Original Research

Survey of Atypical Antipsychotic Prescribing by Canadian Child Psychiatrists and Developmental Pediatricians for Patients Aged Under 18 Years

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Objective: To describe self-reported patterns of prescribing atypical antipsychotics (ATAs) and monitoring practices of child psychiatrists and developmental pediatricians in Canada.

Method: We surveyed members of the Canadian Academy of Child and Adolescent Psychiatry and members of the Developmental Paediatrics Section of the Canadian Paediatric Society regarding the types and frequencies of ATAs they prescribed, the ages and diagnoses of patients for whom they prescribed these medications, and the types and frequencies of monitoring used.

Results: Ninety-four percent of the child psychiatrists (95%CI, 90% to 97%) and 89% of the developmental pediatricians (95%CI, 75% to 96%) prescribed ATAs, most commonly risperidone (69%). Diagnoses included psychotic, mood, anxiety, externalizing, and pervasive developmental disorders. Prescribing for symptoms such as aggression, low frustration tolerance, and affect dysregulation was also common. Twelve percent of all prescriptions were for children under age 9 years. Most clinicians monitored patients, but there were wide variations in the type and frequency of tests performed.

Conclusions: Despite the lack of formal indications, ATAs were prescribed by this group of clinicians for many off-label indications in youth under age 18 years, including very young children. Neither evidence-based guidelines nor a consensus on monitoring exist for this age group.

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Information on funding and support and author affiliations appears at the end of the article.

Clinical Implications

- Prescribing of ATAs is common by child psychiatrists and developmental pediatricians in Canada.
- The medications are prescribed for various diagnoses and symptoms, and patients include the very young.
- Monitoring is reported to be common, but there is little consensus as to what tests should be done or how often.

Limitations

- The data did not reflect actual prescriptions.
- The data were subject to recall bias.
- The respondents may not represent other clinicians.

Key Words: *antipsychotics, children, youth, Canada*

In the last 2 decades, the treatment of psychosis has been revolutionized by the widespread adoption of ATAs.[1–3] These agents, which in Canada presently include risperidone, olanzapine, quetiapine, and clozapine, have fewer propensities to cause extrapyramidal side effects and carry a significantly lower risk of tardive dyskinesia than do typical agents.[4] For adults, monitoring guidelines and established indications for the use of these medications exist, but not for children, with some exceptions. Some data exist to support the use of clozapine to treat refractory schizophrenia in patients aged under 18 years[5] and to reduce aggression in this population[6]; the review by Kranzler and colleagues[7] cites it as the drug of choice for this indication. Olanzapine has been reported to provide good response in early-onset schizophrenia. The adoption of ATAs as first-line drugs is primarily based on a similar practice for treating adults.

The more acceptable side effect profile and the safety of ATAs have broadened the indications for their use. ATAs are being used increasingly to treat various nonpsychotic disorders, not only in adults but also in children and adolescents.[8–14] As is often the case, controlled trials are rare and are characterized by small sample sizes, diagnostically heterogeneous samples, retrospective designs, short follow-up, and the lack of control groups.[15–18] Some data support short-term, sustained efficacy in reducing aggression,[19–24] tics,[25] and mania.[26,27] Other uses for ATAs, for example, as adjunctive treatment for anxiety and depression, are only supported by data for adults.

Unfortunately, these medications are not without their shortcomings. Most studies of adults and children find weight gain to be a side effect of ATAs.[28–31] Although this is to some extent a class effect, weight gain is generally more common and greater with olanzapine and clozapine.[31] Prior to treatment, adults with psychosis have a higher risk of glucose intolerance than do control subjects without psychosis; these medications increase that risk.[32,33] Medications such as olanzapine and clozapine, which cause more weight gain in adults, are generally more likely to disturb glucose metabolism, but this change has been found with use of all these medications in adult populations to differing extents. Finally, undesirable effects on lipid metabolism have also been identified in adults.[33–35] Weight gain with ATA use is by no means universal or inevitable. Awareness of this side effect, warning patients about it, and early intervention with diet and exercise have been advised.[36]

The use of ATAs in treating children has been increasing exponentially in the United States, raising concerns as to the appropriateness of this practice.[37,38] Evidence-based guidelines on frequency and type of monitoring do not exist. Canadian data are even more limited. To better appreciate current practices, we surveyed Canadian CPs and DPs to quantify their prescribing of this class of medications, the disorders and symptoms being treated, and the type and frequency of monitoring being used currently. We hypothesized that many doctors in this group were using the medications for various indications that are presently off-label. Further, we hypothesized that doctors varied widely in the kinds and frequency of tests they used to monitor these medications.

