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A RETROSPECTIVE STUDY OF HOSPITALIZED ADOLESCENTS SUFFERING FROM DEPRESSIVE CONDUCT DISORDER

ABSTRACT

The present study evaluated the use of psychotropic medications in hospitalized adolescents suffering from depressive conduct disorder. In addition, the efficacy of the hospital treatment was estimated. The study sample comprised 13 to 17-year-old adolescents (n = 39) treated due to depressive conduct disorder in the two psychiatric inpatient units for adolescents in Kuopio University Hospital, Finland during the years 2002–2011. The demographic and clinical data of the adolescents as well as medication details were collected from the adolescents' medical files. In addition to psychosocial interventions, psychotropic medications were frequently utilized in the inpatient treatment. Antidepressants were utilized in two out of every three hospitalizations and they were prescribed similarly to both genders. Fluoxetine, mirtazapine, citalopram and escitalopram were the most commonly prescribed antidepressants. Antipsychotic drugs were prescribed more often to girls than to boys. Quetiapine and olanzapine were the most often utilized antipsychotic drugs. Quetiapine was used, especially to treat girls and also those in voluntary treatment, whereas olanzapine was often prescribed to the adolescents involuntarily hospitalized. Other types of disorder-specific medications were also used to relieve the symptoms of concomitant sleep disorder or anxiety. During the psychiatric inpatient treatment, the psychosocial functioning of the adolescents improved markedly, and their depressive symptoms and feelings of hopelessness became relieved. The treatment outcome was estimated by the staff of the psychiatric units to be satisfactory in 25.5% of inpatient treatments. Over 40% of hospitalizations were discontinued due to the poor efficacy of the treatment. Depressive conduct disorder is a challenging disorder to treat. In addition to psychosocial interventions, pharmacological interventions aiming at specific clinical symptoms, such as depression, anxiety, sleeping disorders and aggression, represent an important part of a comprehensive therapeutic approach.

KEY WORDS: ADOLESCENT, DEPRESSION, CONDUCT DISORDER, DRUG TREATMENT, HOSPITALIZATION

INTRODUCTION

In ICD-10, a depressive conduct disorder simultaneously fulfills the general diagnostic criteria for a conduct disorder (F91) and those for one of the mood disorders (F30-F39). A conduct disorder is characterized by a variety of repetitive antisocial behaviours in which the basic rights of others or major age-appropriate social norms or rules are violated (1). Conduct disorder symptoms can be classified into four main subscales: 1. aggression towards people and animals, 2. destruction of property, 3. deceitfulness or theft, and 4. serious violations of rules. The typical signs of depression are: 1. depressed mood for at least for two weeks, 2. loss of interest or pleasure in activities that are normally pleasurable, 3. decreased energy or increased fatigability, and in addition at least one of the following symptoms: loss of confidence or self-esteem, unreasonable feelings of self-reproach or excessive and inappropriate guilt, recurrent thoughts of death or suicide, or any suicidal behaviour, evidence of a diminished ability to think or concentrate such as indecisiveness or vacillation, change in psychomotor activity, with agitation or retardation, sleep disturbance, change in appetite with a corresponding weight change (5).

The prevalence of conduct disorder in adolescents is approximately 5–10%, and it is more common in boys than in girls (2,3,4). However, it has been reported that a conduct disorder in conjunction with a depressive disorder occurs more frequently in girls (2).

Although a depressive conduct disorder should be treated primarily in an outpatient setting (5), when psychiatric inpatient treatment is needed, a short-term hospitalization focusing on the management of an acute crisis is usually recommended. There are situations that may require serious consideration of involuntary psychiatric hospitalization, such as severe impulse control problems with uncontrolled or threatened violence and severe suicidal ideation. In their review, Tcheremissine and Lieving postulated (6) that several drug groups could be effective therapeutic options for children and adolescents with conduct disorder and comorbid psychiatric conditions. However, the Finnish current care guidelines for conduct disorder in children and adolescents (7) recommend the use of risperidone or lithium, whereas fluoxetine, escitalopram, sertraline and duloxetine are the first-line medicines to treat adolescent depression (5,8).

The aims of this study were to examine the efficiency of the hospital treatment in hospitalized adolescents suffering from a depressive conduct disorder, gender differences of symptoms and to especially evaluate the use of psychotropic medications during hospitalization.

METHODS

This study sample comprised 13 to 17-year-old adolescents (n = 39; 23 girls, 16 boys) treated due to depressive conduct disorder (F92.0) in the two psychiatric inpatient units for adolescents in Kuopio University Hospital, Finland during the years 2002–2011. The decision for hospital treatment was made by psychiatrist. The psychiatric diagnoses were assessed using the ICD-10 classification. The demographic and clinical data of the adolescents as well as medication details were collected from the adolescents' medical files.

These two psychiatric units followed the principles of community care. Inpatient treatments involved several interventions including a thorough psychiatric examination, individual therapy, sessions with parents or guardians, assessments by a psychologist or occupational therapist, physiotherapy, somatic consultation and psychotropic medication when appropriate (9). Both voluntary and involuntary treatments were provided. These two psychiatry units operated as a tertiary care centre for the catchment area of North Savo District serving around one million inhabitants.

