ORIGINAL ARTICLE

Asthma control in adolescents: the importance of assessing adherence

Giorgio Ciprandi[1], Amelia Licari[2], Riccardo Castagnoli[2], Riccardo Ciprandi[3], Gian Luigi Marseglia[2]

[1]Allergy Clinic, Casa di Cura Villa Montallegro, Genoa, Italy; [2]Department of Paediatrics, Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy; [3]Cystic Fibrosis Unit, Istituto G. Gaslini, Genoa, Italy

Abstract. *Background and aim* Asthma control is the goal of the management, but some patients do not achieve adequate control. Adherence to prescriptions is a relevant factor in this issue. As very few studies addressed this problem in adolescents, we investigated this aspect in this setting. *Methods* This cross-sectional study consecutively enrolled 87 adolescents (60 males, 27 females, median age 14.2 years) with asthma visited at a third-level pediatric clinic. We used two questionnaires: Morisky Medication Adherence Scale (MMAS-8) and TAI. *Results* As regards MMAS-8, 23 (26.6%) adolescents had low adherence, 34 (39%) medium, and 30 (34.4%) high. Concerning TAI, 34 (39%) had low adherence, 43 (49.5%) medium, and 10 (11.5%) high. After stratification per asthma control grade, adolescents with partly-controlled asthma had the highest scores for medium adherence (p=0.0017 and 0.049, respectively for MMAS-8 and TAI). *Conclusions* Adolescents with asthma have poor adherence independently to the asthma control grade. This failure implicates that more attention should be paid to this issue in clinical practice. (www.actabiomedica.it)

Key words: asthma, adherence, adolescents, asthma control

Introduction

Adherence to medications is still a challenging issue in clinical practice (1). The World Health Organization defines adherence as "the extent to which a person's behavior taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider."

Adherence can be measured, and self-reported questionnaires are currently the most common and effective used tools (2). In this regard, Plaza and colleagues assessed adherence in 816 adult patients with asthma or COPD, combining the adherence test with inhalers (TAI) with pharmacy refill records (3). TAI test demonstrated a 58.1% non-adherence rate, and pharmacy refill recorded 28.6%; the combined measures showed a 64.6% rate. The concordance between tools was weak. Therefore, the authors suggested the concomitant use of both tests.

On the other hand, adolescence is a critical period of life characterized by emotional distress (4). Consistently, prevalence, morbidity, and mortality are high among asthmatic adolescents, with higher exacerbation rates, hospitalization, and death than in younger children (5). Reported adherence to inhaled corticosteroids (preventer inhalers) in adolescents is poor, ranging from 25% to 35%, and associated with adverse outcomes, including death (4). Asthma exacerbations are effectively reduced when adherence to preventer inhalers is greater than 80% (6).

The poor adherence rates in adolescents with asthma can be attributed to the many developmental, psychosocial, and environmental changes across adolescence. For example, in early adolescence (12-15 years), cognitive functioning shifts from concrete to abstract thinking, transitioning a simplified asthma perception into a more complex understanding of the illness (4). Adolescence is also characterized by increased attention to peer acceptance and desire for autonomy from

parents. Therefore, adolescents may conceal symptoms and dismiss medication to avoid embarrassment, stigma, or seeming different from their peers.

Moreover, asthma management pursues the target of optimally controlling asthma as recommended by the guidelines. However, unfortunately, despite the widespread dissemination of asthma guidelines, only half of the adolescents have well-controlled asthma (7). This failure depends on many factors, including, indeed, poor adherence. Based on this background, we evaluated the adherence grade in a group of adolescents with asthma, considering the asthma control grade.

Methods

This cross-sectional study included adolescents with asthma visited at a third-level pediatric clinic.

Inclusion criteria were: age between 12 and 18 years, both genders, and asthma diagnosis. Exclusion criteria were: current respiratory infections, severe chronic disorders (e.g., metabolic disorders, autoimmunity, neuropsychiatric diseases, cancer), and medications, including immune-suppressants, psychiatric drugs, chemotherapy, able to interfere with the interpretation of the results.

