

KIRSI KAKKO, RIINA PESONEN, LEENA PIHLAKOSKI, RAILI SALMELIN, REIJA LATVA

STRUCTURED MONITORING OF PSYCHOTROPIC MEDICATION IN UNIVERSITY HOSPITAL CHILD PSYCHIATRY IN FINLAND

ABSTRACT

Introduction: The use of psychotropic medications has emerged in children, but the monitoring practices are diverse. With the aim of systematizing psychotropic medication practices in children, the Medication Unit was launched at the department of child psychiatry of Tampere University Hospital (TAUH) in February 2021. Aims and methods: The aim of this retrospective patient report-based study was to examine the performed psychotropic medication monitoring in the Medication Unit between 1 February and 31 December 2021. Results: The median age of the study patients (n = 57) was 10.7 years and 77% were males. The most common medications at the first visit to the Medication Unit were methylphenidate (44%) and risperidone (23%). Performed somatic monitoring followed the medication group-specific guidelines well, but target symptom reporting and dialogue concerning adverse effects was not as systematic. Conclusion: The monitoring of psychotropic medications in the Medication Unit was well executed, systematic and followed the local guidelines well. During this study, co-operation with the nursing staff, clearly defined tasks, predefined protocols and proper facilities probably benefitted the monitoring. Further studies on strategies to improve psychotropic medication practices within the child psychiatric service system are needed.

KEY WORDS: PSYCHOTROPIC MEDICATION, MONITORING, GUIDELINES, CHILDREN, CHILD PSYCHIATRY

INTRODUCTION

The global trend in using psychotropic medications in children and adolescents has been rising in recent years, including in Finland (1–6). The use of methylphenidate, which is the first-line medication for attention-deficit/ hyperactivity disorder (ADHD), increased 5-6-fold in children and adolescents between 2006 and 2016 (4,7). Also, the use of antipsychotic medications, most commonly second-generation antipsychotics (SGAs), increased 1.4-fold in Finnish children and 2.2-fold in adolescents between 2008 and 2017 (1). The use of antidepressants, mostly selective serotonin reuptake inhibitors (SSRIs), doubled in Finnish minors between 2008 and 2018. Most of this increase appeared in adolescents (8). In primary schoolers the increase was smaller and in pre-schoolers the SSRI use has decreased (8). Further, the use of psychotropic polypharmacy has emerged (6,9,10). Except for ADHD and some SSRI medications, due to the limited number of paediatric pharmacological trials, official indications for psychotropic medications are few in children under the age of 13 years (*Table 1*), thus off-label prescribing is common (11-14).

The treatment of ADHD consists of multimodal psychosocial support methods, combined with medication (15). ADHD medications (*Table 1*) are usually well tolerated and effective in reducing the core symptoms in children (15,16). The common adverse effects are a diminished appetite, elevation of blood pressure (BP) or heart rate (HR), and sleep disturbances (15). However, alpha-2 agonists may cause hypotension and bradycardia (15,16). Several countries, including Finland, have created clinical guidelines for the initiation and monitoring of ADHD medication (*Table 2*) (15,16).

SGAs in children are mostly prescribed off-label (*Table 1*). Risperidone, aripiprazole and quetiapine are often prescribed for the symptomatic treatment of severe aggression and behavioural disorders comorbid with ADHD and autism spectrum disorders, and further, for anxiety and depressive disorders (1,5,17). SGAs are associated with metabolic adverse effects. An increased appetite, weight gain and deviations in lipid and glucose metabolism may affect up to 60% of children using SGAs (18,19). Neurological adverse effects, such as extrapyramidal symptoms, akathisia, neuroleptic malignant syndrome or tardive dyskinesia, may also emerge (19,20). SGAs may prolong the QT interval (21,22). Even though the risk seems to be small in healthy children, an individual assessment is needed (21,22).

International guidelines for initiation and monitoring of SGA treatment in children have analogous principles, but follow-up frequency and monitoring methods may differ (*Table 2*) (23–25).

Fluoxetine and sertraline are the most commonly used antidepressants in children and adolescents (*Table 1*) (6,8). They are generally well tolerated and most of the adverse effects appear in the early stages of treatment or after a dose increase (19). Nausea, changes in appetite or headache are usually transient (19,26). Activation, agitation and insomnia may also appear and the elevated risk of suicidal thinking and behaviour should be noted (19,27). Further, there is a risk of QT interval prolongation and, extremely rare but potentially life-threatening, serotonin syndrome (19). Monitoring recommendations for SSRIs are described in *Table 2*.

