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## ADOLESCENT INPATIENTS WITH A DEPRESSIVE DISORDER: TREATMENT OUTCOMES AND PSYCHOPHARMACOLOGICAL MEDICATION

### ABSTRACT

*This study examined the efficacy of psychiatric inpatient treatment and the use of psychopharmacological medication in adolescents with a depressive disorder. The study sample consisted of 13–17 years old adolescents (n=256) treated due to a depressive disorder in the two adolescent psychiatric units of Kuopio University Hospital, Finland, during the ten years 2002–2011. The data concerning demographic and clinical characteristics, treatment outcomes and medication were collected from the patients' medical records. Approximately 70% of hospitalizations terminated with satisfactory clinical results. Inpatient treatment was more beneficial for the patients with a non-psychotic depression, whereas every second adolescent with a psychotic depression had still low psychosocial functioning at discharge (median GAS scores at discharge 45 vs. 40,  $p=0.001$ ). Psychotropic medication was utilized in 95% of all hospitalizations. Mirtazapine, selective serotonin reuptake inhibitors (SSRIs) and atypical antipsychotics were the most frequently prescribed medications. Antidepressants and antipsychotics induced adverse events rather frequently (23% and 31%, respectively), but serious side effects such as worsening of psychiatric symptoms, cardiac problems and metabolic changes were rare. Psychopharmacological medication has to be individually tailored and require frequent monitoring of the clinical response, side effects and safety. Both clinical and controlled trials investigating the utility of psychopharmacological treatments in young patients are needed.*

**KEYWORDS: ADOLESCENT, DEPRESSIVE DISORDER, PSYCHIATRIC INPATIENT TREATMENT, TREATMENT OUTCOME, PSYCHOPHARMACOLOGICAL MEDICATION**

## INTRODUCTION

Depression is a common and serious psychiatric disorder in adolescents; the 12-month prevalence has been estimated to be 7.5% among US and 10.5% among European adolescents, but many more young persons, almost three out of every ten (29.2%) are estimated to have a subthreshold depression [1,2]. The lifetime prevalence of psychotic depression is estimated to be 0.5% [3]. The prevalence of depression is higher among girls, and it increases as adolescence proceeds [2].

Depression may have many long-term effects on the course of an individual's life, such as severe role impairment, problems at school and difficulties with social relationships [2,4]. Depressed adolescents have a higher risk for substance misuse, self-harm and suicidal behaviour. Furthermore, the occurrence of comorbid mental disorders, especially anxiety and behavioural disorders, is common. It is evident that the efficacious treatment of depression would not only reduce costs to society, but would also increase the quality of life of the adolescent and improve his/her mental health in the transition to adulthood.

Most depressive disorders in adolescents are treated in outpatient care, but hospitalization is needed if there is a high risk of serious self-harm, suicidality, self-neglect or severe impairment in psychosocial functioning. The principal treatment of depression in these young people consists of various therapeutic interventions [5,6]. First-line treatment of adolescents with mild or moderate depression is not antidepressant medication, but psychopharmacological intervention is needed in cases of severe and psychotic depression.

Psychopharmacological medication is often used “off-label” in underage patients, i.e., without an official indication. According to the database of the Social Insurance Institution of Finland, the number of prescriptions for antidepressants for young people has increased significantly in recent decades, with the same trend also being observed in other countries [7-10]. The prescribing of psychotropic medication to adolescents in hospital settings became more common in the 1990s; in 1991 only 29% of depressive adolescent inpatients were medicated, by 1999 that percentage had risen to 71% [11].

Although there are many antidepressants on the market, fluoxetine is the only compound that has shown therapeutic efficacy in clinical trials in the treatment of depression of teenage individuals [12] and the guidelines recommend it as the first-line antidepressant [5,6]. It is essential that patients must be monitored carefully at the start of therapy because

adverse events, even suicidal behaviour, are possible. If fluoxetine is inefficient or induces side effects, sertraline, citalopram and escitalopram are recommended. After remission, antidepressant medication should be continued for at least six months to prevent relapse.

The aims of this study were to examine the efficiency of the psychiatric inpatient treatment of adolescents suffering from depressive disorders and the use of psychopharmacological medication utilized during hospitalizations.

