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Short title: Asthma control and physical activity in children

Asthma control is not associated with physical activity level in children with asthma during regular follow-up

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Abstract

Objective: Engagement in physical activity (PA) is one of the important aims of long-term asthma treatment. The objective of this study is to evaluate whether improvement of asthma control is associated with enhanced PA during regular follow-up in children with asthma.

Methods: Children, 6-18 years, with asthma were eligible for inclusion when their asthma was uncontrolled at a regular follow-up visit. Participants completed a seven-day recall questionnaire to assess engagement in different physical activities (Physical Activity Questionnaires for Children) at baseline and at the time asthma control was achieved according to predefined criteria. They were also instructed to wear an accelerometer (ActigraphTM GT1M) for seven consecutive days at these timepoints.

Results: Thirty children (21 boys), aged 10.5 (2.9) years, with uncontrolled asthma were included. After a median (IQR) follow up time of 163 (94-253) days PA was assessed again. Accelerometer obtained moderate vigorous PA (median (IQR) 56 (43-66) versus 53 (35-63) minutes) as well as self-reported PA (median (IQR) PAQ score 7.4 (5.9-10.1) versus 7.2 (6.5-11.0)) were not significantly different at the time of uncontrolled and controlled asthma. Moderate vigorous PA increased in 46.2%, was comparable in 23.1%, and decreased in 30.7% of patients, respectively. Self-reported PA increased in 19.0%, was comparable in 52.4%, and decreased in 28.6% of patients, respectively.

Conclusions: Based on the results of this study we conclude that asthma control is not associated with self-reported and accelerometer obtained level of physical activity during regular follow-up in children with asthma.

Keywords asthma, child, physical activity, activity tracker, questionnaire

Introduction

It is widely acknowledged that a physically active lifestyle is beneficial for healthy children as well as children with a chronic condition such as asthma (1-3). In international asthma guidelines, engagement in physical activity (PA) is advocated for children with asthma, and one of the important aims of long-term asthma treatment is to maintain normal PA (4). However, the guidelines do not recommend how to obtain reliable information about an individual's PA in daily practice. Especially if serial measurements of PA are required during regular follow-up this may be feasible by means of self-reported questionnaires, in contrast to objective measurements with activity trackers.

Recently, Cassim et al. performed a systematic review and did not find any evidence that children and adolescents with and without asthma engaged in different amounts of physical activity when measured objectively by accelerometers (5). Intuitively, improvement of asthma control is associated with improvement of PA. However, in several cross-sectional studies neither asthma status nor severity was associated with moderate vigorous physical activity measured by self-reported questionnaires or accelerometers (6-10). To date, little is known about the effect of improvement of asthma control on PA level of an individual during follow-up. To the best of our knowledge only Vahlkvist et al. demonstrated that improvement of asthma control was associated with an increase in objectively measured PA in children with newly diagnosed untreated asthma. Improvement of asthma control resulted in an increase of moderate vigorous activity from approximately 30 to 45 min per day after one year of treatment, which was comparable to their healthy peers (11).

In this study, we hypothesized that improvement of asthma control is associated with enhanced PA during regular follow-up in children with asthma. Therefore, we evaluated whether improvement of asthma control is associated with increased self-reported and objectively measured PA in individual children with asthma in daily practice.

Methods

Children, 6 to 18 years of age with uncontrolled asthma, were recruited during a regular visit to our ambulatory pediatric clinic. Eligible patients were included between January 2017 and December 2018 only during presence of one of the researchers to ensure that comprehensive information could be provided. After informed consent was obtained, oral and written instructions were given and study devices provided. This study was approved by the institutional review board (MEC 2016-083).

Asthma control

Level of asthma control was based on the global initiative of asthma (GINA) guidelines in which the following items were determined for the past four weeks: daytime symptoms more than twice/week, night waking due to asthma, use of reliever medication more than twice/week, and/or any activity limitation. Asthma was classified as partly uncontrolled if one or two of these items were confirmed, and uncontrolled if three or more of these items were confirmed by the patient and/or parents (4). Asthma control was based on GINA guidelines instead of the asthma control test, as the latter does not inquire about use of reliever medication for children under 12 years of age. In addition, it has been demonstrated that in comparison to the GINA guidelines the ACT might underestimate the number of children with uncontrolled asthma due to low sensitivity (12-14). We also determined whether the patient had contacted or visited the general practitioner, pediatrician, emergency department and/or was admitted to the pediatric department because of acute asthma in the previous three months. An episode of acute asthma was defined as an increase of symptoms for which frequent use of bronchodilators and/or systemic steroids were prescribed.

Patients were eligible for inclusion if asthma was partly uncontrolled (GINA score 1-2) in combination with bronchial obstruction and/or an exacerbation in the previous three months, or if asthma was uncontrolled (GINA score 3-4) with or without bronchial obstruction at baseline and/or an exacerbation in the previous three months. Treatment of uncontrolled asthma was adjusted according to the guidelines. Children with cognitive or motor limitations as well as children with anatomical respiratory changes or cardiac comorbidities with significant haemodynamic changes were excluded.