Diagnostics, target symptom definition, individual risk assessment and careful monitoring are key issues when prescribing psychotropics in children, especially with offlabel prescriptions and polypharmacy (14,15). Despite the guidelines, clinical monitoring practices may be inadequate (28–34). Special concerns have arisen with SGAs, which are mostly prescribed off-label and carry a significant risk of metabolic effects. The lack of SGA monitoring was also noted in a Finnish study performed in Tampere University Hospital's (TAUH) department of child psychiatry (35). It revealed that the frequency of growth and BP measurements and metabolic laboratory tests at SGA initiation varied from 27% to 49%, and 46-77% of the patients had enough measurements to estimate possible metabolic changes during the follow-up (35). The means to improve SGA monitoring in children have been investigated in several studies (36,37). It seems that national guidelines are not sufficient but the implementation of local clinical guidance and monitoring protocols may be helpful although their effects seem to wane as time passes (36,37). To improve monitoring more permanently, the protocols need to be tailored to fit the local practices and organizational commitment is necessary (37). A paediatric SGA monitoring protocol was also implemented at TAUH in 2015 (35). Despite temporary improvement, a yet unpublished study by Honkola et al. (2022) showed that the protocol did not spread to common clinical practice (35,38). Thus, more effective means were needed. To address the contradiction between increasing psychotropic prescriptions and insufficient monitoring practices, the Medication Unit at TAUH's department of child psychiatry was launched in February 2021.

Table 1. Official indications of attention-deficit/hyperactivity disorder (ADHD) medications, second-generation antipsychotic (SGA) medications and selective serotonin reuptake inhibitors (SSRIs) available in the market for children under the age of 13 years in Finland (according to the Duodecim lääketietokanta) and the United States (according to the Food and Drug Administration, FDA)(27,44)

	Indication for children under the age of 13 years							
	In Finland	According to the FDA						
ADHD medications								
Methylphenidate	ADHD > 6 years of age	ADHD > 6 years of age						
Lisdexamfetamine	ADHD > 6 years of age if methylphenidate is not effective	ADHD > 6 years of age						
Dexamfetamine	ADHD > 6 years of age if methylphenidate is not effective	ADHD > 6 years of age						
Atomoxetine	ADHD > 6 years of age	ADHD > 6 years of age						
Guanfacine	ADHD > 6 years of age if stimulants are not suitable or effective	ADHD > 6 years of age as monotherapy and as adjunctive therapy to stimulant medications						
SGAs ¹								
Risperidone	Aggression and/or conduct disorder in patients > 5 years of age with diagnosis of intellectual disability (max 6 weeks)	Bipolar mania (≥ 10 years of age) Irritability associated with autism (> 5 years of age)						
Quetiapine		Bipolar mania (≥ 10 years of age)						
Aripiprazole		Bipolar mania (≥ 10 years of age) Irritability associated with autism (≥ 6 years of age) Tourette's disorder (≥ 6 years of age)						
Asenapine		Bipolar mania (≥ 10 years of age)						
Lurasidone		Bipolar depression (≥ 10 years of age)						
Paliperidone		Schizophrenia (≥ 12 years of age)						
Ziprasidone	Manic or mixed episodes of bipolar disorder (> 10 years)							
SSRIs ²								
Fluoxetine	MDD ³ > 8 years of age	MDD > 8 years of age OCD ⁴ > 7 years of age						
Sertraline	OCD > 6 years of age	OCD > 6 years of age						
Fluvoxamine	OCD > 8 years of age	OCD > 8 years of age						
Escitalopram		MDD > 12 years of age						

¹ Available SGAs with no official indications either in Finland or the USA: Olanzapine, Sertindole, Cariprazine, Brexpiprazole, Loxapine, Clozapine

² Available SSRIs with no official indications either in Finland or the USA: Paroxetine, Citalopram

³ Major depressive disorder

⁴ Obsessive-compulsive disorder

Table 2. Recommendations for the monitoring of psychotropic medications in children (15,16,19,22-24,26,37,39-41,44)

Medication	Upon initiation	Monitoring (Regularly during the follow-up) ¹	Somatic monitoring (Regularly during the follow-up) ¹	Laboratory tests
ADHD medications				
All	Assessment of target symptoms Physical examination Growth ² BP ³ , HR ⁴ Individual risk assessment Cardiac disease or risk factors	Symptoms Efficacy Sleep Appetite Mental health changes Adverse effects	Growth BP, HR Neurological examination	No systematic testing is needed upon initiation or during monitoring ECG ⁵ when necessary ⁶
Special considerations				
Stimulants				
Atomoxetine		Pay special attention to possible emergence of suicidality		Liver enzymes if symptoms of liver dysfunction appear
Guanfacine			Pay special attention to BP and HR (bradycardia and hypotension) Close monitoring is needed during the initiation and with each dose increase	
SGAs	Definition and assessment of target symptoms Physical examination Growth Waist circumference BP, HR Neurological status Individual risk assessment Cardiac disease or risk factors Metabolic disease Neurological adverse effects Information if prescription is off-label Lifestyle education	Symptoms Efficacy Mental health changes Nutritional status Adverse effects Lifestyle	Growth • Weekly weight monitoring during the first 6 weeks • Waist circumference • BP, HR • Neurological examination	Upon initiation and regularly during follow-up • Metabolic parameters ⁷ • Blood count • Alanine aminotransferase • Prolactin ⁸ • ECG ⁸