## METHODS

### SAMPLE

The study sample consisted of 13–17 years old adolescents (n=256, 87% females) treated due a depressive disorder in the two adolescent psychiatric units of Kuopio University Hospital, Finland, during the years 2002–2011. These units serve as a tertiary care centre for a catchment area of North Savo District, which has around one million inhabitants. Both voluntary and involuntary forms of treatment were provided. The treatment was individualized and consisted of therapeutic sessions with a case manager nurse at least once a week, along with different activities, family sessions, and somatic consultation and psychopharmacological medication when appropriate [13].

The criteria for inclusion in the study were a duration of hospitalization of at least five days and that data collected via the Beck Depression Inventory questionnaire (BDI) was available at both admission and discharge. Patients with a bipolar disorder or dysthymia were excluded from this study. In addition, patients with a depressive conduct disorder were excluded from the study because the results relating to these individuals have been published earlier [14]. Patients with cyclothymia were included.

### Data collection and assessment methods

The diagnosis of depression was made by a psychiatric interview according to ICD-10 (International Classification of Diseases, version 10) criteria as part of the clinical examination performed by a psychiatrist specializing in adolescent care. The patients' diagnoses at discharge were categorized into three groups according to the severity of depression diagnosis as follows: 1) mild/moderate depression or cyclothymia (F32.0, F32.1, F33.1, F34.0), 2) severe depression without psychotic symptoms (F32.2, F33.2) and 3) severe depression with psychotic symptoms (F32.3, F33.3) (*Table 1*). The clinical results are presented for these diagnostic groups.

Table 1. Characteristics of the psychiatric inpatient treatment periods of the adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

	Mild/moderate depression or cyclothymia	Severe depression without psychotic symptoms	Severe depression with psychotic symptoms	p-value
Treatment periods, n	85	183	81	
The first psychiatric hospitalization, n (%)	54 (64%)	113 (62%)	27 (33%)	< 0.001 ( $\chi^2(2)=21.234$ )
Involuntary treatment, n (%)	11 (13%)	29 (16%)	29 (36%)	< 0.001 ( $\chi^2(2)=17.400$ )
The length of hospitalization (days), median (range)	13 (5 – 86)	22 (5 – 96)	25 (5 – 369)	< 0.001

Demographic and clinical characteristic data including estimations of depressive symptoms (Beck Depression Inventory, BDI), hopelessness (Beck’s Hopelessness Scale, HS) and psychosocial functioning (Global Assessment Scale, GAS) were collected from the patients’ medical records.

BDI is a numeric self-rated scale used to measure the severity of depression in a subjective manner [15]. The scores range from zero to sixty-three; higher scores represent more severe depressive symptoms. Scores less than 13 indicate minimal depression, scores from 13 to 18 point to mild depression, scores from 19 to 29 refer to moderate depression and scores from 30 to 63 are evidence of severe depression.

HS is a numeric self-rated scale used to measure subjectively feelings of pessimism and hopelessness [16]. Its scores range from 0 to 20; values under nine refer to mild or insignificant hopelessness whereas scores of fifteen or more represent critical hopelessness.

GAS is a numeric scale used to assess an individual’s psychosocial functioning [17]. GAS scores were evaluated by the hospital staff team. The scores range from one to a hundred with the scale being divided into ten equal intervals. Low scores indicate poor psychosocial functioning with the upper value of a hundred representing superior functioning. Constant monitoring is needed when an individual’s scores are less than ten, scores less than 41 refer to severe psychosocial functional impairment in several areas whereas scores of seventy or more are regarded as a good functional capability.

In addition to BDI, HS and GAS scores, the data assessing the efficacy of psychiatric hospitalizations were collected from

the medical case summaries. The outcome of treatment was assessed as a dichotomous variable (satisfactory/non-satisfactory) and it was based on the estimation by the staff team. The data concerning psychotropic drug therapy including antidepressants, antipsychotics and anxiolytics as well as sedatives and other psychopharmacological medication, such as mood stabilizers, methylphenidate and naltrexone, were collected from the medical records.

#### STATISTICAL ANALYSES

The data were analysed using IBM SPSS Statistics 27 Software. Continuous variables were categorized as means or medians, and categorical variables as percentages. The statistical significance for categorical variables was analysed using Chi-squared test. For numeric variables of independent samples, Mann-Whitney U test was used to compare two groups and Kruskal-Wallis test to compare more than two groups. P values below 0.05 were used to indicate a statistically significant difference.