The permission for this study was provided by the ethical committee of Kuopio University Hospital and University of Eastern Finland and by the Medical Director of the University Hospital of Kuopio. Notification of the research was delivered in advance of data collection to Data Protection Ombudsman.

PSYCHIATRIC ASSESSMENTS

Depressive symptoms of adolescents were assessed by patients' self-rating with the Beck Depression Inventory (BDI) scale (10), which yields a total score from 0 to 63. The following interpretation of severity of depression scores was used: 0-9 minimal depressive symptoms, 10-18 mild to moderate, 19-29 moderate or severe depressive symptoms, and 30-63 severe depression symptoms.

Feelings of hopelessness in the adolescents were assessed by a self-rating questionnaire of hopelessness (Beck Hopelessness Scale, BHS), which is a 20-item, self-administered rating scale measuring an adolescent's negative expectancies concerning him/herself and their future life

(11). The total score ranges from 0 to 20, and the level of hopelessness increases with increasing scores. Based on the original cut-off points, the subjects were classified into four groups: 0–3 = no hopelessness at all, 4–8 = mild hopelessness, 9–14 = moderate hopelessness, and 15–20 = severe hopelessness (11).

The staff team assessed patients' psychosocial functioning by the Children's Global Assessment of Scale (CGAS), which measures psychological and social functioning. CGAS scores range from 100 (extremely high functioning) to 1 (severely impaired) (12). The scores of BDI, BHS and CGAS were taken into account for the assessment of treatment outcome only if they were reported both at entry and on discharge.

STATISTICAL ANALYSIS

The data were analysed using the GraphPadPrism program. Continuous variables were categorized as mean (±SD, range) and categorical variables as percentages. The statistical significance for categorical variables was analysed using Chi-squared test or Fisher´s exact test when the groups were small. Mann-Whitney U test was used for numeric variables of independent samples, whereas for dependent variables (BDI, BHS, CGAS) Wilcoxon signed rank test was applied to compare group means. In all analyses, a significance level of $p<0.05$ was set.

RESULTS

The adolescents examined in this study had a total of 51 inpatient treatment periods, which meant there were 1.3 inpatient treatments per adolescent. Twenty-one treatment periods (41.2%) represented the first time that these adolescents had been hospitalized in the psychiatric ward (*Table 1*). In both genders, the median length of hospital treatment was 8 days (range 2-60 days).

ADOLESCENTS' PSYCHIATRIC SYMPTOMS

Self-destructive behaviour, a wish to die and behavioural/conduct problems were the most common symptoms encountered in these adolescents (*Table 1)*. Self-injury and sleep disorders tended to be typical symptoms more evident in girls, whereas theft and vandalism were more common behaviours in boys. Anxiety and substance/alcohol misuse were also relatively common symptoms and comorbid psychiatric diagnoses were reported in 15.4% of the adolescents. Mental and behavioural disorders due to alcohol or other psychoactive substance misuse were the most common comorbidity (n = 3).

At entry, girls had statistically significantly higher BDI and BHS scores than their male counterparts, but there was no gender difference in the CGAS scores (*Figure 1*). On discharge, BDI scores had become significantly reduced and CGAS scores increased both in girls and in boys, but BHS scores were reduced statistically significantly only in girls.

Table 1: The characteristics of the study sample

	Hospitalizations		
	Girls (n=30) n (%)	**Boys (n=21) n (%)**	**Statistical significance**
Mean age at admission, mean (SD)	15.6 years (1,0)	15,7 (1.3)	ns
First psychiatric inpatient treatment	14 (51.9 %)	7 (33.3 %	ns
Voluntary treatment	24 (80.0 %)	11 (52.4 %)	$p<0.05$ ($\chi2=4,377$, df=1)
Living in primary family (at least with one biological parent)	6 (22.2 %)	11 (52.4 %)	$p<0.05$ ($\chi2=5,829$, df=1)
Self-destructive thoughts, death wishes	22 (73.35 %)	11 (52.4 %)	ns
Self-injury	23 (76.7 %)	8 (38.1 %)	$p<0.01$ ($\chi2=7,710$, df=1)
Behavioural/conduct problems	18 (60.0 %)	17 (81.0 %)	ns
Sleep disorders	17 (56.7 %)	7 (33.3 %)	ns
Anxiety symptoms	15 (50.0 %)	13 (61.9 %)	ns
Substance abuse	15 (50.0 %)	11 (52.4 %)	ns
Suicide attempt	5 (16.7 %)	2 (9.5 %)	ns
Theft, vandalism	1 (3.3 %)	6 (28.6 %)	$p<0.01$ ($\chi2=6,645$,.df=1)
Comorbid psychiatric diagnosis	4 (13.3 %)	2 (9.5 %)	ns

SD = standard deviation, ns = not significant, $\chi2$ = chi square test, df = degree of freedom

