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Clinical Practice Study

Audit of physical health monitoring in children and adolescents receiving antipsychotics in neurodevelopmental clinics in Northumberland

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Abstract**AIM**

To ascertain performance against the standards set by National Institute for Clinical Excellence (NICE) guidelines on physical health monitoring of thirty children and adolescents prescribed antipsychotics in neurodevelopmental clinics in Northumberland and identifying areas for improvement in practice.

METHODS

The audit involved a review of recorded documentation pertaining to physical health monitoring in patient electronic records pertaining to children and adolescents attending neurodevelopmental clinics in Northumberland prescribed antipsychotics. Clients were also contacted by telephone if relevant documentation could not be identified or retrieved to confirm the details. 32 case notes were perused of which 2 were excluded as they had refused to have venepuncture which was documented in the electronic records.

RESULTS

The overall audit results demonstrated partial compliance with NICE guidelines on physical health monitoring in children and adolescents prescribed antipsychotics. Bi-annual recording of height, weight, blood pressure, pulse rate and review of side effects

was completed in 100% of subjects. However, annual monitoring for blood tests including liver function, renal function full blood count as well as biannual monitoring of serum prolactin, serum lipid profile was completed only in 56% of subjects. Comparative baseline characteristics between the two groups (compliant and non-compliant with guidelines) found no differences based on any socio-demographic or clinical variables. However, the proportion of patients in the group compliant to guidelines was higher in the age group of 12-17 years as compared to < 12 years (70.58% vs 38.46%), though not statistically significant ($\chi^2 = 1.236$; $P = 0.24$).

CONCLUSION

Development of tailored and specific guidelines for physical health monitoring in children and adolescents prescribed antipsychotics taking into consideration clinical effectiveness and safety profile is likely to improve adherence rates.

Key words: Antipsychotic; Children; Physical health; Guidelines

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Core tip: A number of clinical guidelines have been developed for physical health monitoring in children and adolescents on antipsychotics. However, none of them capture the intricacies and complexities involved in prescribing antipsychotics to children and adolescents, which is distinct from adults. The typically shorter duration of prescribing, lower doses used and lack of data on long term adverse effects with antipsychotics in this population have not been taken into account. This audit aimed to ascertain if physical health of children and adolescents attending neurodevelopmental clinics in Northumberland and prescribed antipsychotics followed National Institute for Clinical Excellence guidelines. The overall audit findings were partially compliant with the guidelines. Logistic and ethical challenges as well as lack of awareness about the guidelines could underpin these findings.

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INTRODUCTION

Despite limited literature on long term effectiveness and side effects of antipsychotics in children and adolescents, antipsychotics are frequently used in this population in Europe and North America. In fact,

recent trends of increased antipsychotic prescribing for this population has been well-documented. In a recent German nation-wide prescribing audit by health care insurers it was demonstrated that the rise in antipsychotic prescriptions was particularly marked among 10- to 14-year-olds (from 0.24% to 0.43%) and among 15- to 19-year-olds (from 0.34% to 0.54%)^[1]. Psychosis, challenging behaviour in autism spectrum disorder (ASD) and Tourette's syndrome are the most common reasons for child and adolescent psychiatrists to prescribe antipsychotics. In addition, use of antipsychotics in other neurodevelopmental disorders like attention deficit hyperactivity disorder (ADHD) is not uncommon though "off-label" for this purpose^[2]. In terms of symptom profiles targeted by antipsychotic use in this population, the most common indications were chronic behavioural disturbance with persistent aggression (34%), followed by agitation/anxiety (31%) and psychotic symptoms (31%) in a recent nation-wide audit of antipsychotic prescribing in children and adolescents in United Kingdom^[3].

A survey of antipsychotic prescribing among child and adolescent psychiatrists in the United Kingdom found that over 95% had prescribed antipsychotics over a 12 mo period with the majority (almost 90%) choosing one of the second generation antipsychotics (SGAs)^[4]. Risperidone followed by aripiprazole and olanzapine are the favoured antipsychotics in this population^[4]. There is a relatively limited but gradually expanding evidence-base of randomised clinical trials to support antipsychotic prescribing in children and adolescents with non-psychotic illnesses. This includes management of challenging behaviour in ASD with risperidone; aripiprazole and risperidone for management of aggression with conduct disorder and learning disability^[5-8].