#### ETHICAL CONSIDERATIONS

The permission for this study was provided by the Research Ethics Committee of the Northern Savo Hospital District (the approval number 272/2016) and University of Eastern Finland and by the Medical Director of the University Hospital of Kuopio. Notification of the research was also delivered in advance of data collection to the Data Protection Ombudsman.

## RESULTS

### PATIENT CHARACTERISTICS

During the ten-year study period (2002–2011), there were 349 inpatient treatment periods (Table 1). Each patient had on average 1.4 (range of 1–9) hospitalizations during the study period. Over 60% of treatment periods with a diagnosis of cyclothymia or mild, moderate or severe depression without psychotic symptoms represented an individual’s first psychiatric hospitalization, whereas two out of every three patients with psychotic symptoms had been previously hospitalized for psychiatric symptoms. The median length of hospital treatment was 20 days (range 5–369 days). The longest treatment periods were observed in those patients with psychotic depression.

Most of the adolescents were females (Table 2). Self-destructive thoughts and/or behaviour, sleep problems and anxiety were common symptoms. A suicide attempt preceded every fifth hospitalization. Every fifth adolescent exhibited a comorbid psychiatric disorder. Neurotic, stress-related and somatoform disorders (6%), as well as eating disorders (5%) were the two most common comorbid psychiatric diagnoses. The first of these disorders was particularly evident in the patients diagnosed with either mild/moderate depression or cyclothymia with the latter comorbidity being more common in the adolescents suffering from severe depression without psychotic symptoms.

Table 2. Demographic and clinical characteristics of the adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

	Mild/moderate depression or cyclothymia	Severe depression without psychotic symptoms	Severe depression with psychotic symptoms	p-value
Age at admission, mean (range)	16.2 (13.6 – 17.9)	15.9 (13.3 – 17.9)	16.2 (13.6 – 17.9)	ns
Female, n (%)	76 (89%)	159 (87%)	75 (93%)	ns
Fostered, n (%)	16 (19%)	32 (17%)	17 (21%)	ns
Suicide attempts, n (%)	13 (15%)	47 (26%)	18 (22%)	ns
Self-destructive thoughts and/or behaviour, n (%)	76 (89%)	163 (89%)	78 (96%)	ns
Sleep disturbances, n (%)	56 (66%)	139 (76%)	50 (62%)	0.04 ( $\chi^2(2)=6.435$ )
Anxiety symptoms, n (%)	53 (62%)	126 (69%)	68 (84%)	0.007 ( $\chi^2(2)=10.040$ )

ns = not significant

**TREATMENT OF PATIENTS WITH MILD OR MODERATE DEPRESSION OR CYCLOTHYMIA**

At the end of hospital treatment, the outcome of treatment was estimated by the staff team. Most hospitalizations (78%) of the patients with mild or moderate depression or cyclothymia ended with satisfactory clinical results. In line with this, psychosocial functioning was still low (GAS <41)

in 19% of patients at discharge (Table 3). Positive changes were observed in all psychiatric assessments (BDI, HS, GAS). However, almost every second inpatient treatment (48%) was followed by a psychiatric hospitalization during the ten-year study period.

Table 3. BDI, GAS and HS scores of the adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

	Mild/moderate depression or cyclothymia	Severe depression without psychotic symptoms	Severe depression with psychotic symptoms
Severe depression			
BDI ≥ 30 at admission, n (%)	26 (31%)	106 (58%)	48 (59%)
BDI ≥ 30 at discharge, n (%)	6 (7%)	51 (28%)	17 (21%)
Moderate depression			
BDI = 19–29 at admission, n (%)	39 (46%)	48 (26%)	21 (26%)
BDI = 19–29 at discharge, n (%)	13 (15%)	36 (20%)	27 (33%)
Mild depression			
BDI = 13–18 at admission, n (%)	12 (14%)	13 (7%)	5 (6%)
BDI = 13–18 at discharge, n (%)	20 (24%)	26 (14%)	13 (16%)
Minimal depression			
BDI < 13 at admission, n (%)	8 (9%)	16 (9%)	7 (9%)
BDI < 13 at discharge, n (%)	46 (54%)	70 (38%)	24 (30%)
Critical hopelessness			
HS ≥ 15 at admission, n (%)	14 (25%) <sup>a</sup>	58 (50%) <sup>b</sup>	27 (42%) <sup>c</sup>
HS ≥ 15 at discharge, n (%)	6 (11%) <sup>a</sup>	28 (24%) <sup>b</sup>	17 (26%) <sup>c</sup>
Severe psychosocial functional impairment			
GAS < 41 at admission, n (%)	59 (92%) <sup>d</sup>	101 (92%) <sup>e</sup>	58 (100%) <sup>f</sup>
GAS < 41 at discharge, n (%)	12 (19%) <sup>d</sup>	24 (22%) <sup>e</sup>	31 (53%) <sup>f</sup>