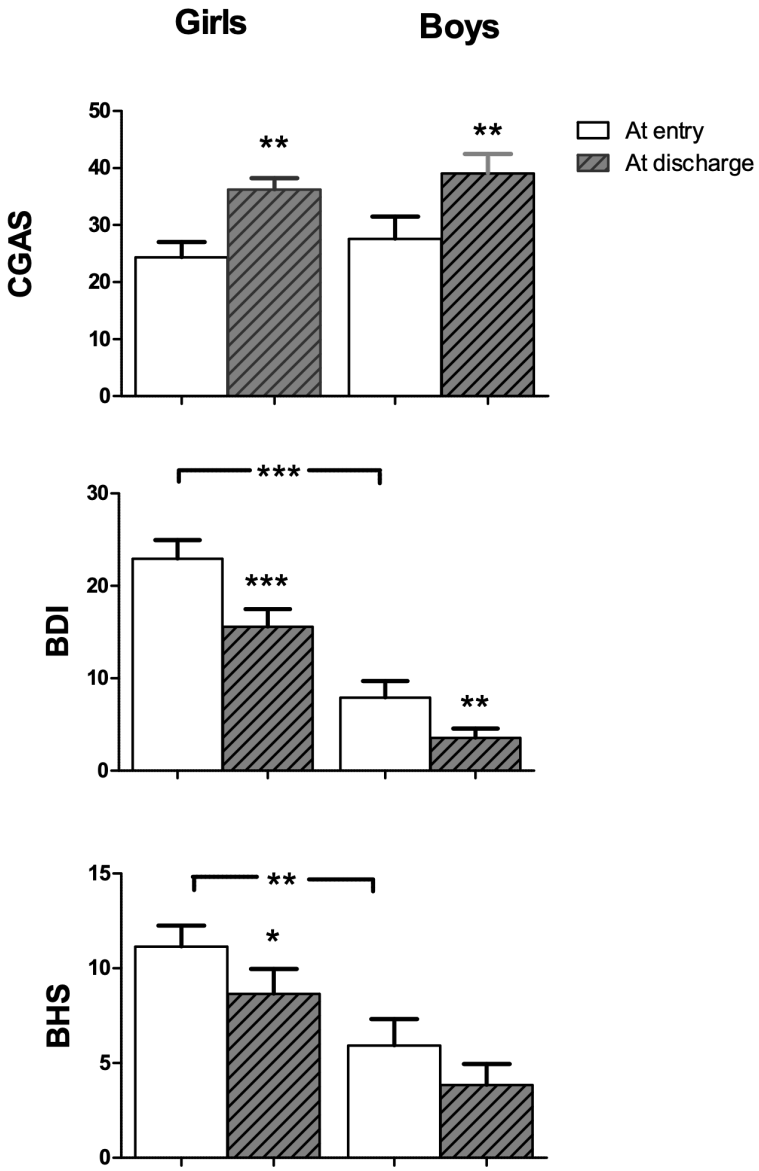

Figure 1: The scores of Children's Global Assessment of Scale (CGASa), depressive symptoms (BDI) and feeling of hopelessness (BHSb) at entry and at discharge in girls and boys (n=30 and n=21 treatment periods, respectively) suffering from a depressive conduct disorder; adata missing from 22 treatment periods, bdata missing from 18 treatment periods. Mean+SEM. Statistical significance: * p<0.05, ** p<0.01, ***p<0.001.

TREATMENT OUTCOME

At the end of hospital treatment, the outcome of the treatment was estimated by the staff team despite the positive changes in the psychiatric assessments (BDI, BHS, CGAS). Only every fourth hospitalization (25.5%) ended with satisfactory clinical results. Poor efficacy of the treatment was the most common reason (43.1%) to end the psychiatric inpatient treatment. This could be due to the motivational deficits in some of the adolescents.

PSYCHOTROPIC MEDICATIONS

Psychotropic medications were utilized very often in the inpatient treatment, i.e., in 80% of the treatment periods. Adolescents were administered approximately 1.9 medications (range 0-6) during their hospital stay.

The majority of adolescents had started their antidepressant medications before being hospitalized. Only 36% of antidepressant medications were started during the psychiatric inpatient treatment, usually for adolescents who were in a psychiatric ward for the first time. Antidepressants were utilized in two out of every three hospitalizations (*Table 2*) and they were prescribed similarly to both genders. Fluoxetine, mirtazapine, citalopram and escitalopram were the most commonly prescribed antidepressants; duloxetine was also used occasionally. Every third girl and every fourth boy were being treated with antidepressants together with an antipsychotic medication.

Most of the antipsychotic medications were also initiated before the adolescents were taken into the psychiatric ward, i.e., only 38% of antipsychotic medications were started during the hospital treatment. Antipsychotic drugs were prescribed more often to girls than to boys (*Table 2*). Quetiapine and olanzapine were the most often utilized antipsychotic drugs followed by risperidone and aripiprazole. Clozapine, flupentixol, haloperidol and ziprasidone were prescribed to only a few individual patients. Quetiapine was prescribed especially to girls; this drug was also administered to those who were hospitalized voluntarily, whereas olanzapine was most often prescribed to adolescents subjected to involuntary treatment. There were no other differences in the medications of adolescents hospitalized voluntarily and those hospitalized involuntarily.