Abbreviations used in this article

AIMS	Abnormal Involuntary Movement Scale
ATA	atypical antipsychotic
CACAP	Canadian Academy of Child and Adolescent Psychiatry
CI	confidence interval
CP	child and adolescent psychiatrists
DP	developmental pediatricians
EKG	electrocardiogram

Method

Subjects

We obtained approval from the Review Board for Research Involving Human Subjects at the University of Western Ontario, the Executive of the CACAP, and the Canadian Paediatric Society. We surveyed CPs and DPs after obtaining approval from their professional organizations.

Questionnaire

We developed a questionnaire asking whether the physicians prescribed these medications, for which indications, and in which age groups. We also inquired as to the kinds of hematological and other monitoring these doctors used and how often these tests were done. We revised the instrument, using input from members of the CACAP. Questionnaires were returned by mail, fax, or email. A copy of the questionnaire is available from the authors.

Analysis

We used SPSS Version 14.0 (SPSS Inc, Chicago, Il, 2006) to analyze the results. Percentages with 95%CIs were used to summarize binary variables. Fisher's exact test was used to compare differences in categorical outcome variables between CPs and DPs. P values ≤ 0.05 were used to signify statistical significance.

Results

Participants

The CACAP has 361 members, 12 of whom do not practise in Canada. We invited the remaining 349 members to participate by written questionnaire. We also invited all 97 members of the Developmental Paediatrics Section of the Canadian

Paediatric Society to participate, sending them the same questionnaire by fax or email.

Of the 349 questionnaires mailed to CACAP members, 6 were ineligible because of retirement or non-MD status or were returned because of an incorrect address. One questionnaire was returned incomplete, preventing use of the data. The usable questionnaires totalled 176, a return rate of 48.8%. Of the 97 members of the Developmental Paediatrics Section, 36 returned completed questionnaires, for a return rate of 37.1%. Thus a total of 212 usable questionnaires were obtained from both organizations, yielding an overall return rate of 46.3%.

Questionnaire Results

Respondents were asked, "Do you prescribe atypical antipsychotics?" Of the CPs, 94% (95%CI, 90% to 97%) and of the DPs, 89% (95%CI, 75% to 96%) answered "yes," representing a nonsignificant difference (P = 0.197) between groups. Therefore, we combined the 2 groups in further analyses.

Use of Medications. The 198 respondents who prescribed this class were asked to estimate what percentage of each particular medication they prescribed. ("If you prescribe atypical antipsychotics approximately what percentage of each do you prescribe?") Table 1 presents the average percentages for the respondents who answered this question.

Risperidone was much more commonly prescribed (69%) than the other newer medications (quetiapine 24%, olanzapine 21%, clozapine < 1%). Clozapine remained in very limited use, presumably because of its more serious side effect profile and the frequent hematological monitoring that it requires.

Respondents were asked to state for which mental health diagnoses and symptoms they prescribed ATAs (Table 2). Most respondents prescribed ATAs for numerous diagnoses and symptoms. Many respondents added aggression (n = 32), psychosis (n = 22), and tics (n = 11) to the list provided of symptoms treated.

We inquired about the percentage distribution of the age groups of patients for whom ATAs were being prescribed. A few respondents (n = 6) gave answers totalling much less than 100%; since they appeared to misunderstand the question, their responses were eliminated. For the remaining responses, we calculated the average percentage of prescriptions for each age group (under 18 years). Although most prescriptions were for youth aged over 13 years, a surprising number of prescriptions were for the very young—12% for the group aged 8 years or under (Figure 1).

Screening. Screening appeared to be common in this sample, with 94% of CPs routinely screening their patients (95%CI, 89% to 97%), compared with 97% of DPs (95%CI, 83% to 99%), P = 0.46. When asked to estimate the proportion of patients screened, most responded that they screened 76% to 100% of the time.