Abbreviations: BDI = Beck Depression Inventory, HS = Beck’s Hopelessness Scale, GAS = Global Assessment Scale

<sup>a</sup> data missing from 28 treatment periods  
<sup>b</sup> data missing from 67 treatment periods  
<sup>c</sup> data missing from 16 treatment periods  
<sup>d</sup> data missing from 21 treatment periods  
<sup>e</sup> data missing from 73 treatment periods  
<sup>f</sup> data missing from 23 treatment periods

Psychotropic medication was administered to most patients (Table 4). Over half of the antidepressants (60%) and antipsychotics (53%) had been initiated during outpatient care. While mirtazapine and selective serotonin reuptake inhibitors (SSRIs) were the most often prescribed antidepressants, venlafaxine, duloxetine and agomelatine were also administered in a few cases. Every fourth adolescent was treated with antidepressants together with an antipsychotic

medication. These combinations were more rarely used during the first hospitalization as compared to subsequent ones (13% vs. 42%). Antidepressants evoked adverse events rather frequently (in 21% of medications) (Table 5). In fact, psychiatric symptoms that demanded a discontinuation of antidepressant medication occurred only in three patients. In addition, a course of citalopram therapy was discontinued once due to tachycardia.

Table 4. The most frequently prescribed psychotropic medications in the hospitalization of adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

	Mild/moderate depression or cyclothymia		Severe depression without psychotic symptoms		Severe depression with psychotic symptoms	
	n	%	n	%	n	%
<b>Psychotropic medication</b>	73	86	177	97	81	100
<b>Antidepressant</b>	53	62	156	85	46	57
Mirtazapine	24	28	88	48	15	19
Escitalopram	12	14	53	29	20	25
Fluoxetine	11	13	48	26	8	10
Citalopram	7	8	13	7	3	4
<b>Antipsychotic</b>	36	42	91	50	77	95
Quetiapine	28	33	74	40	40	49
Olanzapine	6	7	9	5	36	44
Clozapine	0	0	4	2	24	30
Aripiprazole	1	1	4	2	19	23
<b>Antidepressant + antipsychotic</b>	20	24	72	39	42	52
<b>Anxiolytic</b>	21	25	62	34	50	62
Oxazepam	19	22	55	30	39	48
<b>Sedative</b>	37	44	72	39	37	46
Zopiclone	26	31	55	30	22	27

Table 5. The adverse events of antidepressant treatment of adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

Adverse event	Mirtazapine (n=127)	Escitalopram (n=85)	Fluoxetine (n=67)	Citalopram (n=23)	Venlafaxine (n=21)	Sertraline (n=9)	Duloxetine (n=6)
Psychiatric							
- provoked psychiatric symptoms (n)	4	13	3	2	1	1	0
- sleep disorder (n)	2	2	0	0	0	0	1
Nervous system							
- fatigue (n)	15	3	2	1	0	1	0
- headache (n)	0	4	0	0	1	0	0
- dizziness (n)	4	0	1	0	1	0	0
- drowsiness (n)	3	0	0	0	0	0	0
- tremor (n)	1	1	0	0	0	0	0
- convulsion (n)	1	0	0	0	0	0	0
Cardiac							
- tachycardia (n)	0	1	0	1	0	0	0
Vascular							
- low blood pressure / fainting (n)	0	0	0	0	1	0	0
Autonomic							
- dry mouth (n)	1	1	0	0	0	0	0
Gastrointestinal							
- nausea (n)	1	2	3	1	1	1	1
- abdominal pain (n)	0	0	1	0	0	0	0
Metabolism and nutrition							
- increased appetite (n)	4	0	1	0	0	0	0
- weight gain (n)	2	0	1	0	0	0	0
Respiratory							
- breathing difficulty (n)	1	0	0	0	0	0	0
Skin and subcutaneous tissue							
- exanthema (n)	1	0	0	0	0	0	0
- sweating (n)	0	0	1	0	0	0	0
Musculoskeletal							
- arthralgia (n)	1	0	0	0	0	0	0
Eye							
- mydriasis (n)	0	2	0	0	0	0	0
Reproductive system							
- sexual adverse events (n)	0	0	0	1	0	0	0
Hepatobiliary							
- elevated liver enzymes (n)	0	1	1	0	0	0	0