It is to be noted that, children and adolescents are more sensitive to antipsychotic-related adverse effects than adults. This includes extrapyramidal side effects (EPS) with first generation antipsychotics (FGAs) and metabolic side effects with SGA^[9,10]. However, it is also worth noting that most literature relating to tolerability of antipsychotics in children and adolescents are based on the treatment of severe mental illnesses like psychotic disorders in typically short-term clinical trials lasting 6 to 12 wk. There is scant literature on the adverse effects associated with longer term prescribing of antipsychotics (the distal health outcomes as opposed to more proximal health outcomes) and more particularly, involving lower doses that are typically used in non-psychotic developmental disorders in children and adolescents. Possibly, as an extension to this, we do not know if these physical side effects are reversible, partially or completely with discontinuation of antipsychotics or are these irreversible side effects.

Individual antipsychotics (even within the same class) differ in terms of side effect profiles when prescribed to children and adolescents. For example, in this population, EPS are more common with haloperidol and high-

dose risperidone than with olanzapine. Weight gain is more common in olanzapine than with risperidone^[10,11]. There is also some evidence for differential response to same medication based on age groups. For example, children and adolescents experience more weight gain on second generation antipsychotics than do adults^[10]. However, most of the guidelines do not differentiate their physical health monitoring requirements, particularly in the maintenance phase between those on different antipsychotics or between different age groups. Also, first and second generation antipsychotics are different chemically and heterogeneous with respect to safety profile. Hence, having common monitoring requirement seems flawed, in practical terms.

The commonly followed guidelines for physical health monitoring in children and adolescents receiving antipsychotics include NICE (National Institute for Clinical Excellence guidelines) (CG155); AACAP (American Academy of Child and Adolescent Psychiatry) - practice parameter for the use of atypical antipsychotic medications in children and adolescents; CAMESA - Canadian Alliance for Monitoring Effectiveness and Safety of Antipsychotics in Children and TRAY (Treatment recommendations for the use of antipsychotics for aggressive youth) centre for the Advancement of Children's Mental Health^[12-14]. The specificity of recommendations for ongoing monitoring for metabolic parameters varies, with some guidelines recommending "appropriate" monitoring while others identifying specific tests and pre-determined follow-up intervals.

The parameters specified in these guidelines include physical measurements like height, weight, blood pressure and pulse rate as well as those measured in laboratory with a blood sample like liver function test, renal function tests and blood glucose. Usually, there are specifications for monitoring parameters at baseline as well as during the maintenance phase in the guidelines mentioned above.

This audit was identified with a view to ascertaining performance against the standards set by National Institute for Clinical Excellence (NICE) guidelines on physical health monitoring of thirty children and adolescents prescribed antipsychotics in neurodevelopmental clinics in Northumberland and identifying areas for improvement in practice^[15]. The audit focused only on those clients who had already been initiated and stabilised on a dose of antipsychotic medication for at least a period of one year prior to the time frame chosen for audit. The time frame covered was from 1st November 2015 to 30th October 2016.

MATERIALS AND METHODS

The audit involved a review of recorded documentation pertaining to physical health monitoring in patient electronic records pertaining to those children and adolescents attending neurodevelopmental clinics in Northumberland prescribed antipsychotics. Clients were

also contacted by telephone if relevant documentation could not be identified or retrieved to confirm the details. Thirty-two case notes were perused of which 2 were excluded as they had refused to have venepuncture which was documented in the electronic records. Hence, the total number of clients included in the audit was 30. The sample was collated by means of consecutive sampling of convenience. Data collection took place from 1 November 2016 to 30 March 2017 and data analysis was completed in 30 April 2017. A quality review of the results of this audit was undertaken by the second author during July 20, 2017 to August 03, 2017 to provide assurance on the accuracy of the findings in this report. The audit was registered with the audit department of Northumberland, Tyne and Wear NHS foundation trust.