Medication	Upon initiation	Monitoring (Regularly during the follow-up) ¹	Somatic monitoring (Regularly during the follow-up) ¹	Laboratory tests
SSRIs	Definition and assessment of target symptoms Physical examination Individual risk assessment • Cardiac disease or risk factors	Symptoms Efficacy Adverse effects Close monitoring needed during the first weeks and months. • Pay special attention to possible emergence of suicidality		ECG when necessary

¹ Timing of monitoring varies in recommendations

THE MEDICATION UNIT

TAUH is one of the five university hospitals in Finland, with a catchment area of approximately 900,000 inhabitants. The department of child psychiatry consists of an acute and inpatient unit, where children come mostly with emergency and urgent referrals, and four non-urgent outpatient units. All the units offer specialist level psychiatric services for children aged 0-12 years. On a yearly basis approximately 1800 children are treated in TAUH department of child psychiatry. The Medication Unit serves all units of TAUH's department of child psychiatry. Patients are referred to the Unit for initiation or monitoring of psychotropic medication. The referring physician stays in charge of the overall psychiatric treatment, while the Medication Unit is responsible for medication monitoring. The Unit operates one and a half days a week in an office that has sufficient equipment for monitoring. Child psychiatric residents work in co-operation with two trained nurses, who, e.g., schedule visits and laboratory tests and perform measurements of growth, BP and HR. A senior consultant is available for an hour per day.

For the Medication Unit, medication group-specific instructions and a checklist for initiating and monitoring were created based on the available guidelines for ADHD (15), SGA (39–41) and SSRI (26) medications (*Table 2*). With all medications, the evaluation of growth, BP and HR - and with ADHD and SGA medications also neurological examination – are recommended at 1 month and 4 months after initiation, and every 6 months thereafter. A phone contact is recommended 1-2 weeks after baseline or after a dose increase. Further, with SGAs, regular monitoring of relevant laboratory tests (*Table 2*) and ECG are recommended. An easy to order set of laboratory tests is available for SGA monitoring. With SSRIs, a weekly evaluation of psychiatric symptoms (especially suicidality) is emphasized during the first month of treatment. The use of psychiatric rating scales is recommended with all medications at all visits. A tightening of the schedule is recommended after a dose increase or if adverse effects emerge.

² Weight and height

³ Blood pressure

⁴ Heart rate

⁵ Electrocardiogram

⁶ Before initiation when there is an individual or family history of cardiological disease or a doubt of previous arrhythmias

⁷ Fasting blood glucose and lipids

⁸ Recommendations vary

AIMS

The aim of this study was to examine how the monitoring of psychotropic medication was performed in the newly launched Medication Unit of TAUH's department of child psychiatry.

MATERIAL AND METHODS

This retrospective patient report-based study was performed at TAUH's department of child psychiatry between 1 February and 31 December 2021 and was approved by the director of the TAUH Research Services. The inclusion criteria were: 1) a referral to the Medication Unit between January and August 2021, 2) at least one contact with the Unit (visit or a phone call), and 3) the patient's age was below 13 years. These criteria were met by 57 patients who were followed until either the discontinuation of the treatment in the Medication Unit or 31 December 2021, whichever came first. The following data were collected from the electronic patient records: background information (age, gender, family status), diagnoses, information concerning the referral and monitoring visits (the referring unit, the reason for the referral), the medication (generic name), performed somatic monitoring (weight, height, BP, HR, neurological status, ECG, laboratory tests), the assessment of target symptoms, medication response and adverse effects (whether discussed or not), and the use of a psychiatric rating scale (whether used or not). Due to different medication group-specific monitoring instructions, the study sample was divided into three groups: 1) patients using ADHD medications (stimulants, atomoxetine, guanfacine) and possibly SSRIs but not SGAs (ADHD medication group 47%, n = 27), 2) patients using SGAs (with or without other medications, SGA group 40%, n = 23), and 3) patients using only SSRIs (SSRI group, 12%, n = 7).

Categorical variables are described with frequencies, and the statistical significance of the possible differences between patient groups was tested with Fisher's or Fisher-Freeman-Halton exact test. Continuous variables are described with medians (Md) and quartiles (IRQ = Q1-Q3), and group differences were tested with the Kruskal-Wallis test. P-values < 0.05 are considered statistically significant and values between 0.05 and 0.10 indicative. IBM SPSS Statistics, version 28 was used for all statistical analyses.

RESULTS

The median age of the study patients at baseline (BL) was 10.7 years and 77% were males. The patients in the SSRI group were statistically significantly older compared to the other patients. Background information, ICD-10 F-category (psychiatric) diagnoses and psychotropic medications at BL are described in Table 3. The most common diagnoses were ADHD and conduct or mixed conduct and emotional disorder. Over 80% of the patients had at least two diagnoses and 26% also had an ICD-10 Z-category diagnosis reflecting environmental factors, e.g., family circumstances, influencing the patient's health. One third of the patients were referred to the Medication Unit from acute or inward units. The most common reason for referral was a request for the monitoring of an ongoing medication. At BL, 77% of the patients used psychotropic medication as a monotherapy, most commonly methylphenidate and risperidone. During the follow-up, the number of patients using only one psychotropic medication decreased to 63%. Three quarters of the patients had at least two contacts with the Unit during the study period (*Table 3*). Thirty-two per cent of all contacts were conducted by

