Monitoring of Metabolic, Cardiac, and Endocrine Indicators in Youth Treated With Antipsychotics as Reported by Health Care Professionals

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Abstract:

Background: It is unclear how youth treated with antipsychotics are monitored. The purpose of this study was to assess monitoring of metabolic, cardiac, and endocrine indicators in youth (<18 years old) treated with antipsychotics as reported by health care professionals in the Netherlands.

Methods: A questionnaire was designed to collect information from health care professionals regarding the monitoring of youth treated with antipsychotics. Data were collected at a national conference.

Findings and Results: Fifty-nine health care professionals completed the questionnaire, of which 53 (89.8%) were child and adolescent psychiatrists (approximately 20% of all child and adolescent psychiatrists in the Netherlands). More than 80% of respondents reported monitoring physical indicators—weight, height, body mass index, heart rate, and blood pressure—and over 50% reported monitoring laboratory indicators—lipid profile, blood glucose, and prolactin level. Most of the respondents reported monitoring physical indicators more than twice per year and laboratory indicators once per year. Almost all respondents (56/59, 94.9%) reported monitoring according to a clinical guideline or protocol. Only 1 respondent reported monitoring the indicators completely according to the clinical guideline. Respondents mentioned that facilitating factors for monitoring, such as access to electrocardiogram facilities, were insufficiently available.

Conclusions: Although all health care professionals reported monitoring metabolic, cardiac, and endocrine indicators in youth treated with antipsychotics, great variability exists in reported monitoring practices. Factors contributing to this variability must be assessed to optimize the benefit-risk ratio for the individual patient.

Key Words: antipsychotics, monitoring, youth, metabolic indicators

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Antipsychotics are frequently prescribed to youth to treat psychiatric disorders, including attention-deficit/hyperactivity disorder, autism spectrum disorder, and disruptive behavior disorders.[1,2] Individual antipsychotics have received marketing authorization for some of these indications, but off-label prescribing is common.[3,4] Frequent and off-label use of antipsychotics in youth is concerning because of the risks of serious adverse effects and limited evidence regarding the (long-term) benefit-risk ratio.

Antipsychotics have been associated with clinically relevant endocrine and cardiometabolic adverse effects, including weight gain, dyslipidemia, development of type 2 diabetes mellitus, hyperprolactinemia, and prolonged QT interval.[5–8] These may occur in both adults and youth, but less is known about adverse effects in youth, and younger age is an established risk factor for greater weight gain with atypical antipsychotics.[9]

Pharmacotherapy with antipsychotics should consist of not only prescribing but also monitoring for efficacy and adverse effects to periodically evaluate the benefit-risk ratio in individual patients and adjust pharmacotherapy when necessary. Several clinical guidelines worldwide describe how to monitor for adverse effects of antipsychotics in youth. However, these guidelines differ not only in which indicators to monitor and the frequency of monitoring but also in treatment options when the outcome deviates from the baseline or reference value. For example, some guidelines recommend continual monitoring of the lipid profile,[10–12] whereas other guidelines recommend monitoring the lipid profile only when risk factors, such as a high body mass index (BMI), are present[13] or depending on the type of antipsychotic used.[14]

Considering this variability in monitoring guidelines, the purpose of this study was to assess monitoring of metabolic, cardiac, and endocrine indicators in youth (<18 years old) treated with antipsychotics as reported by health care professionals in the Netherlands.

MATERIALS AND METHODS

Questionnaire Design

A questionnaire was designed to collect information related to current clinical practices regarding monitoring of metabolic, cardiac, and endocrine indicators in youth treated with antipsychotics. The questionnaire was pretested and reviewed by 4 child and adolescent psychiatrists from an outpatient clinic in Utrecht who have experience in prescribing antipsychotics, as well as 6 colleagues of the division of Pharmacoepidemiology and Clinical Pharmacology of Utrecht University.