Table 1 Percentage of prescribers by medication

Medication	%
Risperidone	69.0
Olanzapine	21.0
Quetiapine	24.0
Clozapine	0.7

Table 2 Percentage of prescribers by indication

Indication	%
Schizophrenia	78.8
Bipolar mood disorder	81.8
Depression	30.0
Tourette syndrome	73.5
Eating disorder	25.9
Obsessive–compulsive disorder	52.3
Posttraumatic stress disorder	33.5
Other anxiety disorders	30.0
Pervasive developmental disorder	89.4
Mental retardation	48.2
Attention-deficit hyperactivity disorder	51.2
Oppositional defiant disorder	51.2
Conduct disorder	59.4
Impulsivity	65.3
Poor frustration tolerance	74.7
Affective dysregulation	84.7
Insomnia	35.9

Respondents were asked to select the tests that they ordered routinely. Table 3 shows the percentage of respondents who ordered each test. In addition to these tests, many clinicians listed complete blood count (n = 22), thyroid function (n = 11), and renal function (n = 9) tests. Respondents appeared to use ATAs to monitor numerous areas that have proven to be of concern in adult patients (Table 3). No consistent pattern of appropriate follow-up intervals emerged from the results given by the respondents (Table 4).

We also explored the use of nonhematological monitoring, electrocardiograms, and AIMS testing. The AIMS is a formal examination for extrapyramidal signs for use in patients taking antipsychotics. Some respondents (n = 8) wrote that, although they did not do formal AIMS testing, they did

Figure 1 Percentage of prescribers by age of patients

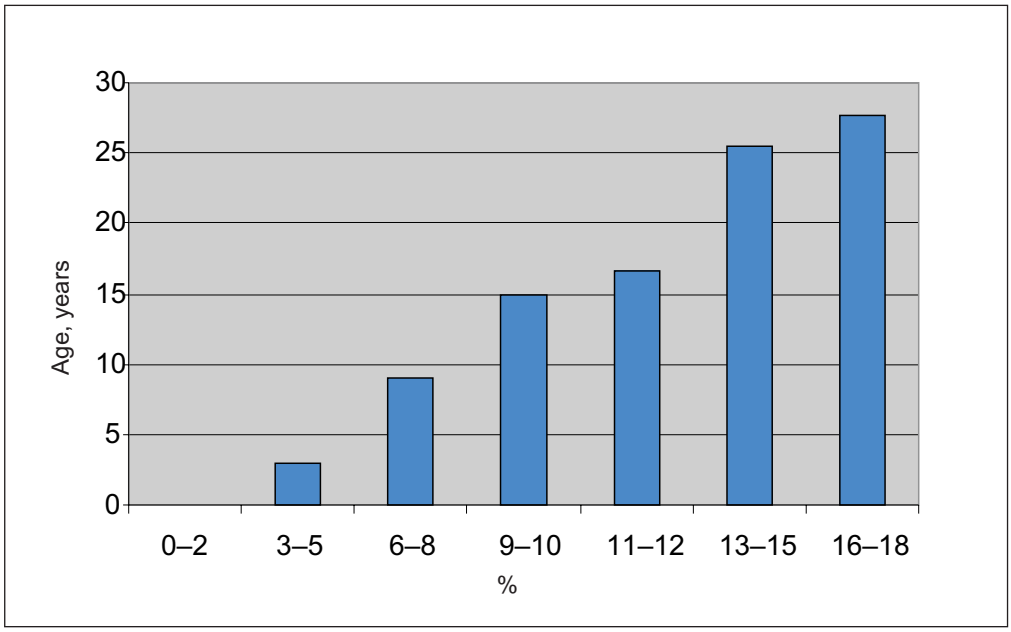

Table 3 Percentage of prescribers by screening test

Screening test	%
Fasting blood sugar	75.0
2 hour post-cibum	17.7
Hemoglobin A1c	19.5
Total cholesterol	76.2
Low density lipoprotein	67.1
High density lipoprotein	65.2
Triglycerides	73.8
Prolactin	72.0
Liver function tests	87.2
EKG	50.0
AIMS	43.9

Table 4 Follow-up intervals

Interval	% ordering hematological monitoring	% performing EKG and (or) AIMS
Baseline	76.8	58.0
1 month	21.3	12.8
3 months	43.9	28.7
6 months	56.1	27.4
1 year	56.7	29.3

examine patients regularly for extrapyramidal signs and symptoms ($n = 8$). Others commented that they regularly measured weight and height, body mass index, and (or) waist circumference.