The frequencies of target symptom reporting, conversations about medication response and adverse effects, use of psychiatric rating scales and performed somatic monitoring in the medication groups are described in Table 4. At BL, target symptoms were reported in approximately half of the patients in the SGA and SSRI groups and in one quarter of the ADHD group. A conversation about medication response was carried out with 71–100% and of adverse effects with 43–83% of patients at BL, both statistically significantly or indicatively more often with patients using SGAs. During the study period, the response and adverse effects were discussed, and a psychiatric rating scale was used at least once with almost all patients. Measurements of growth, BP and HR were performed for almost all patients at BL and at least once during the study period. Repeated measures were available for 74-81%. In the SGA group, monitoring of laboratory tests was significantly more common, and monitoring of ECG and repeated neurological examinations were indicatively more common (Table 4).

Table 3. Background information of the study patients in the Medication Unit of Tampere University Hospital's child psychiatric department, for three medication groups and the whole sample

		N	Medication group	p	All		
	_	ADHD ¹ (n = 27)	SGA ² (n = 23)	SSRI ³ (n = 7)	_		
		Md (IQR) ⁴	Md (IQR) ⁴	Md (IQR) ⁴		Md (IQR) ⁴	
Age at baseline		9.8 (8.9–10.9)	11.0 (10.2–12.3)	12.8 (11.8–12.9)	< 0.001	10.7 (9.4–12.3)	
		0/0	%	%		%	
Gender					ns		
Boy		78	83	57		77	
Caregiver					ns		
Both biological parents		44	27	50		37	
Parents separated		44	46	33		43	
Foster care		13	27	17		20	
Number of ICD-10 F-diagnoses					ns		
1		33	39	57		39	
2		52	30	43		42	
3-4		15	30	0		19	
F-diagnoses with a frequency > 10%	in All						
Obsessive-compulsive disorders	F42	4	13	29	ns	11	
Reaction to severe stress and adjustment disorders	F43	4	26	14	0.060	14	
Hyperkinetic disorders	F90	96	57	0	< 0.001	68	
Conduct or mixed conduct and emotional disorder	F91-92	37	57	14	ns	42	
Childhood emotional disorders	F93	15	9	29	ns	14	
Referred from TAUH's child psychiatric					ns		
Acute and in-patient units		22	39	29		30	
Out-patient units		78	61	71		70	

Reason for referral				ns	
Medication initiation	19	4	29		14
Monitoring ongoing medication	82	96	71		86
Medication at baseline					
ADHD medication	100	44	0	< 0.001	65
Methylphenidate	70	26	0	< 0.001	44
Lisdexamfetamine	7	9	0	ns	7
Guanfacine	7	9	0	ns	7
Atomoxetine	19	0	0	0.076	9
SGA medication	0	91	0	< 0.001	37
Risperidone	0	57	0	< 0.001	23
Aripiprazole	0	35	0	< 0.001	14
SSRI medication	0	13	100	< 0.001	18
Sertraline	0	13	43	0.003	11
Fluoxetine	0	0	57	< 0.001	7
Number of contacts per patient				0.019	
1	15	30	29		23
2	7	35	29		21
≥ 3	78	35	43		56

¹ Patients using ADHD medication without SGAs, possibly combined with SSRIs

² Patients using second-generation antipsychotics alone or combined with ADHD and/or SSRI medications

³ Patients using solely SSRIs

⁴ Median and quartiles (lower-upper quartile)

Table 4. Frequencies of clearly reported target symptoms, discussing response and adverse effects and performing measurements during the first visit (baseline), at least once, and at least twice during the whole follow-up period for the patients of the Medication Unit of Tampere University Hospital's child psychiatric department, for three medication groups

	Baseline				At least one measurement			į	At least two measurements ⁴			
	Medication group		p	Medication group		p	Medication group		p			
	ADHD ¹ (n = 27)	SGA^{2} $(n = 23)$	SSRI ³ (n = 7)	_	ADHD¹ (n = 27)	SGA^{2} $(n = 23)$	SSRI ³ (n = 7)	_	ADHD ¹ (n = 23)	SGA ² (n = 16)	SSRI ³ (n = 5)	-
	%	%	%		%	%	%		%	%	%	ns
Clearly reported target symptoms	26	44	57	ns	33	52	71	ns	17	38	60	ns
Medication response discussed	74	100	71	0.012	96	100	100	ns	91	94	80	ns
Adverse effects discussed	74	83	43	0.097	93	100	100	ns	87	75	60	ns
A psychiatric rating scale used	85	83	86	ns	100	100	100	ns	83	75	60	ns
Somatic measurements performed												
Weight	89	91	100	ns	100	100	100	ns	78	81	80	ns
Height	89	91	100	ns	100	100	100	ns	74	81	80	ns
BMI ⁵	89	91	100	ns	100	100	100	ns	74	81	80	ns
Blood pressure	93	91	100	ns	100	100	100	ns	78	75	80	ns
Heart rate	89	91	100	ns	100	100	100	ns	74	75	80	0.069
ECG	30	61	43	0.094	33	83	43	< 0.001	4	31	20	
Neurological examination	59	65	43	ns	70	78	57	ns	17	50	20	0.067
Some laboratory tests taken	4	65	29	< 0.001	4	87	43	< 0.001	4	56	0	<0.001
Blood count	4	65	29	< 0.001	4	87	43	< 0.001	0	38	0	0.002
Fasting blood lipids	0	57	29	< 0.001	0	78	29	< 0.001	0	31	0	0.011
Fasting blood glucose	0	52	29	< 0.001	0	74	29	< 0.001	0	38	0	0.002
Prolactin	0	48	14	< 0.001	0	70	14	< 0.001	0	31	0	0.011