Antipsychotics were utilized in nearly half of the hospitalizations; quetiapine and other atypical antipsychotics were prescribed more commonly (Table 4). The average daily doses of quetiapine and olanzapine were 197mg and 9mg, respectively. Quetiapine was occasionally used for off-label indications as a sedative and/or as an anxiolytic (according to 25% of the prescriptions) and the average daily dose in these indications was 58mg. One olanzapine medication was administered due to its sedative and anxiolytic properties. In addition, lithium was prescribed in a few cases (n=3). Every fourth antipsychotic medication (27%) resulted in adverse effects (Table 6). However, only one patient experienced such severe quetiapine-induced fatigue and restless legs that this medication had to be terminated.

Table 6. The adverse events of antipsychotic treatments most used by adolescents with a depressive disorder treated in the two adolescent psychiatric units of Kuopio University Hospital in 2002–2011

Adverse event	Queti- apine (n=142)	Olan- zapine (n=51)	Clozapine (n=28)	Aripip- razole (n=24)	Chlorpro- thixene (n=13)	Risper- idone (n=11)
Psychiatric						
- provoked psychiatric symptoms (n)	5	1	1	1	0	0
- sleep disorder (n)	2	1	0	0	0	0
Nervous system						
- fatigue (n)	27	5	8	0	0	0
- headache (n)	3	1	0	2	0	0
- dizziness (n)	7	0	3	2	0	0
- drowsiness (n)	2	0	0	0	1	0
- tremor (n)	0	2	2	0	0	0
- restless legs (n)	2	0	0	0	0	0
- motor difficulties (n)	1	0	0	0	0	0
- oculogyric crisis (n)	1	0	0	0	0	0
- stiffness (n)	0	1	0	0	0	0
Cardiac						
- tachycardia (n)	2	0	1	0	0	0
- arrhythmia (n)	3	0	0	0	0	0
- QTc prolongation (n)	0	1	0	0	0	0
Vascular						
- low blood pressure / fainting (n)	1	0	1	0	0	0
Autonomic						
- dry mouth (n)	3	1	0	0	0	0





Adverse event	Queti- apine (n=142)	Olan- zapine (n=51)	Clozapine (n=28)	Aripip- razole (n=24)	Chlorpro- thixene (n=13)	Risper- idone (n=11)
Gastrointestinal						
- nausea (n)	1	0	3	2	0	0
- heartburn (n)	2	0	0	0	0	0
- constipation (n)	1	0	1	0	0	0
- hypersalivation (n)	0	0	13	0	0	0
Metabolism and nutrition						
- increased appetite (n)	1	3	0	0	0	0
- weight gain (n)	3	6	5	0	0	0
- hyperlipidemia (n)	0	1	0	0	0	0
Respiratory						
- breathing difficulty (n)	3	0	1	0	0	0
Skin and subcutaneous tissue						
- exanthema (n)	1	0	0	0	0	0
- oedema (n)	1	0	0	0	0	0
Eye						
- dry eyes (n)	1	0	0	0	0	0
Reproductive system						
- galactorrhoea (n)	0	1	0	0	0	1
- hormonal imbalance (n)	0	1	0	0	0	0
Renal and urinary						
- dysuria (n)	1	0	2	0	0	0

Oxazepam was the most often prescribed anxiolytic drug and zopiclone was the most common sedative (*Table 4*). In two patients, the anxiolytic medication had to be discontinued due to adverse effects: oxazepam due to confusion and chlordiazepoxide due to neck twinges. Sedatives induced adverse effects very rarely. In addition, lamotrigine was administered to a single patient.

#### TREATMENT OF PATIENTS WITH SEVERE DEPRESSION WITHOUT PSYCHOTIC SYMPTOMS

Over half of hospitalizations (66%) of the patients with severe depression without psychotic symptoms ended with satisfactory clinical results. Although there were positive changes in psychiatric assessments, psychosocial functioning was low (GAS <41) at discharge in every fifth patient (22%) (*Table 3*). Patients also returned to psychiatric hospital treatment rather often; after 53% of inpatient treatments.