Anti-anxiety medications were more often needed in the treatment of girls compared to boys (*Table 2*). Oxazepam (n = 5) was the most common anxiolytic used in this study. Sedatives also tended to be more often prescribed to girls (*Table 2*), with zopiclone (n = 13) being the most commonly prescribed sedative. In ten (19.6%) treatment periods, the adolescents were treated in the hospital's psychiatric ward without being administered any psychotropic medication.

Figure 2 shows CGAS, BDI and BHS scores of those adolescents (n = 10) receiving no psychotropic drug treatment during their hospital stay in comparison to the adolescents with psychotropic medication. The comprehensive treatment in the psychiatric wards increased CGAS scores significantly in these ten patients, but because their BDI and BHS scores were low already at entry, the inpatient treatment caused no change in these values. From these ten adolescents, seven required no more psychiatric hospitalization in the years 2002-2011.

Table 2: Psychotropic drug treatments in adolescents with depressive conduct disorder

	Hospitalizations		
	Girls (n=30) n (%)	**Boys (n=21) n (%)**	**Statistical significance**
Antidepressants	**19 (63.3 %)**	**14 (66.7 %)**	ns
Fluoxetine	6 (20.0 %)	2 (9.5 %)	ns
Mirtazapine	4 (13.3 %)	4 (19.0 %)	ns
Citalopram	3 (10.0 %)	4 (19.0 %)	ns
Escitalopram	2 (6.7 %)	4 (19.0 %)	ns
Duloxetine	4 (13.3 %)	0	ns
Antipsychotics	**24 (80.0 %)**	**10 (47.6 %)**	$p<0.05$ ($\chi2=5,829$, df=1)
Quetiapine	11 (36.7 %)	2 (9.5 %)	$p<0.05$ ($\chi2=4,792$, df=1)
Olanzapine	7 (23.3 %)	3 (14.3 %)	ns
Risperidone	1 (3.3%)	3 (14.3 %)	ns
Aripiprazole	3 (10.0 %)	0	ns
Other	2 (6.7 %)	2 (9.5 %)	ns
Antidepressants + antipsychotics	**11 (36.7 %)**	**5 (23.8 %)**	ns
Anxiolytics	**10 (33.3 %)**	**2 (9.5 %)**	$p<0.05$ ($\chi2=3,892$, df=1)
Sedatives	**11 (36.7 %)**	**4 (19.0 %)**	ns

SD = standard deviation, ns = not significant, $\chi2$ = chi square test, df = degree of freedom