The final questionnaire included 15 questions concerning monitoring, based on current clinical guidelines[10,12–15] and the items used for the Systematic Information for Monitoring score.[16] Most questions were multiple choice, with the option to include additional comments. The questions concerned (1) reasons to start and stop monitoring; (2) which metabolic, cardiac, and endocrine indicators were monitored; (3) time frames of treatment in which these indicators were monitored; (4) frequency of monitoring; (5) response to monitoring results; (6) whether a clinical guideline or protocol was followed and which clinical guideline or protocol was followed; and (7) whether facilitating factors or barriers for monitoring were present. The indicators included in the questionnaire

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were lipid profile, blood glucose, prolactin, antipsychotic drug level, weight, height, BMI, fat mass or fat percentage, waist and hip circumference, heart rate, blood pressure, and QTc interval or electrocardiogram (ECG). Three time frames for monitoring were specified: at start of antipsychotic treatment, during the first 3 months of treatment, and after 3 months of treatment. The frequency of monitoring at start and during the first 3 months of treatment was defined as "never," "sometimes, in case of …" and "always/almost always," and the frequency after 3 months as "never," "less than once per year," "once per year," "twice per year," "more than twice per year," and "other, namely: …." Facilitating factors for monitoring included access to a laboratory, tape measure, scale, and the ability to obtain an ECG. The full questionnaire can be found in Supplementary Item 1 (Dutch), Supplemental Digital Content 1, http://links.lww.com/JCP/A526 and Supplementary Item 2 (English), Supplemental Digital Content 2, http://links.lww.com/JCP/A527.

The institutional review board of the Department of Pharmaceutical Sciences of Utrecht University approved the study. A review by the ethics committee was not required because the data collected were anonymous and included no information on individuals; no patient data were used.

Setting, Study Population, and Data Collection

Data were collected at the national conference *Van Wijk tot Wetenschap* for child and adolescent psychiatry in Utrecht, the Netherlands, in November 2016. All prescribers present at the conference were invited by trained undergraduate students of Utrecht University to complete the questionnaire during the conference. Prescribers did not receive incentives to participate. The questionnaire required approximately 10 minutes to complete.

Analysis

Data entry and review were conducted by the first author (L.M.). Discrepancies and indistinct answers were discussed and resolved by consensus with 2 additional reviewers (E.H. and T.E.). Descriptive statistics were performed using SPSS Statistics version 24.

RESULTS

Fifty-nine health care professionals completed the questionnaire (Table 1); this number amounts to 46% of the physicians and clinical nurse specialists present at the conference. Fifty-three (89.8%) respondents were child and adolescent psychiatrists; this is approximately 20% of the total number of practicing child and adolescent psychiatrists in the Netherlands.

The respondents reported that the main reasons to start monitoring metabolic, cardiac, and endocrine indicators were early detection of changes in physical or laboratory indicators (48/59, 81.4%), presence of risk factors including diabetes mellitus before start of antipsychotic treatment (44/59, 74.6%), and recommendation by a guideline (42/59, 71.2%). The main reasons reported to stop monitoring were end of antipsychotic therapy (39/59, 66.1%) and youth not willing to provide a blood sample anymore (21/59, 35.6%).

More than 80% of respondents reported monitoring (sometimes or always) the physical indicators weight, height, BMI, heart rate, and blood pressure when antipsychotic treatment was started in youth, during the first 3 months of treatment and after 3 months (Fig. 1). More than half of respondents reported monitoring the laboratory indicators lipid profile, blood glucose, and prolactin level when antipsychotic treatment was started in youth, during the first 3 months of treatment, and after 3 months. Indicators least frequently monitored were fat mass or fat percentage and waist and hip circumference. Not a single respondent reported monitoring all laboratory and physical indicators (Fig. 1) when starting antipsychotic treatment in youth, during the first 3 months of treatment, and after 3 months. When monitoring of fat mass or fat percentage was excluded, 3.4% (2/59) of respondents reported monitoring all remaining laboratory and physical indicators in all 3 time frames. When monitoring of fat mass or fat percentage and monitoring of waist and hip circumference were excluded, 20.3% (12/59) of respondents reported monitoring all remaining laboratory and physical indicators in all 3 time frames.