Demographic data, symptom perception assessment by visual analogic scale (VAS), lung function, and asthma control test (ACT) were evaluated. The asthma control was assessed according to the global initiative for asthma (GINA) guidelines (www.ginasthma.org)

The internal ethics review Committee approved the study (code number: 22253/2017). Both the parents signed informed consent. The study was conducted before the COVID-19 pandemic as started in January 2019 and ended in June 2019.

Medication adherence was assessed by two questionnaires: the Morisky Medication Adherence Scale (MMAS-8) and TAI.

MMA-8 is a simple, reliable, and widely used instrument for determining adherence to prescribed medications; it includes eight questions (score range: 0–8), with each item measuring a specific medication adherence behavior (8). The first seven items are Yes-or-No questions, and the last item has five options. Adherence levels of a high, medium, and low level are defined with MMAS-8 scores of 8 points, 6 to <8 points, and <6 points, respectively.

The TAI is a validated self-report instrument designed to assess adherence to inhaler therapy (9). The TAI-10 includes ten patient-rated items with a total score ranging from 10 to 50; patients who scored <50 were classified as non-adherent.

Descriptive statistics of the study patients were firstly calculated; quantitative data were reported in terms of absolute frequencies and percentages; quantitative data were reported in terms of medians, first and third quartiles (1st − 3rd q). The normality of distributions was evaluated using the Shapiro-Wilk test. Quantitative data of three groups were analyzed using the non-parametric Analysis of Variance (Kruskal-Wallis test). Bonferroni's correction was used as a *post–hoc* test to avoid multiple comparisons error. All statistical tests were 2-sided, and a P value less than 0.05 was considered statistically significant. The statistical software "Statistica" (version 9, StatSoft Corporation, Tulsa, OK, USA) was used.

Results

This cross-sectional study consecutively enrolled 87 adolescents (60 males, 27 females, median age 14.2 years).

Table 1 shows the clinical outcomes. The subjects were stratified into three subgroups considering the asthma control, such as well-controlled (48), partly-controlled (30), and uncontrolled (9).

Adolescents with uncontrolled asthma perceived more severe symptoms (p=0.002), had lower FEF_{25-75} (i.e., an early marker of bronchial impairment) values and ACT scores (p=0.034 and <0.0001, respectively). As regards MMAS-8, 23 (26.6%) adolescents had low adherence, 34 (39%) medium, and 30 (34.4%) high. Concerning TAI, 34 (39%) had low adherence, 43 (49.5%) medium, and 10 (11.5%) high. Considering the asthma control grade, adolescents with partly-controlled asthma had the highest scores for medium adherence (p=0.0017 and 0.049, respectively for MMAS-8 and TAI).

Discussion

These results underlined that the adolescents globally had poor adherence as only 34.4% (using the

Table 1. Comparison among the 3 groups of patients: well controlled, partially controlled and uncontrolled according to GINA guidelines.