Discussion

These data suggest a high rate of prescribing ATAs by Canadian CPs and DPs for various indications and symptoms. A significant proportion of these prescriptions are given to children aged under the age of 9 years. These medications are currently being used off-label without clear guidelines for indications, dosing, and monitoring. Subjects report that they monitor patients extensively and frequently, but the practices are not uniform. This situation may be due to lack of data and guidelines. A 43.9% rate of AIMS testing is impressive; however, this means that 56.1% of patients under the age of 18 years who are being prescribed this medication are not being monitored in this way. Further, there are significant discrepancies in the timing of follow-up (3 months, 6 months, or 12 months.) Although these survey results do not establish the total number of patients being treated with ATAs, they do establish that the prescribing of ATAs by CPs and DPs in Canada is ubiquitous. There is an urgent need for more data regarding safety and monitoring of these medications in children.

Design Limitations

Although most questions in the survey were responded to and answered appropriately, physicians misunderstood one question regarding the percentage distribution of various age groups of patients for whom ATAs were currently being

prescribed. Inaccuracy or bias is also possible in self-reports, as is the phenomenon of recall bias. The low return rate also limits the external validity of these survey results.

Conclusions

Despite the lack of formal indications of any kind for patients under the age of 18 years, ATAs are widely prescribed by Canadian CPs and DPs. This survey demonstrates that this group of clinicians prescribes ATAs for many off-label indications in youth aged under 18, including patients who are very young. Although these clinicians report the use of many investigations to follow up with their patients, neither a consensus on monitoring nor evidence-based guidelines exist for this age group. Further studies are needed to clarify these issues. Until more data are available to provide evidence-based recommendations, a consensus-based guideline is needed to aid Canadian clinicians who are currently prescribing ATAs for patients under age 18 years and who reluctantly must rely on their own judgment. Perhaps a national body such as the Canadian Psychiatric Association or the CACAP might appoint an expert panel to review the existing data and current practice and produce such recommendations. This study suggests that such recommendations would be gratefully received.

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Résumé : Enquête sur la prescription d'antipsychotiques atypiques par les pédopsychiatres et les pédiatres du développement canadiens aux patients de moins de 18 ans

Objectif : Décrire les modèles autodéclarés de prescription d'antipsychotiques atypiques (APA) et les pratiques de surveillance des pédopsychiatres et des pédiatres du développement au Canada.

Méthode : Nous avons interrogé les membres de l'Académie canadienne de psychiatrie de l'enfant et de l'adolescent et les membres de la section pédiatrie du développement de la Société canadienne de pédiatrie concernant les types d'APA qu'ils prescrivaient et à quelle fréquence, l'âge et les diagnostics des patients à qui ils prescrivaient ces médicaments, et les types et fréquences de surveillance utilisés.

Résultats : Quatre-vingt quatorze pour cent des pédopsychiatres (95 % IC, 90 % à 97 %) et 89 % des pédiatres du développement (95 % IC, 75 % à 96 %) prescrivaient des APA, le plus souvent la rispéridone (69 %). Les diagnostics comprenaient des troubles psychotiques, de l'humeur, anxieux, d'externalisation et des troubles envahissants du développement. Les prescriptions pour des symptômes comme l'agressivité, la faible tolérance à la frustration, et le dérèglement de l'affect étaient aussi répandues. Douze pour cent de toutes les prescriptions étaient pour des enfants de moins de 9 ans. La plupart des cliniciens surveillaient les patients, mais il y avait de larges variations entre le type et la fréquence des tests effectués.

Conclusions : Malgré l'absence d'indications officielles, les APA étaient prescrits par ce groupe de cliniciens pour de nombreuses utilisations non indiquées sur l'étiquette, chez des jeunes de moins de 18 ans, y compris de très jeunes enfants. Il n'existe ni lignes directrices fondées sur des données probantes, ni consensus sur la surveillance pour ce groupe d'âge.