TABLE 1. Characteristics of the Study Population (n = 59)

Characteristic	n (%)
Specialism	
Child and adolescent psychiatrist	53 (89.8)
Pediatrician	3 (5.1)
General practitioner	2 (3.4)
Clinical nurse specialist	1 (1.7)
Health care setting*	
Mental health services, youth	48 (81.4)
(Academic) Hospital	7 (11.9)
Private practice	6 (10.2)
Mental health services, general	5 (8.5)
Other	4 (6.8)
Years prescribing	
0–1	0 (0.0)
2–5	9 (15.3)
6–10	13 (22.0)
>10	37 (62.7)
No. youth prescribed antipsychotics to (last 6 months)	
<10	21 (35.6)
10–20	15 (25.4)
>20	23 (39.0)
Use of a guideline	
Yes	56 (94.9)
No	3 (5.1)

*Ten respondents worked in more than 1 health care setting; therefore, total n > 59 (>100%).

Most respondents reported monitoring laboratory indicators once per year when treatment with antipsychotics lasted longer than 3 months; lipid profile was monitored once per year by 55.9% (33/59) of respondents, blood glucose by 57.6% (34/59), and prolactin level by 40.7% (24/59). The physical indicators weight, height, BMI, heart rate, and blood pressure were reported to be monitored more frequently by the majority of respondents (more than twice per year); weight and height were each monitored more than twice per year by 44.1% (26/59) of respondents, BMI by 40.7% (24/59), heart rate by 35.6% (21/59), and blood pressure by 37.3% (22/59). The majority of respondents who reported monitoring the QTc interval or ECG indicated that they monitored this indicator only when risk factors were present.

In total, 16 (27.1%) respondents reported that they have not changed therapy because of monitoring results within the last 6 months, 38 (64.4%) respondents reported that they have changed therapy for less than 25% of the youth for whom they had prescribed antipsychotics, and 5 (8.5%) respondents have changed therapy for 25% to 50% of the youth for whom they had prescribed antipsychotics.

In total, 94.9% (56/59) of respondents reported monitoring according to a guideline or protocol. Most of the respondents followed a Dutch guideline (39/59, 66.1%),[13] an international