The NICE guidelines recommend annual physical health monitoring of following parameters for patients already stabilised on antipsychotic medications: Biannual monitoring for weight, height, pulse, blood pressure, fasting blood glucose, HbA1c and blood lipid levels, review of side effects and annual monitoring for liver function tests, renal function tests and serum electrolytes as well as full blood count. The expected compliance rate was 100% (gold standard) with respect to all the above parameters.

Statistical analysis

The data was analysed using SPSS 15.0 (Statistical package for social science). The data was analysed using appropriate parametric and non-parametric tests based on the distribution of data including χ^2 test for categorical variables and *t*-test for continuous variables. *P* < 0.05 was considered significant.

RESULTS

The study sample included 28 males and 2 female clients (male: female ratio of 14:1). The two antipsychotics prescribed were risperidone (77%) (*n* = 23) and aripiprazole (23%, *n* = 7). The daily dose range for risperidone was 0.25-2 mg and for aripiprazole was 0.5-4 mg. The mean dose of risperidone used was 0.88 mg (SD: 0.11) and mean dose of aripiprazole used was 1.87 mg (SD: 0.23). The mean age of initiation of antipsychotic in this sample was 13.45 years (SD: 1.23). The average duration of antipsychotic use in months was 15.67 mo (SD: 1.98) (Table 1).

Bi-annual recording of height, weight, blood pressure, pulse rate and review of side effects was completed in 100% of subjects. However, annual monitoring for blood tests including liver function, renal function full blood count as well as biannual monitoring of serum prolactin, serum lipid profile was completed only in 56% of subjects. It was also noted that in five of the subjects in whom the physical health monitoring was carried out according to guidelines, the initial lab result summary did not contain serum prolactin which

Table 1 Baseline characteristics of the audit sample (*n* = 30)

Variable	Mean	SD
Age (yr)	13.45	1.23
Duration of antipsychotic use (mo)	15.67	1.98
Average number of clinical reviews	3.43	0.46
Variable	<i>n</i>	%
Age groups (yr)		
12-17	17	56.67
< 12	13	43.33
Gender		
Male	28	93.33
Female	2	6.67
Antipsychotic		
Risperidone	23	76.67
Aripiprazole	7	23.33
Psychiatric diagnosis		
ADHD	12	40.00
ASD	4	13.33
ADHD + ASD	6	20.00
ADHD + other diagnosis	6	20.00
ASD + other diagnosis	2	6.67

ADHD: Attention deficit hyperactivity disorder; ASD: Autism spectrum disorder.

was subsequently carried out after a second request (possibly missed out initially due to oversight).

Comparing the baseline characteristics between the groups for whom antipsychotic physical monitoring guidelines were followed and not followed, there were no differences based on antipsychotic prescribed, duration of antipsychotic use or number of reviews carried out in the neurodevelopmental clinics. However, the proportion of patients who were monitored for physical health according to guidelines was higher in the age group of 12-17 years as compared to < 12 years, though not statistically significant ($\chi^2 = 1.236$; $P = 0.24$). There were also no significant differences in the proportion monitored for physical health based on the diagnosis (ADHD; ASD; ADHD+ASD; ADHD + other mental health disorders; ASD + other mental health disorders) ($\chi^2 = 1.345$; $P = 0.27$). The "other" diagnoses included oppositional defiant disorder ($n = 3$), tic disorder ($n = 3$) and conduct disorder ($n = 2$). We did not carry out a gender-wise comparison, since there were only two female clients in the audit sample (Table 2).

The overall audit results demonstrated partial compliance with NICE guidelines on physical health monitoring in children and adolescents prescribed antipsychotics. However, it was interesting to note that, the monitoring guidelines were followed in a larger proportion of patients in 12-17 year age range as compared to < 12 years (though not statistically significant). To summarise, there was no statistical difference between the groups that completed and did not complete physical health monitoring according to NICE guidelines based on any baseline socio-demographic or clinical variables.