Almost all, 97% of patients, received psychopharmacological medication (*Table 4*). Slightly over half of antidepressants (52%) and antipsychotics (51%) had been initiated during outpatient care. Mirtazapine and SSRIs were the most frequently prescribed antidepressants, but venlafaxine, duloxetine and agomelatine were administered to some patients. Antidepressants were combined with antipsychotics in 39% of the hospitalizations. The patients who were treated with these combinations had higher average BDI depression scores (33 vs. 29,  $p=0.042$ ) and HS scores (15 vs. 12,  $p=0.008$ ) at admission than the other adolescents. In addition, the length of their hospitalizations was also longer (median 24 days vs. 14 days,  $p=0.043$ ). Antidepressant therapy was often associated with adverse events (in 22% of medications); for example, a worsening of psychiatric symptoms led to the termination of the drug therapy in four patients (*Table 5*).

Antipsychotics were used in every second psychiatric inpatient treatment (*Table 4*) with quetiapine and other atypical antipsychotics being most often prescribed. The average daily doses of quetiapine and olanzapine were 175mg and 10mg, respectively. Quetiapine was administered mostly due to its antipsychotic, antidepressant and mood stabilizing properties. However, in 34% of the prescriptions, it was used as a sedative and/or as an anxiolytic (an average daily dose 81mg). Chlorprothixene (regular use n=1, irregular use n=5), lithium (n=1) and irregularly used levomepromazine (n=1) were also prescribed to some adolescents. Every fourth antipsychotic medication (26%) resulted in adverse effects (*Table 6*). A major increase in the body weight of one patient led to the discontinuation of olanzapine medication and quetiapine-induced fatigue and drowsiness were reasons to terminate this medication in two individuals.

Anxiolytics and sedatives were prescribed in 34% and 39% of the treatment periods, respectively (*Table 4*). Oxazepam and zopiclone were the most commonly used medicines from these two drug groups. Anxiolytics and sedatives caused adverse effects very rarely. Oxazepam triggered symptoms of fatigue in one patient and zopiclone caused hallucinations and/or an unpleasant taste in two patients; for these reasons, the medications were discontinued. Other psychotropic medications (lamotrigine n=3, methylphenidate n=1 and topiramate n=1) were rarely needed.

## TREATMENT OF PATIENTS WITH SEVERE DEPRESSION WITH PSYCHOTIC SYMPTOMS

Although over half of the hospitalizations (58%) of the patients with severe depression with psychotic symptoms ended with satisfactory clinical results, 53% of these adolescents had severely impaired psychosocial functioning (GAS <41) at discharge (*Table 3*). Therefore, it was not surprising that adolescents from this patient group often returned to inpatient care (after 83% of inpatient treatments) during the ten-year study period.

All patients received psychotropic medication during their inpatient treatment (*Table 4*). In fact, most of them had started antidepressant and antipsychotic medications already during their outpatient care, 65% and 73%, respectively. SSRIs and mirtazapine were the most generally prescribed antidepressants, but venlafaxine, duloxetine and agomelatine were also occasionally administered. Antidepressants were often combined with antipsychotics. Antidepressant-induced adverse events were observed in 28% of medications (*Table*

5). For example, a worsening of psychiatric symptoms led to discontinuation of antidepressants in three patients.

Antipsychotics were prescribed to 95% of these patients (*Table 4*). Atypical antipsychotics were utilized most frequently, but other drugs such as chlorprothixene (regular use n=1, irregular use n=6), lithium (n=2), irregularly used haloperidol (n=2) and regularly used levomepromazine (n=1) were administered to some patients. Quetiapine and olanzapine were used occasionally as sedatives and/or as anxiolytics (10% of quetiapine and 14% of olanzapine) and the average daily doses in these indications were 81mg and 14mg, respectively. In this patient group, higher doses of quetiapine, olanzapine and clozapine were needed (the average daily doses 326mg, 15mg, 346mg, respectively) as compared to the other patients in this study (in them, the average daily doses were 181mg, 10mg, 113mg, respectively). The average daily doses of aripiprazole and chlorprothixene were 12mg and 100mg, respectively.

