulty S, Vitiello B, Severe J. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents with Depression Study (TADS) randomized controlled trial. JAMA 2004; 292: 807-820.

45) Treatment for Adolescents with Depression Study Team. Treatment for Adolescents with Depression Study (TADS): rationale, design, and methods. J Am Acad Child Adolesc Psychiatr 2003; 42: 531-542.

46) March JS, Vitiello B. Clinical messages from the treatment for adolescents with depression study (TADS). Am J Psychiatr 2009; 166: 1118-1123.

47) Dubicka B, Elvins R, Roberts C, Chick G, Wilkinson P, Goodyer I-M. Combined treatment with cognitive-behavioural therapy in adolescent depression: meta analysis. B J Psychiatr 2010; 197: 433-440.

48) Brunstein-Klomek A, Zalsman G, Mufson L. Interpersonal Psychotherapy for Depressed Adolescents (IPT-A). Isr J Psychiatr Relat Sci 2007; 44: 40-46.

49) Gunlicks-Stoessel M, Mufson L, Jekal A, Turner JB. The impact of perceived interpersonal functioning on treatment for adolescent depression: IPT-A versus treatment as usual in school-based health clinics. J Consult Clin Psychol 2010; 78: 260-267.

50) Klein JB, Jacobs RH, Reinecke MA. Cognitive-behavioural therapy for adolescent depression: a meta-analytic investigation of changes in effect-size estimates J Am Acad Child Adolesc Psychiatr 2007; 46: 1403-1413.

51) Scott A. Cognitive behavioural therapy and young people: An introduction. J Fam Health Care 2009; 19: 80-82.

52) Muñoz RF, Cuijpers P, Smit F, Barrera AZ, Leykin Y. Prevention of major depression. Annu Rev Clin Psychol 2010; 27: 181-212.

53) Harrington R, Campbell F, Shoebridge P, Whittaker J. Meta-analysis of CBT for depression in adolescents. J Am Acad Child Adolesc Psychiatr 1998; 37: 1005-1007.

54) Cheung AH, Zuckerbrot RA, Jensen PS, Ghalib K, Laraque D, Stein RE. GLAD-PC Steering Group. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): II. Treatment and ongoing management. Pediatrics 2008; 121: 227.

55) DeRubes RJ, Siegle GJ, Hollon SD. Cognitive therapy versus medication for depression: Treatment outcomes and neural mechanisms. Nat Rev Neurosci 2008; 9: 788-796.

56) Kennard B, Emslie GJ, Mayes TL, Nightingale-Teresi J, Nakonezny PA, Hughes JL, Jones JM, Tao R, Stewart SM, Jarrett RB. Cognitive-behavioral therapy to prevent relapse in pediatric responders to pharmacotherapy for major depressive disorder. J Am Acad Child Adolesc Psychiatr 2008; 47: 1395-1404.

57) Guidano VF, Liotti G. Cognitive Processes and Emotional Disorders. New York: Guilford; 1983.

58) Guidano VF. Complexity of the Self. New York: Guilford; 1987.

59) Guidano VF. The Self in Progress. New York: Guilford; 1991.

60) Nardi B, Pannelli G. Adolescent depression: How to cope with turmoil and development of self negativity. Med Mind Adol 1998; 13: 65-78.

61) Nardi B, Bellantuono C. A new adaptive and evolutionary conceptualization of the Personal Meaning Organization (P.M.O.) framework. Eur Psychother 2008; 8: 5-16.

62) Nardi B. Guidelines on the construction of a post-rationalist therapeutic approach. Eur Psychother 2010; 9: 57-67.