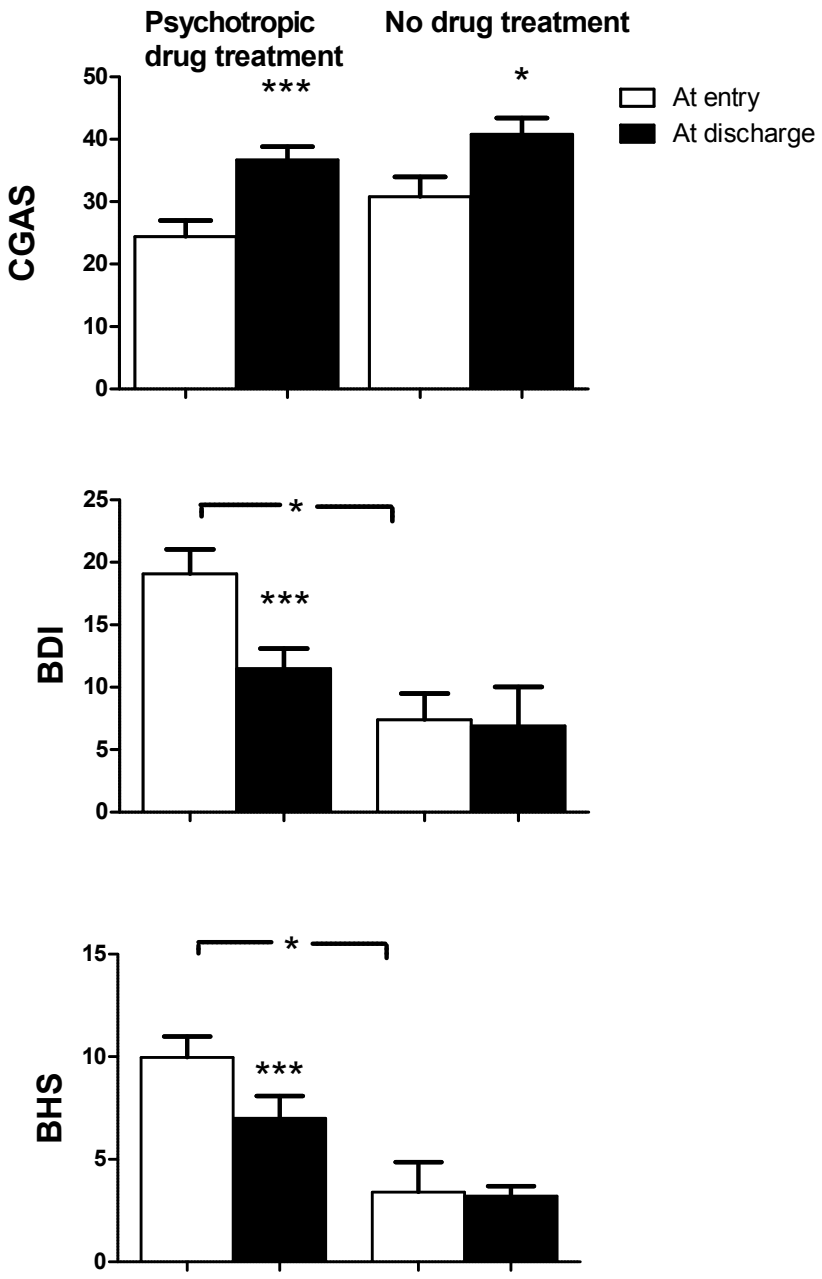

Figure 2: The scores of Children's Global Assessment of Scale (CGASa), depressive symptoms (BDI) and feeling of hopelessness (BHSb) at entry and at discharge in adolescents with psychotropic medication and those without drug treatments (n=41 and n=10 treatment periods, respectively); adata missing from 22 treatment periods; bdata missing from 18 treatment periods. Mean+SEM. Statistical significance: * p<0.05, ***p<0.001.

ADOLESCENTS WITH SEVERAL HOSPITALIZATIONS

Fourteen adolescents in this study (35.9%) required several hospitalizations (range 2-6) in the years 2002-2011. In a six-month period, girls tended to return to the hospital's psychiatric ward more often than boys (46.7% vs. 19.0% $\chi 2 = 4{,}126$, df = 1, $p<0.05$), but later, at 12 months, the difference was no longer statistically significant (54.9% vs. 28.6%).

Those adolescents who returned to inpatient care within six months exhibited high BDI and BHS scores on discharge when compared to the values of the other subjects (*Figure 3*). All of them had exhibited self-destructive thoughts and/or wish to die (*Table 3*), many of them had displayed signs of self-harm or had a history of a suicide attempt and some also suffered from hallucinations. Background information from the medical files revealed that most of them (83.3%) had lived in an out-of-home placement. Common reasons to end the inpatient care had been poor efficacy of the treatment (38.9%) and a need for short-term inpatient care due to acute crisis of adolescents (22.2%). A better clinical situation was mentioned as a reason to end the hospitalization only in 16.7% of treatment periods.

Table 3. Comparison of adolescents returning to hospital treatment in six months with others

	Hospitalizations		
	Back in six months (n=18)	**Others (n=33)**	**Statistical significance**
Self-destructive thoughts, death wishes	18 (100.0 %)	22 (66.7 %)	$p<0.01$ ($\chi 2=7{,}65$, df=1)
Self-injury	16 (88.9 %)	14 (42.4 %)	$p<0.01$ ($\chi 2=10{,}38$, df=1)
Anxiety symptoms	12 (66.7 %)	16 (48.5 %)	ns
Sleep disorders	8 (44.4 %)	16 (48.5 %)	ns
Hallucinations	8 (44.4 %)	4 (12.1 %)	$p<0.01$ ($\chi 2=8{,}36$, df=1)
Suicide attempt	5 (27.8 %)	2 (6.1 %)	$p<0.05$ ($\chi 2=4{,}64$, df=1)