¹ Patients using ADHD medication without SGAs, possibly combined with SSRIs

² Patients using second-generation antipsychotics alone or combined with ADHD and/or SSRI medications

³ Patients using solely SSRIs

⁴ Among patients who had at least two contacts

⁵ Body Mass Index

DISCUSSION

At TAUH's child psychiatry, special attention has been put into safe medication practices during the last decade. As a result, a Medication Unit was established in 2021. The main finding of this study was that in the Medication Unit, the monitoring of psychotropic medications was well executed, systematic and followed the local medication group-specific guidelines well.

At TAUH, the prior SGA-monitoring protocol implemented in 2015 substantially improved monitoring during the study period (35). However, as in previous studies (37,42), a yet unpublished study by Honkola et al. (2022) performed at TAUH showed that the mode of action did not spread to overall clinical practices (38) and an organizational change was needed. Studies show that in order to succeed, monitoring practices should be tailored locally and supported with concrete tools and reminders (25,37). These principles were used as guidelines when planning the Medication Unit. During the present study in the Medication Unit, the frequency of somatic monitoring was good in all medication groups. Further, in the SGA medication group, for which reference data from the same location was available, the frequencies were considerably better than before the implementation of the monitoring protocol and the Medication Unit (35). Further, non-invasive methods such as growth monitoring were used systematically in the Medication Unit and over half of the patients had a neurological examination, which is important for the estimation of possible neurological adverse effects (20). As was recommended, ECG and laboratory tests, targeting the detection of possible cardiological and metabolic adverse effects, were more common in children with SGAs compared to other medications. These findings were probably influenced by the collaboration and the clearly defined tasks of the residents and the nurses. The systematic measurement of growth and BP were tasks clearly entrusted to the nurses in the Unit, as was scheduling of the visits according to the protocol. Also, previous studies indicate that multidisciplinary collaboration can facilitate psychotropic medication monitoring, especially in outpatient settings (31,33). Further, a well-defined medication-specific monitoring protocol, a checklist, a predetermined set of laboratory tests and proper facilities in the Unit may have supported the monitoring during this study.

Besides somatic monitoring, dialogue with patients and caregivers regarding medication target symptoms, response and adverse effects is essential (14,15). According to the findings of this study, these still need attention. Medication

response was discussed at least once with most of the patients. However, despite a clear reminder in the checklist, target symptoms often remained unreported, especially with ADHD medications. This is an interesting finding and may reflect the idea that target symptoms of ADHD medications are widely known. Nevertheless, patients and caregivers may not be familiar with them and may have other expectations than the clinicians. The finding does not necessarily indicate that the target symptoms were not evaluated, but rather that they were not clearly reported. Exact definition and reporting are essential in order to evaluate the response. Furthermore, psychotropic medications are often used as symptomatic treatment, and in children they are often offlabel. This highlights the need for careful evaluation and reporting of symptomatic changes and the risk-benefit balance. The importance of reporting is especially evident when there is more than one physician attending to the medication monitoring. A promising finding in this study was, however, that psychiatric rating scales were used with most of the patients during the study period. This, also, was probably influenced by the checklist and the monitoring routine, which recommended their use, and the collaboration with the nurses who ensured that the scales were available.

Dialogue regarding adverse effects took place at least once with most of the patients during the study period. However, at the first visit to the Unit, the adverse effects of SSRIs received far less attention than those of ADHD and SGA medication, or at least they were not noted in the patient reports. Dialogue on adverse effects with the child and the caregiver is an important part of monitoring, and with SSRIs caregivers need to be informed of the risk of possible suicidality in order to safeguard the patient when needed (27). It is possible that the medication group differences are due to physicians' better knowledge of the adverse effects of ADHD and SGA medications. The national guidelines for ADHD and the prior local study concerning SGA monitoring may also have influenced the result. Based on this finding, more emphasis should be put on educating physicians of the adverse effects of psychotropics, and means to inform patients and caregivers about them, especially concerning the medications less commonly used in children.