Antipsychotics caused adverse effects rather often (in 35% of medications) (*Table 6*). Quetiapine and clozapine caused such severe weight gains that it led to a discontinuation of the medications in two patients. Quetiapine also induced cardiac problems in one patient and fatigue in another one, both being reasons to cease drug treatment. Olanzapine and risperidone triggered hormonal disturbances in two patients leading to a discontinuation of these medications.

Anxiolytics and sedatives were often utilized (*Table 4*). These drugs evoked rather few adverse effects, but drowsiness caused by lorazepam was a reason to stop this medication in one patient. Other psychotropic medications (lamotrigine n=3, valproic acid n=2 and naltrexone n=1) were administered only occasionally.

## DISCUSSION

This clinical study examined the efficacy of psychiatric hospital treatment and the use of psychopharmacological medication in adolescents suffering from a depressive disorder. The treatment of depressed adolescents needing inpatient psychiatric treatment is demanding; it should be conducted by a multi-professional team and often psychopharmacological treatment is also required. According to the assessments of the treatment teams, two-thirds of hospitalizations ended with satisfactory clinical results. Although there are only a few medicines with an official indication for young patients, psychopharmacological treatment was commonly used

with mirtazapine, SSRIs and atypical antipsychotics being the most frequently prescribed medications. Serious side effects of psychotropic medication, such as worsening of psychiatric symptoms, cardiac problems and metabolic changes, was rare.

According to the changes of BDI, HS and GAS scores, patients' symptoms of depression and feelings of hopelessness were relieved and their functional capacity improved significantly during the hospital stay. Inpatient treatments were particularly successful for those patients without psychotic depression. These adolescents were mainly in voluntary treatment and many of them were in the psychiatric ward for the first time, which might partly explain the good treatment outcome. Most hospitalizations (70%) of the patients in these diagnostic groups ended with satisfactory clinical results, but still every second adolescent returned to psychiatric inpatient care during the study period. Although there is a trend for short stays in psychiatric wards, some researchers have linked a short length of stay to increased rates of rehospitalization [18]. If patients are discharged with residual symptoms and clinical problems (e.g., psychosocial issues have not been addressed), this may diminish their potential to experience a sustained recovery. It has also been reported that an older age and lower GAS scores at admission are factors affecting the improvement of children and adolescents treated in psychiatric inpatient units [19,20]. Though most of the adolescents with a mild or moderate depression or cyclothymia can be treated in outpatient care, hospitalizations may have been needed, e.g., due to a comorbid psychiatric disorder, suicidality or inadequate outpatient care.

The treatment outcomes of adolescents with severe psychotic depression were less impressive. Over half of hospitalizations ended with satisfactory clinical results, but still every second adolescent had severely impaired psychosocial functioning at discharge although they had longer inpatient treatment periods compared to the patients without psychotic depression. In addition, these patients required hospitalization again after 83% of the initial treatment periods. This result highlights the seriousness of this disorder. However, the inpatient treatment seems to be more beneficial for the adolescents with depression compared to the young patients with a depressive conduct disorder because only 25.5% of the hospitalizations ended with satisfactory clinical results in the latter group [14]. In conclusion, psychiatric inpatient care seems to be effective for the majority of young people though research in adolescent inpatient settings is rather limited [18-21].

Psychotropic medication was prescribed to almost all adolescents during their hospital stay. Antidepressants were commonly used, although their efficacy has not been unequivocally demonstrated [22]. According to the recent meta-analysis of Hetrick et al. [23], most of the newer generation antidepressants reduce depression symptoms to some extent. In this study, mirtazapine was the most widely prescribed antidepressant although fluoxetine has been demonstrated to possess therapeutic efficacy [12,22] and it is recommended as the first-line antidepressant for patients under 18 years of age [5,6]. The popularity of mirtazapine can be partly explained by its sedative and anxiolytic effects [24]. Most adolescents in this study had been treated as outpatients and many of them also as inpatients, and therefore it is possible that fluoxetine may have been prescribed previously for some of them. According to Finnish guidelines, sertraline and escitalopram are recommended as second-line treatments if fluoxetine is not suitable either due to side effects or poor efficacy [5]. Other SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) such as duloxetine can also be considered [5,23].