ns = not significant, $\chi 2$ = chi square test, df = degree of freedom

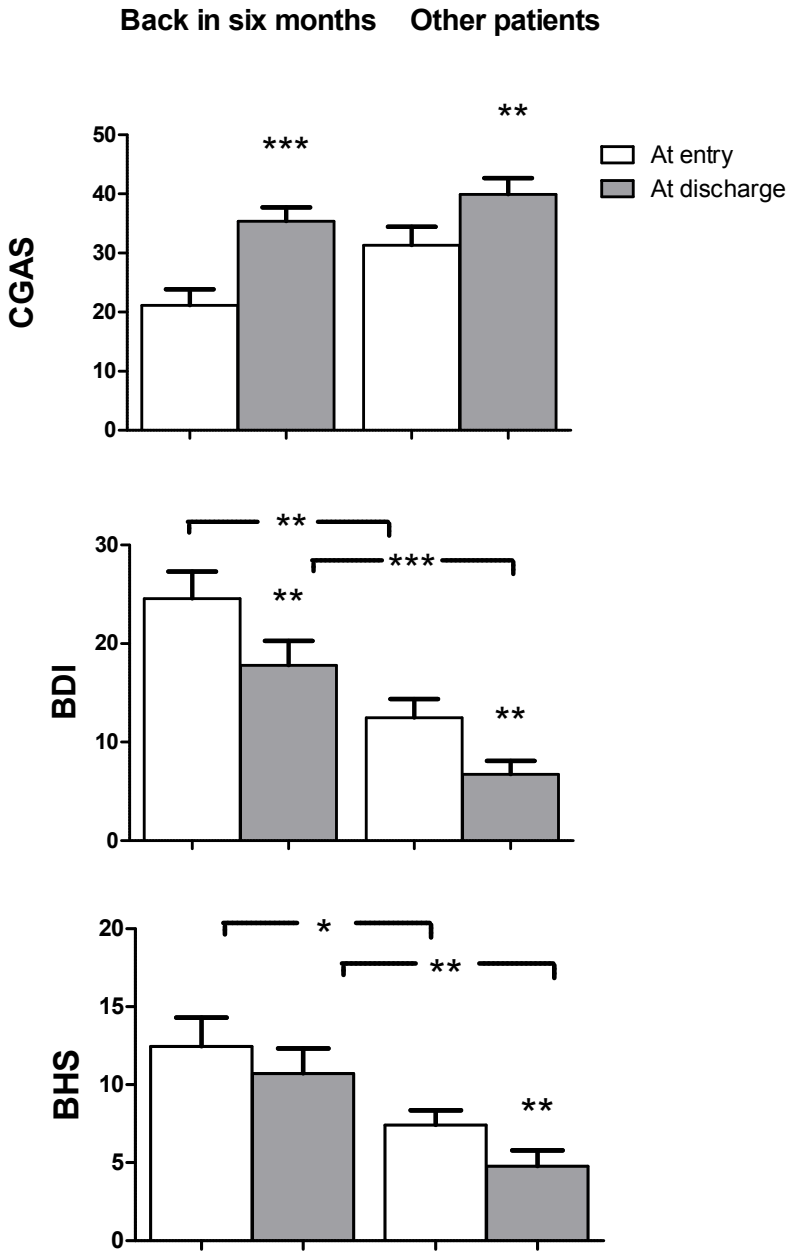

Figure 3: The scores of Children's Global Assessment of Scale (CGASa), depressive symptoms (BDI) and feeling of hopelessness (BHSb) at entry and at discharge in adolescents who were rehospitalized within six months compared to other adolescents in this study (n=18 and n=33 treatment periods, respectively); adata missing from 22 treatment periods, bdata missing from18 treatment periods. Mean+SEM. Statistical significance: * p<0.05, ** p<0.01, ***p<0.001

DISCUSSION

This clinical study examined the efficacy and especially the use of psychotropic medications in adolescents hospitalized due to a depressive conduct disorder. The inpatient treatment of adolescents with depressive conduct disorder is demanding: while it is multi-professional, quite often psychotropic drugs are also needed as a part of the psychiatric therapy. The psychiatric treatment outcome estimated by the staff teams was satisfactory in only 25% of the inpatient treatments, but most of the adolescents in this study no longer needed to return to psychiatric inpatient treatment during the ten-year study period (2002-2011). Psychotropic drugs, particularly antidepressants and antipsychotics, were commonly used in the treatment of adolescents. Antipsychotics and anti-anxiety drugs were more often prescribed to girls than to boys. The use of antipsychotic was often off-label use.

Conduct disorders are more common in boys than in girls (2,3,4), but in this study most of the adolescents with a depressive conduct disorder were girls. It may be that there is a lower threshold for girls with severe depressive conduct disorder being hospitalized. On the other hand, it has been reported that a conduct disorder frequently co-occurs with a depressive disorder, especially in girls (2). In line with this, at the time of arrival to the hospital, the BDI and BHS scores of girls were clearly higher when compared to the respective values of boys.

Disorders with conduct problems should primarily be treated with psychosocial interventions (7). However, medications may be included as a part of the therapy in order to help in the control of aggressive or impulsive behaviour, and they may promote the adolescent's ability to benefit from the psychosocial interventions. In addition, a disorder-specific medication may be useful to treat concomitant sleep disorder or anxiety. Nowadays, psychotropic drugs are more commonly prescribed for children and adolescents (13,14), although scientific evidence about medication efficacy in young people tends to be scarce with the drugs often being prescribed off-label. The present study identified the frequent use of psychotropic medication in psychiatric wards for adolescents with a depressive conduct disorder. Both antidepressants and antipsychotics were often utilized in the inpatient care. This result is in line with the study of Dean et al. (15) who reported that most of the children and adolescents using mental health services in Brisbane, Australia, were receiving psychotropic medications. Here, psychotropic drugs were prescribed mainly to those with high depression BDI scores and intense feelings of hopelessness.

According to the current Finnish depression care guidelines (5), any antidepressant medication for children and adolescents should be started with fluoxetine. Sertraline, escitalopram and duloxetine are also thought to be effective in the treatment of depression in young people (5,8), but other selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs) can also be considered (5), although with caution. There are some reports that serotonergic antidepressants are able to reduce aggressive symptoms in children and adolescents with disruptive behaviour disorders, including conduct disorder (6). Here, SSRIs (fluoxetine, escitalopram and citalopram) as well as mirtazapine were the most frequently prescribed antidepressants. Since sleep disorders and anxiety were common symptoms of the adolescents, the sedative and anxiolytic effects of mirtazapine may partly explain why it was chosen so often as an antidepressant.