	Well controlled [N = 48]	Asthma control (GINA) Partly controlled [N = 30]	Uncontrolled [N = 9]	##P
Gender: Male, n/N (%)	33/48 (68.7 %)	22/30 (73.3 %)	5/9 (55.5 %)	0.59
Age *(years)*	14.8 [13 – 17]	14.5 [13.5 – 17.3]	14 [12.7 – 17.1]	0.85
VAS for asthma symptoms	9 [8 – 10]	8 [8 – 8]	7 [7 – 8]	**0.002**
FVC - at baseline (% pred.)	101.5 [93.7 – 109.5]	101.5 [91.2 – 108.7]	95 [82 – 96]	0.13
FEV_1 - at baseline (% pred.)	97.5 [91.7 – 107.2]	101.5 [93.5 – 111.7]	90 [72 – 100]	0.05
FEV_1/FVC - at baseline	83.4 [79.9 – 87.8]	87.6 [84.1 – 90.9]	83.7 [70 – 90.8]	0.10
FEF_{25-75} - at baseline (% pred.)	89 [75.2 – 99.2]	99 [84.4 – 113.7]	87 [42 – 97]	**0.034**
Asthma Control Test (ACT) score	24 [23 – 25]	22 [21 – 22]	16 [15 – 17]	**< 0.0001**
Level of adherence to treatment MMAS-8				
MMAS-8 <6, low	16/48 (33 %)	5/30 (17 %)	2/9 (22 %)	0.2556
MMAS-8 6-8, medium	11/48 (23 %)	19/30 (63 %)	4/9 (44 %)	**0.0017**
MMAS-8 >8, high	21/48 (44 %)	6/30 (20 %)	3/9 (34 %)	0.0995
Level of adherence to treatment 10-item TAI				
10-item TAI 10-45, low	17/48 (32 %)	13/30 (44 %)	4/9 (44.5 %)	0.7381
10-item TAI 46-49, medium	23/48 (48 %)	16/30 (53 %)	4/9 (44.5 %)	0.8537
10-item TAI 50, high	8/48 (20 %)	1/30 (3 %)	1/9 (11 %)	**0.0491**

Figures represent median values (unless otherwise specified) and figures in squared parentheses represent 1st and 3rd quartiles; figures in round parentheses represent column percentages; in bold significant p value

MMAS-8 tool) or 11.5% (using the TAI tool) presented high adherence scores. Surprisingly, adolescents with partly-controlled asthma displayed the lowest adherence scores. As expected, subjects with well-controlled asthma had the highest adherence, even though the rates were unsatisfactory (44% considering MMAS-8 and only 20% by TAI). Adolescents with uncontrolled asthma had an intermediate situation. This outcome could be consistent with asthma severity as patients experiencing bothersome symptoms tend to take the medicines more frequently. Probably, adolescents with partly-controlled asthma do not feel the need to take medicines correctly.

The current study provided interesting information about the influence of asthma control grade on adherence. Unfortunately, the adherence rate remains a critical issue in asthma management, mainly in adolescents. This fact represents the low effectiveness of the current recommendations in asthma care (10). A recent meta-analysis explored the relevance of measuring adherence in adolescents and young adults with asthma (11). The study included 38 retrospective studies. The primary outcome of this meta-analysis confirmed that subjects with good adherence to asthma medications had less likely to experience asthma exacerbation. Namely, adolescence represents a recognized age period with an increased risk of increased asthma mortality rate (12). Asthma course, indeed, may significantly change during adolescence. Several factors may worsen asthma in adolescents, including anxiety, depression, obesity, puberty (mainly in females), smoking, poor symptom recognition, and low adherence to treatment. In this regard, a European Academy of Allergy and Clinical Immunology task force provided a series of recommendations to adequately manage adolescents during the transition period from adolescence to adulthood (13). In this context, adherence improvement represents a crucial factor in optimizing asthma care. Low adherence has been recognized as a relevant factor in adolescents with loss of asthma control over time (14).

Also, the present findings were consistent with a very recent study conducted on adolescents and children (15). The study included 134 subjects and aimed to evaluate the adherence to inhaled corticosteroids (ICS). Anxiety, depression, and low self-esteem were factors associated with non-adherence to treatment. After providing asthma education, ICS adherence and asthma control significantly improved. Another study demonstrated that using electronic reminders and incentives through an application coupled with an electronic monitoring device increased the adherence rate to asthma medications (16).

Therefore, adherence to prescribed treatments represents a critical issue in adolescents with asthma and deserves adequate attention in clinical practice, as underscored by the present study.

However, this study had some limitations, including the cross-sectional design, the lack of biomarker assessment, and the limited number of subjects. Anyway, the data were collected in a real-life setting, so the findings can mirror what happens in clinical practice.