Table 2 Factors associated with likelihood of testing

Age groups (yr)	Total number	Number monitored
12-17	17	12
< 12	13	5
Antipsychotic		
Risperidone	23	13
Aripiprazole	7	4
Psychiatric diagnosis		
ADHD	12	7
ASD	4	2
ADHD + ASD	6	3
ADHD + other diagnosis	6	4
ASD + other diagnosis	2	1
Average duration of antipsychotic use	Mean	SD
Group A ¹	15.98	1.21
Group B ²	15.42	1.32
Average number of clinical reviews	Mean	SD
Group A ¹	3.52	0.32
Group B ²	3.31	0.36

¹Group A: Group that completed physical health monitoring requirements according to National Institute for Clinical Excellence (NICE) guidelines;

²Group B: Group that did not complete physical health monitoring requirements according to NICE guidelines. ADHD: Attention deficit hyperactivity disorder; ASD: Autism spectrum disorder.

DISCUSSION

The findings from our audit are broadly similar to previous published literature. A similar audit carried out recently in an inpatient setting in United Kingdom on children and adolescents prescribed antipsychotics demonstrated adherence rates of 20%-60% on different parameters^[16]. In comparison, an audit of similar parameters in a community based setting focusing on adult patient's demonstrated partial adherence to guidelines in around half the patients^[17]. Both the above audits were carried out with standards set by NICE as the reference.

Outside the United Kingdom, there are studies or audits published from North America and Europe on the same theme. A large scale longitudinal retrospective cohort study using data from 2000-2006 from the PharMetrics data base (an insurance claims database) in United States demonstrated 12 wk lipid and blood sugar monitoring rates of 6.8% and 9% respectively in patients under 65 years (which also includes children and adolescents) receiving second generation antipsychotics^[18]. It also interestingly demonstrated rise in these rates to 14.1% and 17.9% post introduction of ADA (American diabetic association) guidelines in 2004. Of even more importance, is the fact that 0-11 years and 11-17 years fared the worst when different age groups were compared for 12 wk monitoring of blood glucose and blood lipids^[18].

The limitations of our audit include a small sample size and lack of representation from female patients with neurodevelopmental disorders, receiving an

antipsychotic. Also, the results are specific for our service and cannot be generalised to other parts of the country considering the heterogeneity in the way neurodevelopmental services as well as physical health services are organised in different parts of the country.

Several guidelines based on available evidence base have been developed (mentioned earlier) for both baseline and ongoing monitoring of physical health parameters for children and adolescents prescribed antipsychotics. However, most of these guidelines are extrapolated at least in part from the equivalent guidelines for adults. They fail to capture the complexities and intricacies of antipsychotic prescribing, particularly in younger children, especially the usually short term symptomatic use.

The common barriers cited for non-adherence to guidelines on physical health monitoring in children and adolescents prescribed antipsychotics include ethical and practical difficulties in taking blood from children (*e.g.*, In children with autism and challenging or oppositional behaviours)^[3]. This could also be the possible basis for the audit finding that a higher proportion of adolescents on antipsychotics were monitored for physical health parameters than younger children on antipsychotics (though not statistically significant). This could also possibly reflect the tendency of mental health professionals to treat adolescents more like young adults while in case of children, the attitude of clinicians is generally quite different. There is also uncertainty regarding the impact of abnormal results on clinical management (*e.g.*, asymptomatic hyperprolactinaemia)^[3]. Sometimes, logistic challenges including inadequate number of skilled phlebotomists and lack of a reliable pathway for carrying out these investigations and retrieving the results could be a barrier to following these guidelines (for example, in many cases psychiatrists depend on general practitioners or hospitals for organising blood tests while in some services in house phlebotomy and lab services are offered). However, most clinicians do support the development of physical health monitoring guidelines for antipsychotic use in children and adolescents, albeit advocating guidelines more appropriately constructed for this target population and taking into account the complexities involved.