Adolescents with conduct problems and high levels of reactive aggression and severe emotion dysregulation can be treated with antipsychotics if psychosocial interventions have not led to a meaningful reduction in reactive aggression. In one meta-analysis, risperidone was revealed to exert short-term effects on irritability and reactive aggression in 5 to 18-year-old children and adolescents with disruptive behaviour disorders (16). Finnish current care guidelines for conduct disorder recommend risperidone but lithium may also be an option (7). In the present study, quetiapine and olanzapine were the most often prescribed antipsychotic drugs. Quetiapine was especially used to treat girls but also those in voluntary treatment, whereas olanzapine was often prescribed to the adolescents involuntarily hospitalized. According to some studies (6,17,18,19,20,21), quetiapine, olanzapine and aripiprazole may represent possible treatment options in aggressive youngsters with conduct problems, but the current Finnish care guidelines for conduct disorder (7) do not recommend them. Long-term use of antipsychotics can lead to weight gain, metabolic syndrome, increased prolactin secretion and extrapyramidal adverse effects (22,23) and therefore, the lowest effective dose should be administered for the shortest time possible.

During the psychiatric inpatient treatment, the adolescents' depressive symptoms and feelings of hopelessness were relieved and their psychosocial functioning improved, according to the mean changes in the scores of BDI, BHS and CGAS at entry and to discharge. These changes happened within a relatively short time, since the median

length of the hospitalizations was only eight days. The effects of antipsychotic or antidepressant drugs occur after a delay of weeks. If these medications were started during the psychiatric inpatient treatment, the effects of the medications would not have been soon visible, but the relief of anxiety and better sleep could have already improved adolescents' wellbeing. The psychosocial interventions used during the hospital stay also improved the psychosocial functioning of those young people having no psychotropic medications at all. The psychiatric treatment outcome was estimated by the staff of the psychiatric units, and the outcome was estimated to be satisfactory in only 25 % of the inpatient treatments. In line with this, 72% of adolescents still had low CGAS scores (CGAS<40) at discharge showing severely impaired psychosocial functioning. According to the professional staff, 43% of hospitalizations were discontinued due to the poor treatment efficacy. This treatment outcome differs from that of adolescents hospitalized due to depression. In young people with severe depression, a satisfactory clinical result can be obtained in as many as 66% of inpatient treatments; even in young individuals suffering from severe depression with psychotic symptoms, although a satisfactory clinical result was obtained less often, it was helpful in every second patient, i.e., in 58% of treatment periods (V. Snellman, personal communication). Most of the adolescents (67%), however, no longer needed to return to psychiatric inpatient treatment in our study period (2002-2011).

A small proportion of adolescents returned to psychiatric inpatient treatment within six months, even sometimes within a couple of days. These young people had high BDI and BHS scores at entry: they were suicidal, showed self-destructive behaviour and some of them suffered from psychotic symptoms. These findings are in line with earlier reports (24,25). Over 80% of these adolescents were living in an institution or in foster care. It has been reported that adolescents who have been placed to live away from home experience more psychiatric symptoms than their peers (26). On discharge, the BDI and BHS scores of these adolescents were still high. It could be speculated that the treatment period in the hospital should have been longer in the first place. However, the lack of motivation in cooperating and trying to resolve emotional problems or interpersonal conflicts, or simply the inability of these adolescents to adhere to the rules within the psychiatric units, might partly explain the poor treatment outcome. Thus, the inpatient care was mainly crisis management, whereas other measures involved, in foster care as well as in outpatient care, are needed.

LIMITATIONS OF THE STUDY

One limitation of this study is the small number of adolescents with a depressive conduct disorder. However, the study sample consisted of adolescent psychiatric patients hospitalized in the geographically large area of Eastern Finland, thus representing the most serious cases in this region's general adolescent population. Psychiatric diagnoses were made by clinicians who worked in psychiatric wards and using the ICD-10 diagnostic system without any structured interview, which would be more reliable. Secondly, the data were collected from patients' medical files that were not written for scientific purposes. Therefore, some CGAS and BHS data were missing and the results concerning the functional capacity and pessimistic attitude are not totally reliable. Furthermore, we had no access to the adolescents' outpatient information, and therefore it is not possible to estimate how well the whole psychiatric chain of care was working due to the fact that this important piece of information was lacking.

In conclusion, it is challenging to treat a depressive conduct disorder in adolescents. In addition to psychosocial interventions, pharmacological interventions aiming at specific clinical symptoms, such as depression, anxiety, sleeping disorders and aggression, represent an important component of the comprehensive therapeutic approach. More research concerning treatment of adolescents who have depressive conduct disorder is needed.

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References:

1. World Health Organization, 1992. *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines*. World Health Organization, Geneva

2. Fairchild G, Hawes DJ, Frick PJ, Copeland WE, Odgers CL, Franke B, Freitag CM, De Brito SA: *Conduct disorder*. Nat Rev Dis Primers 5(43):1-23, 2019

3. Ghandour RM, Sherman LJ, VladutiuCJ, Ali MM, Lynch SE, Bitsko RH, Blumberg SJ: *Prevalence and Treatment of Depression, Anxiety, and Conduct Problems in US Children*. J Pediatr 206: 256-267, 2019

4. Loeber R, Burke JD, Lahey BB, Winters A, Zera M: *Oppositional defiant and conduct disorder: a review of the past 10 years, part I*. J Am Acad Child Adolesc Psychiatry 39(12):1468-84, 2000