The good quality monitoring detected in this study suggests that the follow-up of psychotropic medication deserves a time and place of its own, and novel approaches to achieve this goal are needed. This study showed that monitoring may be well performed and medication safety improved even separately from the unit responsible for the child's treatment as a whole. However, when the Unit focuses

on medication, the risk may be that not all aetiological factors associated with the patients' wellbeing and symptoms are sufficiently considered, especially when physicians work in rotation – even when the nurses in the Unit provide some continuity. Despite guidance and supporting structure, the evaluation of the benefits and risks of psychotropic medications in children is always a challenging task. Children with complicated polypharmacy and multiple psychosocial factors affecting their symptoms probably benefit more from a traditional single-physician working model. However, as with all children using psychotropics, medication safety and thorough monitoring practices need to be considered as priorities.

CONCLUSIONS

The monitoring of psychotropic medications in the Medication Unit at TAUH's department of child psychiatry was well executed, systematic and followed the local guidelines well. However, further studies on strategies to improve psychotropic medication practices and affect possible barriers of monitoring within the child psychiatric service system are needed.

STRENGTHS AND LIMITATIONS

A major strength of this study is that it produced naturalistic information of a new clinical working model to improve medication monitoring and safety. However, the short duration, small number of study subjects in different medication groups and the lack of a control group are limitations that may affect the generalizability of these results.

Acknowledgements

We wish to express our gratitude to all the participating patients and physicians at TAUH's child psychiatric department and to the nurses at the Medication Unit.

Disclosures

The authors declare no conflicts of interest regarding this manuscript.

Authors

Kirsi Kakko MD, PhD^{1,2} Riina Pesonen B.M.² Leena Pihlakoski MD¹ Raili Salmelin MSc, PhD^{1,2} Reija Latva MD, PhD^{1,2}

- ¹ Department of Child Psychiatry, Tampere University Hospital, Tampere, Finland
- ² Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

Correspondence:

Kirsi Kakko

Tampere University, Faculty of Medicine and Health Technology FI-33014 Tampere University, Finland and Department of Child Psychiatry, Tampere University Hospital, PO Box 2000, Tampere FI-33521, Finland

Email: kirsi.kakko@tuni.fi

References

- 1. Varimo E, Saastamoinen LK, Rättö H, Mogk H, Aronen ET. *New users of antipsychotics among children and adolescents in 2008–2017: a nationwide register study*. Front Psychiatry. 2020;24(11):316. https://doi.org.10.3389/fpsyt.2020.00316
- 2. Kalverdijk LJ, Bachmann CJ, Aagaard L, Burcu M, Glaeske G, Hoffmann F, et al. *A multi-national comparison of antipsychotic drug use in children and adolescents, 2005–2012*. Child Adolesc Psychiatry Ment Health. 2017;11(1):55. https://doi.org.10.1186/s13034-017-0192-1
- 3. Piovani D, Clavenna A, Bonati M. *Prescription prevalence of psychotropic drugs in children and adolescents: an analysis of international data*. Eur J Clin Pharmacol. 2019;75(10):1333–46. https://doi.org.10.1007/s00228-019-02711-3
- 4. Vuori M, Koski-Pirilä A, Martikainen JE, Saastamoinen L. *Gender- and age-stratified analyses of ADHD medication use in children and adolescents in Finland using population-based longitudinal data, 2008–2018.* Scand J Public Health. 2020;48(3):303–7. https://doi.org.
- 5. Saastamoinen LK, Autti-Rämö I, Tuulio-Henriksson A, Sourander A. *Lasten ja nuorten psykoosilääkkeiden käyttö kasvussa*. Suom Lääkärilehti. 72(9):575–9.
- 6. Lagerberg T, Molero Y, D'Onofrio BM, Fernández de la Cruz L, Lichtenstein P, Mataix-Cols D, et al. *Antidepressant prescription patterns and CNS polypharmacy with antidepressants among children, adolescents, and young adults: a population-based study in Sweden*. Eur Child Adolesc Psychiatry. 2019;28(8):1137–45. https://doi.org. 10.1007/s00787-018-01269-2
- 7. Vuori M, Aronen E, Sourander A, Martikainen J, Jantunen T, Saastamoinen L. *Aktiivisuuden ja tarkkaavuuden häiriön* (ADHD) lääkkeiden käyttö on yleistynyt. Lääketieteellinen Aikakauskirja Duodecim. 2018;134(15):1515–22.
- 8. Hou K. *Lasten ja nuorten masennuslääkkeiden käyttö*. Helsingin yliopisto Farmasian tiedekunta. 2020. [Internet]. Available from: https://helda.helsinki.fi/bitstream/handle/10138/332200/Hou Kathy Maisterintutkielma 2021.pdf?sequence=3