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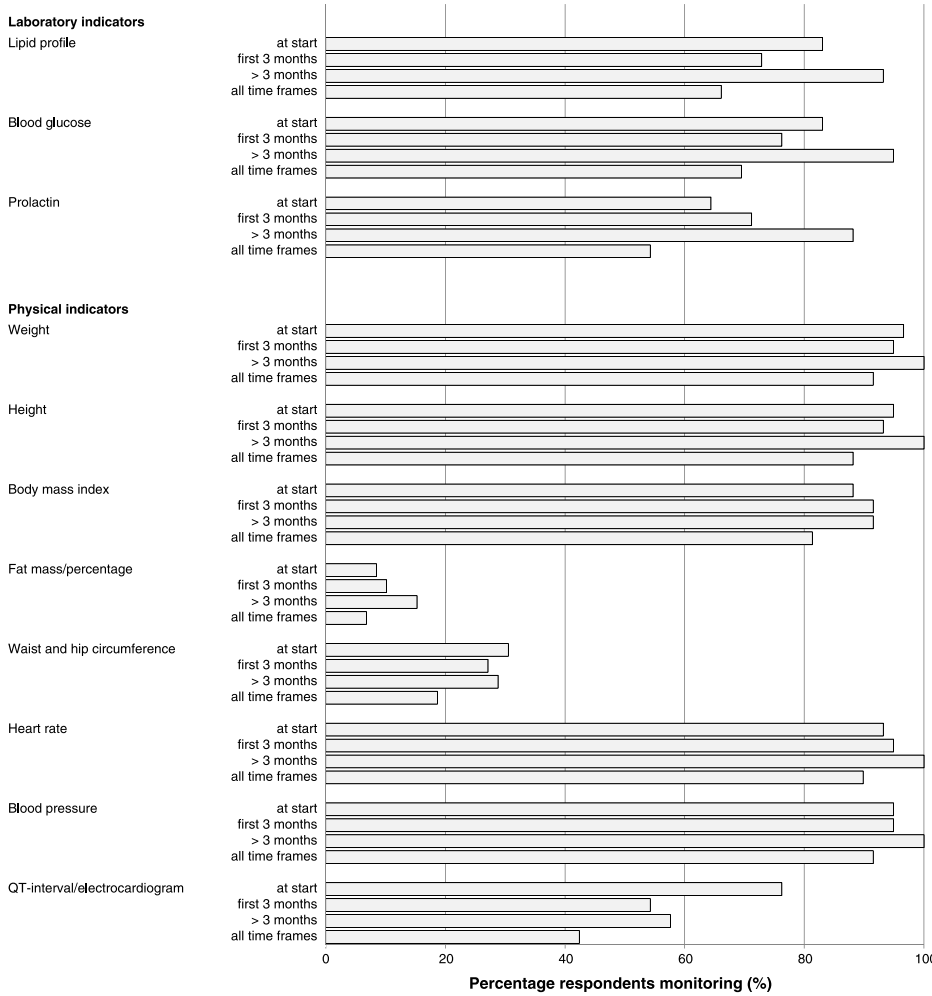

FIGURE 1. Monitoring of metabolic, cardiac, and endocrine indicators in youth treated with antipsychotics as reported by health care professionals (n = 59).

guideline (4/59, 6.8%),[10] or both (4/59, 6.8%). Only 1 of these respondents reported monitoring lipid profile, blood glucose, prolactin level, weight, height and BMI throughout the entire course of treatment according to the guideline followed. More than half of the respondents who claimed to follow a Dutch guideline[13] reported always monitoring lipid profile (23/43, 53.5%) and blood glucose (25/43, 58.1%) when treatment with antipsychotics was started, although the guideline advises monitoring these indicators only when risk factors are present.

Not all respondents reported that factors to facilitate monitoring were sufficiently available. In total, 98.3% (58/59) of respondents reported that a scale was available, 91.5% (54/59) a tape measure, 94.9% (56/59) a blood pressure monitor, 83.1% (49/59) access to outcomes of laboratory indicators, 81.4% (48/59) access to a laboratory, 74.6% (44/59) ability to consult another specialist, 49.2% (29/59) access to facilities to obtain an ECG, and 49.2% (29/59) potential for referral if the child has a fear of needles.

DISCUSSION

Although all health care professionals who completed the questionnaire reported monitoring metabolic, cardiac, and endocrine indicators in youth treated with antipsychotics, there was great variability in monitoring between these respondents. This involved not only which laboratory and physical indicators were monitored in the 3 time frames but also the frequency of monitoring. Although most of the respondents reported monitoring according to a guideline,[10,13] almost none reported actually monitoring all laboratory and physical indicators according to the guideline they claimed to follow.

To optimize monitoring, it is important to know the cause of the variability. First, guidelines differ in type, frequency, and method of monitoring metabolic, cardiac, and endocrine indicators. For example, the National Institute for Health and Clinical Excellence guideline[10] and the guideline of the American Academy of Child and Adolescent Psychiatry[12] offer advice regarding when an ECG should be considered, but neither the guideline of the Canadian Alliance for Monitoring Effectiveness and Safety of Antipsychotics in Children[14] nor the Dutch guideline[13] advises when to monitor for changes in the ECG. Furthermore, previous studies have shown that instructions in guidelines regarding monitoring are often incomplete or do not provide sufficient information to be applicable in daily clinical practice.[17,18] Consequently, physicians may interpret the instructions differently and as a result monitor youth treated with antipsychotics differently. Therefore, guidelines must be uniform, informative, comprehensible, and passably simple for everyday practice.