In conclusion, adolescents with asthma have poor adherence independently to the asthma control grade. This failure implicates that more attention should be paid to this issue in daily practice.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement, etc.) that might pose a conflict of interest in connection with the submitted article

References

1. Duarte-de-Araujo A, Teixeira P, Hespanhol V, Correira-de-Sousa J. COPD: understanding patients' adherence to inhaled medications. Int J COPD 2018;13:2767-2773
2. Pearce CJ, Fleming L. Adherence to medication in children and adolescents with asthma: methods for monitoring and intervention. Exp rev Clin Immunol 2018;14(12):1055-1063
3. Plaza V, Giner J, Curto E, Alonso-Ortiz MB, Orue MI, Vega JM, et al. Assessing adherence by combining the test of adherence to inhalers with pharmacy refill records. J Investig Allergol Clin Immunol 2021;31:58-64
4. De Simoni A, Horne R, Fleming L, Bush A, Griffiths C. What do adolescents with asthma really think about adherence to inhalers? Insight from a qualitative analysis of a UK online forum. BMJ Open 2017;7:e015245
5. Vazquez-Ortiz M, Angier E, Blumchen K, et al. Understanding the challenges faced by adolescents and young adults with allergic conditions: a systematic review. Allergy 2020;75:1850-1880
6. Rehman N, Morais-Almeida M, Wu AC. Asthma across childhood: improving adherence to asthma management from early childhood to adolescence. J Allergy Clin Immunol Pract 2020;8(6):1802-1807.e1
7. Tosca MA, Marseglia GL, Ciprandi G. The real-world "ControL'Asma" study: a nationwide taskforce on asthma control in children and adolescents. Allergol Immunopathol 2021;49:32-39
8. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich). 2008;10:348–354
9. Plaza V, Fernandez-Rodriguez C, Melero C, et al. Validation of the "Test of the adherence to inhalers". J Aerosol med Pulmon Drug Del 2016;29:142-155
10. Kaplan A, Price D. Treatment adherence in adolescents with asthma. J Asthma Allergy 2020;13:39-49
11. Asamoah-Boaheng M, Osei Bonsu K, Farrell J, Oyet A, Midodzi WK. Measuring Medication Adherence in a Population-Based Asthma Administrative Pharmacy Database: A Systematic Review and Meta-Analysis. Clin Epidemiol 2021;13:981-1010
12. Robinson PD, Jayasuriya G, Haggie S, Uluer AZ, Gaffin JM, Fleming L. Issues affecting young people with asthma through the transition period to adult care. Paediatr Respir Rev 2021:S1526-0542(21)00093-2
13. Graham R, Vazquez-Ortis M, Knibb R, et al. EAACI guidelines on the effective transition of adolescents and young adults with allergy and asthma. Allergy 2020;75(11):2734-2752
14. Hauerslev M, Garpvall K, Marckmann M, Hermansen MN, Hansen KS, Chawes BL. Long-term predictors of loss of asthma control in school-aged well-controlled children with mild to moderate asthma: A 5-year follow-up. Pediatr Pulmonol 2021 (in press)
15. Takkinsatian P, Chantaratin S, Sirisakpanit S, et al. Psychosocial factors and lack of asthma knowledge undermine child and adolescent adherence to inhaled corticosteroid. J Asthma 2021:1-14
16. De Simoni A, Fleming L, Holliday L, et al. Electronic reminders and rewards to improve adherence to inhaled asthma treatment in adolescents: a non-randomized feasibility study in tertiary care. BMJ Open 2021;11(10):e053268

Corresponding author:
Received: 22 October, 2021
Accepted: 12 November, 2021
Giorgio Ciprandi
Allergy Clinic, Casa di Cura Villa Montallegro, Genoa, Italy
Via P. Boselli 5, 16146, Genoa, Italy
E-mail: gio.cip@libero.it