- 9. Varimo E, Saastamoinen LK, Rättö H, Aronen ET. *Polypharmacy in children and adolescents initiating antipsychotic drug in 2008–2016: a nationwide register study.* Nord J Psychiatry. 2022;9;1–9. https://doi.org. 10.1080/08039488.2022.2042597
- 10. Kronström K, Kuosmanen L, Ellilä H, Kaljonen A, Sourander A. *National time trend changes in psychotropic medication of child and adolescent psychiatric inpatients across Finland*. Child Adolesc Ment Health. 2018;23(2):63–70. https://doi.org.10.1111/camh.12217
- 11. Putignano D, Clavenna A, Reale L, Bonati M. *The evidence-based choice for antipsychotics in children and adolescents should be guaranteed*. Eur J Clin Pharmacol. 2019;75(6):769–76. https://doi.org.10.1007/s00228-019-02641-0
- 12. Varimo E, Aronen ET, Mogk H, Rättö H, Saastamoinen LK. *Antipsychotic treatment duration in children and adolescents: a register-based nationwide study*. J Child Adolesc Psychopharmacol. 2021;31(6):421–9. https://doi.org. 10.1089/cap.2020.0095
- 13. Braüner JV, Johansen LM, Roesbjerg T, Pagsberg AK. *Off-label prescription of psychopharmacological drugs in child and adolescent psychiatry*. J Clin Psychopharmacol. 2016;36(5):500–7. https://doi.org. 10.1097/JCP.0000000000000559
- 14. Sharma AN, Arango C, Coghill D, Gringras P, Nutt DJ, Pratt P, et al. *BAP Position Statement: Off-label prescribing of psychotropic medication to children and adolescents*. J Psychopharmacol (Oxf). 2016;30(5):416–21. https://doi.org.10.1177/0269881116636107
- 15. Working group set up by the Finnish Medical Society Duodecim and the Finnish Pediatric Neurology Association, Child Psychiatric Society, Adolescent Psychiatric Society. ADHD (attention deficit hyperactivity disorder). Current care guidelines. 2019.
- 16. Brown KA, Samuel S, Patel DR. *Pharmacologic management of attention deficit hyperactivity disorder in children and adolescents: a review for practitioners*. Transl Pediatr. 2018;7(1):36–47. https://doi.org.10.21037/tp.2017.08.02
- 17. Nesvåg R, Hartz I, Bramness JG, Hjellvik V, Handal M, Skurtveit S. *Mental disorder diagnoses among children and adolescents who use antipsychotic drugs*. Eur Neuropsychopharmacol. 2016;26(9):1412–8. https://doi.org. 10.1016/j. euroneuro.2016.07.001
- 18. Libowitz MR, Nurmi EL. *The burden of antipsychotic-induced weight gain and metabolic syndrome in children*. Front Psychiatry. 2021;12:623681. https://doi.org.10.3389/fpsyt.2021.623681
- 19. Romba C, Perez-Reisler M. Management of adverse effects of psychotropic medications. Pediatr Ann. 2020;49(10). https://doi.org. 10.3928/19382359-20200922-03
- 20. Rasimas JJ, Liebelt EL. *Adverse effects and toxicity of the atypical antipsychotics: What is important for the pediatric emergency medicine practitioner?* Clin Pediatr Emerg Med. 2012;13(4):300–10. https://doi.org. 10.1016/j.cpem.2012.09.005
- 21. Jensen KG, Juul K, Fink-Jensen A, Correll CU, Pagsberg AK. *Corrected QT changes during antipsychotic treatment of children and adolescents: a systematic review and meta-analysis of clinical trials*. J Am Acad Child Adolesc Psychiatry. 2015;54(1):25–36. https://doi.org. 10.1016/j.jaac.2014.10.002
- 22. Hiippala, Anita, Happonen, Juha-Matti. *Lapselle tai nuorelle psyykenlääkitys milloin tutkitaan EKG?* Suom Lääkärilehti. 2021;76(5):279–82.
- 23. Dinnissen M, Dietrich A, van der Molen JH, Verhallen AM, Buiteveld Y, Jongejan S, et al. *Prescribing antipsychotics in child and adolescent psychiatry: guideline adherence*. Eur Child Adolesc Psychiatry. 2020;29(12):1717–27. https://doi.org.10.1007/s00787-020-01488-6
- 24. Kealey E, Scholle SH, Byron SC, Hoagwood K, Leckman-Westin E, Kelleher K, et al. *Quality concerns in antipsychotic prescribing for youth: a review of treatment guidelines.* Acad Pediatr. 2014;14(5):S68–75. https://doi.org. 10.1016/j. acap.2014.05.009