Some published literature on quality improvement projects in this regard demonstrated simple methods like a visual prompt questionnaire tool along with review paperwork, new formatting of clinical letters to general practitioners, psychoeducation of both clinical practitioners and patients, easy read leaflets and posters which did produce a significant improvement in adherence to clinical guidelines^[16,17]. On a larger scale, in Europe, the Therapeutic Drug Monitoring (TDM) run by the German-Austrian Swiss "Competence Network on TDM in Child and Adolescent Psychiatry" and the Paediatric Atypical Antipsychotic Monitoring Safety Study (PAMS) in the United Kingdom have been developed as pharmacovigilance projects^[19,20].

Development of tailored and specific guidelines for physical health monitoring in children and adolescents prescribed antipsychotics based on age of initiation, dose and type of antipsychotic is likely to improve adherence rates. Some room for flexibility, taking into consideration appropriate clinical judgement on a case by case basis may also be beneficial in this regard. Similarly, understanding attitudes and psychological barriers in both patients and clinicians to regular monitoring, particularly blood parameters can provide useful insight in addressing the generally low compliance rates to these guidelines worldwide. We also need further studies to identify those children and adolescents with a possibly higher risk of side effects (*e.g.*, a positive family history of physical morbidity) to allow us to tailor a more intensive monitoring regimen for this subset of population receiving antipsychotics. Tailored guidelines for children and adolescents and a customised approach is needed to match clinical effectiveness and safety profile.

ARTICLE HIGHLIGHTS

Research background

Despite limited literature on long term effectiveness and side effects of antipsychotics in children and adolescents, antipsychotics are frequently used in this population in Europe and North America. In fact, recent trends of increased antipsychotic prescribing for this population has been well-documented. These medication are associated with physical health side effects though the extent of these side effects when used in lower doses or prolonged duration in children and adolescents have not been adequately studied. However, a number of popular guidelines exist pertaining to physical health monitoring in children and adolescents on antipsychotics.

Research motivation

The current study is an audit of physical health monitoring in children and adolescents prescribed antipsychotics in neurodevelopmental clinics in Northumberland. A comparative review of similar audits carried out from different regions can address pertinent issues like association between standards set by different guidelines and the concordance rates with the same.

Research objectives

To ascertain performance against the standards set by National Institute for Clinical Excellence (NICE) guidelines on physical health monitoring of thirty children and adolescents prescribed antipsychotics in neurodevelopmental clinics in Northumberland and identifying areas for improvement in practice.

Research methods

The audit involved a review of recorded documentation pertaining to physical health monitoring in patient electronic records pertaining to those children and adolescents attending neurodevelopmental clinics in Northumberland prescribed antipsychotics. Clients were also contacted by telephone if relevant documentation could not be identified or retrieved to confirm the details. 32 case notes were perused of which 2 were excluded as they had refused to have venepuncture which was documented in the electronic records.

Research results

The overall audit results demonstrated partial compliance with NICE guidelines on physical health monitoring in children and adolescents prescribed antipsychotics. Bi-annual recording of height, weight, blood pressure, pulse rate and review of side effects was completed in 100% of subjects. However, annual monitoring for blood tests including liver function, renal function full blood count as well as biannual monitoring of serum prolactin, serum lipid profile was completed only in 56% of subjects. Comparative e baseline characteristics

between the two groups (compliant and non-compliant with guidelines) found no differences based on any socio-demographic or clinical variables. However, the proportion of patients in the compliant group was higher in the age group of 12-17 years as compared to < 12 years (70.58% vs 38.46%), though not statistically significant ($\chi^2 = 1.236$; $P = 0.24$).

Research conclusions

Development of tailored and specific guidelines for physical health monitoring in children and adolescents prescribed antipsychotics taking into consideration clinical effectiveness and safety profile is likely to improve adherence rates.

Research perspectives

The methodology into development of tailored guidelines for antipsychotic monitoring in children and adolescents need to be adequately focused upon. A comparative review of the audits on antipsychotic physical health monitoring guidelines carried out till date in different regions of the world based on different guidelines might shed some light on this important topic.

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