5. Depression. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim and the Finnish Psychiatric Society. Helsinki: The Finnish Medical Society Duodecim, 2022. Available online at: www.kaypahoito.fi

6. Tcheremissine OV, Lieving L M. *Pharmacological aspects of the treatment of conduct disorder in children and adolescents*. CNS Drugs 2006; 20: 549–65

7. Conduct Disorder. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim and the Finnish Society for Child Psychiatry, the Finnish Society for Adolescent Psychiatry and the Finnish Psychiatry Society. Helsinki: The Finnish Medical Society Duodecim, 2018. Available online at: www.kaypahoito.fi

8. Hetrick SE, McKenzie JE, Bailey AP, Sharma V, Moller CI, Badcock PB, Cox GR, Merry SN, Meader N: *New generation antidepressants for depression in children and adolescents: a network meta-analysis*. Cochrane Database Syst Rev. 5(5): CDO13674

9. Hintikka U: *Changes in Adolescents' Cognitive and Psychosocial Functioning and Self-Image During Psychiatric Inpatient Treatment*. Dissertation. Kuopio University Publications, Kuopio, Finland, 2007

10. Beck AT, Steer RA, Garbin MG. *Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation*. Clin Psychol Rev 8:77-/100, 1988

11. Beck AT, Weissman A, Lester D, Trexler L: *The measurement of pessimism: the Hopelessness Scale*. J Consult Clin Psychol 42:861–865, 1974

12. Schorre BEH, Vandvik IH: *Global assessment of psychosocial functioning in child and adolescent psychiatry: A review of three unidimensional scales (CGAS, GAP, GAPD)*. European Child & Adolescent Psychiatry, 13(5): 273-286, 2004

13. Lagerberg T, Molero Y, D'Onofrio BM, Fernandez de la Cruz L, Lichtenstein P, Mataix-Cols D, Rück C, Hellner C, Chang Z (2019) *Antidepressant prescription patterns and CNS polypharmacy with antidepressants among children, adolescents, and young adults: a population-based study in Sweden*. Eur Child Adoles Psy. 28(8):1137–45

14. Vartiainen J, Snellman V, Laukkanen E, Lecklin A: *Evidence on the benefits of antidepressants in the treatment of depression in children and adolescents is limited*. Dosis 2:196-215, 2020

15. Dean AJ, McDermot BM, Marshall RT: *Psychotropic medication utilization in a child and adolescent mental health service*. J Child Adolesc Psychopharmacol 16(3):273-285, 2006

16. Loy JH, Merry SN, Hetrick SE, Stasiak K: *Atypical antipsychotics for disruptive behaviour disorders in children and youths*. Cochrane Database Syst. Rev. 9, CD008559 (2017)

17. Ercan ES, Uysal T, Ercan E, Ardic A: *Aripiprazole in children and adolescents with conduct disorder: a single-center, open-label study*. Pharmacopsychiatry 45(1):13-19, 2012

18. Findling RL, Kauffman R, Sallee FR, Salazar DE, Sahasrabudhe V, Kollia G, Kornhauser DM, Vachharajani NN, Assuncao-Talbott S, Mallikaarjun S, Iwamoto T, McQuade RD, Boulton DW, Blumer J: *An open-label study of aripiprazole: pharmacokinetics, tolerability, and effectiveness in children and adolescents with conduct disorder*. J Child Adolescent Psychopharmacol 19(4):431-439, 2009

19. Kuperman S, Calarge C, Kolar a, Holman T, Barnett M, Perry P: *An open-label trial of aripiprazole in the treatment of aggression in male adolescents diagnosed with conduct disorder*. Ann Clin Psychiatry 23(4): 270-276, 2011

20. Masi G, Milone A, Veitri S, Iuliano R, Pfanner C, Pisano S: *Use of quetiapine in children and adolescents*. Pediatr Drugs 17:125-140, 2015

21. Masi GG, Milone A, Canepa G, Millepiedi S, Mucci M, Muratori F: *Olanzapine treatment in adolescent with severe conduct disorder*. Eur Psychiatry 21(1): 51-57, 2006

22. Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, Infate MC, Weiden PJ: *Antipsychotic-induced weight gain: a comprehensive research synthesis*. Am J Psychiatry 156(11):1686-1696, 1999

23. Correll CU: *Antipsychotic use in children and adolescents: minimizing adverse effects to maximize outcomes*. Am Acad Child Adolesc Psychiatry 47(1): 9-20, 2008

24. Ilomäki E, Hakko H, Ilomäki R, Räsänen P, STUDY-70 workgroup: *Gender differences in comorbidity of conduct disorder among adolescents in Northern Finland*. Int J Circumpolar Health 71:17393:1-8, 2012. doi: 10.3402/ijch.v71i0.17393

25. Simic M, Fombonne E: *Depressive conduct disorder: symptom patterns and correlates in referred children and adolescents*. Journal of Affective Disorders 62: 175-185, 2001

26. Mekonnen R, Noonan K, Rubin D: *Achieving Better Health Care Outcomes for Children in Foster Care*. Pediatr Clin North Am 56:405-415, 2009