While paroxetine seems to lack efficacy in adolescents [25,26], it may reduce depressive symptoms at least to a minor extent in older teenagers [27]. Venlafaxine may be efficient in adolescent depression, but it may carry a risk for suicidality [23,28]. It appears that both paroxetine and venlafaxine induce more adverse events than placebo [25-28], and they are unsuitable for the treatment of juvenile depression [6]. Tricyclic antidepressants may reduce only slightly the symptoms of depression in adolescents [4], but they are not recommended because of their marginal efficacy, adverse events and potential toxicity [5,6]. The administration of these medications seemed to be in line with the guidelines and scientific literature because paroxetine and venlafaxine had been prescribed rarely and tricyclic antidepressants not at all.

Antipsychotic medications were surprisingly commonly administered to young patients, since 42-95% of adolescents in the different diagnostic groups received these pharmaceuticals. Quetiapine was the most common antipsychotic, and while it was most often utilized for its antipsychotic effects, it was also prescribed due to its anxiolytic and/or sedative properties [29]. Antidepressants were combined with antipsychotics particularly in the treatment of psychotic depression.

In this study, antidepressants and antipsychotics induced adverse events rather frequently, but serious side effects were rare. Antidepressants were discontinued due to worsening of psychiatric symptoms in ten adolescents. Antipsychotics were

discontinued mainly due to fatigue and severe weight gain. Clozapine caused most often adverse events and it should never be considered as the first-choice drug [30]. Here, it was prescribed to the adolescents with psychotic depression and infrequently to some patients with severe depression without psychotic symptoms. However, all patients receiving clozapine had been hospitalized due to a psychotic depression at least once during the study period.

Sleeping difficulties and anxiety are commonly encountered when treating patients with depression, and insomnia seems to be a rather ubiquitous symptom in depressed adolescents as compared to adults [31]. These symptoms were reported in 70% of treatment periods, but sedatives and anxiolytics were prescribed only in 42% and 40% of hospitalizations, respectively. Sedatives and anxiolytics may have been avoided possibly due to their risk for addiction; this might partly explain the rather high usage rates of antipsychotics in the patients with cyclothymia and depression without psychotic symptoms. Antipsychotics should be prescribed to patients with sleeping difficulties only in special cases [32]. In the case of young patients, melatonin could reduce sleep latency, but non-drug-based approaches should represent the first-line treatment.

In conclusion, the treatment of adolescents with a depressive disorder consists of various psychosocial interventions and psychopharmacological agents. Overall, the psychotropic medication of the hospitalized adolescents seemed to be in accordance with the guidelines. The main principles of the treatment have remained the same in the last decades and psychotropic medications have been studied for a long time. However, there is not a one-size-fits-all treatment of young patients with a depressive disorder. Therefore, psychotropic medication should be tailored individually, and possible adverse events, such as psychiatric, metabolic, extrapyramidal, cardiovascular and hormonal effects, must be considered and monitored carefully throughout the course of the treatment. It is evident that both clinical and controlled trials clarifying the utility of these medications would be beneficial.

### STRENGTHS AND LIMITATIONS

The present study has some limitations. It was a retrospective study examining psychopharmacological medication used during the inpatient treatment of depressed adolescents. The data were collected from patients' medical records which had not been written for scientific purposes. Because of

missing data of GAS and HS scores, the results concerning the functional capacity and pessimistic attitude may not be totally reliable. However, this method may obtain more authentic results than possible with other approaches such as interviews.

BDI and HS are validated, reliable and globally used measures. It is noteworthy that BDI and HS are self-assessment scales, and it is possible that some patients were not capable of recognizing their own feelings or suicidal ideation. In contrast, the GAS assessments were made by the staff team. The use of these standardized and reliable scales strengthens the results of the study.

While diagnoses were made by psychiatrists using the ICD-10 diagnostic system, structured interviews might have been more reliable. A wider perspective of the depressed adolescents' treatment would have been acquired if we had had access to the data from outpatient care. It could be argued that intensive and effective outpatient care could prevent psychiatric hospitalization. Inadequacy or even a total lack of appropriate outpatient care and feelings of hopelessness can lead to the patient's symptoms deteriorating to the extent that he/she requires psychiatric inpatient treatment.

Inpatient treatment of depressed adolescents is rather rare, because the majority of the patients can be treated as outpatients. Thus, the results provide a perspective of the outcomes of inpatient treatment and the use of psychotropic drugs in everyday practice in a clinical ward treating depressed adolescents.

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