Second, respondents of this study reported that facilitating factors for monitoring were not always sufficiently available. Similarly,

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in a previous study, health care professionals reported inadequate access to factors that facilitate monitoring, such as a tape measure, blood pressure monitor, or laboratory facilities.[19] This lack of facilitating factors should be resolved to adequately monitor youth in daily clinical practice.

Finally, only 1 of the respondents of this study reported complying with the guideline that was claimed to be followed. Lack of adherence by health care professionals to monitoring guidelines has been reported before[20–22] and may have several reasons, including lack of reminder systems, lack of time, insufficient knowledge about monitoring, or attitudes concerning monitoring.[21,23] Furthermore, the attitude of the youth and parents regarding monitoring is essential as well. Youth may resist monitoring because of fear of needles, and parents may feel resistant when their child does not desire to be monitored or when they do not have ample knowledge concerning the need for monitoring.[21]

Treatment of youth with antipsychotics is more than just prescribing medication; it should also involve adequate monitoring for efficacy, adverse effects, and safety, as well as adjustment of therapy when necessary. It is important to be aware of the different factors that can result in variability in monitoring, because only then can these factors be discussed, possibly resolved, and variability minimized. Following this approach, individual children can be offered the same treatment, including adequate monitoring of metabolic, cardiac, and endocrine indicators.

However, this study shows that not every physician agrees upon adequate methods of monitoring. Several respondents indicated that they would like a clear national guideline concerning the manner and frequency of monitoring metabolic, cardiac, and endocrine indicators in youth treated with antipsychotics. In such a guideline, a balance must be found between the benefit and the burden for a child treated with antipsychotics. Not only are knowing which indicators to monitor and the frequency of monitoring significant considerations, but also all health care professionals involved must understand appropriate interventions when the outcome deviates from the baseline or reference value and suitable treatments for somatic consequences of antipsychotics.[19] For this to occur, cooperation between child and adolescent psychiatrists, nurse practitioners, general practitioners, and pediatricians is necessary. Furthermore, electronic medical records could provide reminders when monitoring is due and thus improve adherence to clinical guidelines.

Strengths and Limitations

A strength of this study is that the prescribers included worked in various health care settings throughout the Netherlands. Most were experienced prescribers with greater than 10 years of prescribing antipsychotics. They completed the questionnaire on the spot; therefore, it was not likely that they searched for information elsewhere but reported on actual daily clinical practice.

A limitation of this study is the relatively small number of prescribers who completed the questionnaire and whether these prescribers were representative of all prescribers of antipsychotics to youth in the Netherlands. Although the number is low, approximately 20% of all child and adolescent psychiatrists in the Netherlands completed the questionnaire. Other physicians, including general practitioners and pediatricians, were underrepresented. Social or professional desirability response bias may have led to overreporting of monitoring in youth treated with antipsychotics. In addition, physicians who attended this conference may be more aware and motivated to follow current guidelines, which could also lead to bias.

CONCLUSION

Treatment with antipsychotics includes frequent monitoring for efficacy and adverse effects. Although all health care professionals reported monitoring metabolic, cardiac, and endocrine indicators in youth treated with antipsychotics, there was great variability in which indicators were monitored and the frequency of monitoring. Almost none of the respondents who reported monitoring according to a guideline did follow this guideline completely. Factors contributing to variability, including the availability of facilitating factors and the reasons whether to start of stop monitoring, must be assessed to optimize monitoring practices and the benefit-risk ratio of antipsychotics for the individual patient.

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AUTHOR DISCLOSURE INFORMATION

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The manuscript does not contain clinical studies or patient data.

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