- 25. Minjon L, van den Ban E, de Jong E, Egberts TCG, Heerdink ER. *Monitoring of metabolic, cardiac, and endocrine indicators in youth treated with antipsychotics as reported by health care professionals*. J Clin Psychopharmacol. 2018;38(5):489–93. https://doi.org.10.1097/JCP.00000000000000936
- 26. Stahl SM. *Prescriber's Guide Children and Adolescents: Stahl's Essential Psychopharmacology* [Internet]. 1st ed. Cambridge University Press; 2018 [cited 2022 May 12]. Available from: https://www.cambridge.org/core/product/ identifier/9781108561402/type/book
- 27. Food and Drug Administration. *FDA-Approved Drugs* [Internet]. Available from: Drugs@FDA: FDA-Approved Drugs [cited 2022 May 12].
- 28. Oxley C, Moghraby OS, Samuel R, Joyce DW. *Improving the quality of physical health monitoring in CAMHS for children and adolescents prescribed medication for ADHD*. BMJ Open Qual. 2018;7(2):e000213. https://doi.org. 10.1136/bmjoq-2017-000213
- 29. Mücke K, Plück J, Steinhauser S, Hellmich M, Scholz K, Sonneck A, et al. *Guideline adherence in German routine care of children and adolescents with ADHD: an observational study*. Eur Child Adolesc Psychiatry. 2021;30(5):757–68. https://doi.org. 10.1007/s00787-020-01559-8
- 30. Chen W, Cepoiu-Martin M, Stang A, Duncan D, Symonds C, Cooke L, et al. *Antipsychotic prescribing and safety monitoring practices in children and youth: a population-based study in Alberta, Canada*. Clin Drug Investig. 2018;38(5):449–55. https://doi.org.10.1007/s40261-018-0626-4
- 31. Coughlin M, Goldie CL, Tranmer J, Khalid-Khan S, Tregunno D. *Patient, treatment, and health care utilization variables associated with adherence to metabolic monitoring practices in children and adolescents taking second-generation antipsychotics*. Can J Psychiatry. 2018;63(4):240–9. https://doi.org. 10.1177/0706743717751693
- 32. Hayden JD, Horter L, Parsons T, Ruble M, Townsend S, Klein CC, et al. *Metabolic monitoring rates of youth treated with second-generation antipsychotics in usual care: results of a large US National Commercial Health Plan.* J Child Adolesc Psychopharmacol. 2020 1;30(2):119–22. https://doi.org. 10.1089/cap.2019.0087
- 33. Jazi S, Ben-Amor L, Abadie P, Menard ML, Choquette R, Berthiaume C, et al. *Long-term metabolic monitoring of youths treated with second-generation antipsychotics 5 Years after publication of the CAMESA guidelines. Are we making progress?* Can J Psychiatry. 2021;66(7):645–56. https://doi.org. 10.1177/0706743720974847
- 34. Okumura Y, Usami M, Okada T, Saito T, Negoro H, Tsujii N, et al. *Glucose and prolactin monitoring in children and adolescents initiating antipsychotic therapy*. J Child Adolesc Psychopharmacol. 2018;28(7):454–62. https://doi.org. 10.1089/cap.2018.0013
- 35. Kakko K. *Second-generation antipsychotic medications in child psychiatric patients: prescribing and monitoring practices* [Internet] [Doctoral thesis]. Tampere university; 2021. Available from: https://urn.fi/URN:ISBN:978-952-03-2211-3
- 36. Kara I, Penner M. *Impact of antipsychotic guidelines on laboratory monitoring in children with neurodevelopmental disorders*. J Child Adolesc Psychopharmacol. 2021;31(1):79–83. https://doi.org. 10.1089/cap.2020.0096
- 37. Melamed OC, LaChance LR, O'Neill BG, Rodak T, Taylor VH. *Interventions to improve metabolic risk screening among children and adolescents on antipsychotic medication: a systematic review*. J Child Adolesc Psychopharmacol. 2021;31(1):63–72. https://doi.org.10.1089/cap.2020.0115
- 38. Honkola R, Puura K, Salmelin R, Kakko K. *Psykoosilääkkeitä käyttävien lasten kasvun seuranta on edelleen usein puutteellista. 2022.* (Unpublished manuscript fmj-2022–0117).
- 39. Pringsheim T, Panagiotopoulos C, Davidson J, Ho J, Canadian Alliance for Monitoring Effectiveness and Safety of Antipsychotics in Children (CAMESA) guideline group. *Evidence-based recommendations for monitoring safety of second-generation antipsychotics in children and youth.* Paediatr Child Health. 2011;16(9):581-589.

- 40. National Institute for Health and Care Excellence (NICE). *Psychosis and schizophrenia in children and young people:* recognition and management [Internet]. London: 2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK554921/ [cited 2022 May 24].
- 41. Sourander A, Marttunen M, Voutilainen A, Koskentausta T, Tolmunen, T, Haapasalo-Pesu K-M, et al. *Lasten ja nuorten psykiatrinen lääkehoito*. In: Lastenpsykiatria ja Nuorisopsykiatria [Internet]. Kustannus Oy Duodecim. 2016.
- 42. Ronsley R, Rayter M, Smith D, Davidson J, Panagiotopoulos C. *Metabolic monitoring training program implementation in the community setting was associated with improved monitoring in second-generation antipsychotic-treated children*. Can J Psychiatry. 2012;57(5):292–9. https://doi.org.10.1177/070674371205700504
- 43. McLaren JL, Brunette MF, McHugo GJ, Drake RE, Daviss WB. *Monitoring of patients on second-generation antipsychotics: a national survey of child psychiatrists*. Psychiatr Serv. 2017;68(9):958–61. https://doi.org.10.1176/appi. ps.201500553
- 44. Duodecim lääketietokanta [Internet]. Available from: https://www.terveysportti.fi/apps/laake/[cited 2022 May 20].