Physical activity

At baseline, PA was determined objectively by means of an activity tracker (accelerometer) and self-reported by using the Physical Activity Questionnaires for Children (PAQ-C). Regular follow-up visits were planned according to our standard practice, at approximately three, six and twelve months after baseline. Asthma control was assessed at each visit. In case asthma control was achieved according to the GINA guidelines, and asthma exacerbations had not occurred in the preceding three months, PA was determined again.

Self-reported PA was determined using the Physical Activity Questionnaires for Children (PAQ-C) (15). The physical activity questionnaire has been translated into Dutch and validated for children aged 5-17 years (16). PAQ-C is a self-administered seven-day recall questionnaire to assess engagement in different physical activities. The questionnaire consists of ten questions. Item 10 determines whether the child was prevented from performing normal physical activities, and is not included in the calculation of the PAQ score. Questionnaire items are scored from one to five, a higher score indicating that the activity was performed more often. The final composite score is the mean of nine items. The PAQ score was also adjusted for age and gender, by using the formula reported by Saint-Maurice et al. (17).

The ActigraphTM GT1M accelerometer was used as an activity tracker. The children were instructed to wear the ActigraphTM accelerometer for seven consecutive days starting the day after the visit, and remove the accelerometer only before showering, swimming, and during sleep. The ActigraphTM was attached with an elastic band to the hip. The ActigraphTM data was preprocessed with Actilife software (Actigraph Corporation, Pensacola, FL). Raw data was downloaded from the devices with an epoch length of 15 s. Wear time was assessed using the algorithm of Troiano et al. (18). The activity was classified according to the criteria of Evenson (19). Activity parameters (sedentary, light, moderate, and vigorous activity) were averaged per day over the total period of home-measured activity. The World Health Organization (WHO) recommends that children perform at least 60 min of moderate vigorous PA (MVPA) per day and therefore MVPA was calculated (20). Data was only used for analysis if the accelerometer was worn for at least three days and at least six hours per day (21, 22).

The following characteristics were obtained from the electronic patient chart: age, sex, atopic comorbidity, results of lung function tests expressed as FEV1%predicted, duration of physician diagnosed asthma, duration and daily dose of inhaled corticosteroids, participation in community sports. Lung function tests were obtained at the initial visit, and repeated each year as recommended in the guidelines and earlier if indicated.

As we aimed to resemble daily practice as much as possible we allowed patients and parents to return the accelerometer and questionnaire by post. A return envelope was provided. Patients or parents were contacted by phone if the accelerometer and/or questionnaire was not returned within four weeks.

Statistical analysis

This was an explorative study, therefore, no initial power analysis was performed to calculate a required sample size. We aimed to include 30 participants in accordance with recent studies on PA in children and adolescents with a chronic disease.(23, 24)

Categorical data were presented as absolute and relative frequencies and continuous variables were expressed as mean (SD) or median (IQR) values depending on normal distribution.

Primary outcome was the difference in MVPA at the time asthma was uncontrolled and controlled, and difference in PAQ-c score a secondary outcome.

Statistical analysis was conducted using the paired t-test or the Wilcoxon matched-pairs signed rank test. P values <0.05 were considered significant. Statistical analyses were performed using R Statistical Software (version 4.0.2; R Foundation for Statistical Computing, Vienna, Austria) and RStudio.

Results

During the study period 35 children were eligible for inclusion. From 30 children informed consent was obtained to participate, five were not willing to participate due to the burden of the study. Twenty one patients had partly uncontrolled asthma (GINA score 1-2) with either bronchial obstruction ($n = 11$), exacerbation in previous three months ($n = 3$) or both ($n = 7$). Nine patients had uncontrolled asthma (GINA score 3-4) with either bronchial obstruction ($n = 3$), exacerbation in previous three months ($n = 3$) or both ($n = 3$). The patient characteristics are presented in Table 1. Nine (30%) of the patients were newly referred, and 19 (63.3%) were using maintenance inhaled corticosteroids. Of these nineteen patients, four were using a low dose, and fifteen a medium dose of inhaled corticosteroids according to the GINA guidelines. Two of the patients had been recommended to taper down and discontinue maintenance inhaled corticosteroids during a previous visit as their asthma was controlled at that time. In 29 patients PA was actually registered as one of the included patients did not wear the accelerometer due to social circumstances. Two patients did not return for a follow-up visit and were contacted by telephone. These patients were not willing to perform the second accelerometer recording because they found it too demanding. During the second recording the accelerometer malfunctioned in one patient. Overall, twenty-six patients wore the accelerometer twice (Figure 1).

After a median (IQR) follow up time of 163 (94–253) days, PA was determined at the time the asthma was controlled. In 73.7% of the patients a lung function test was performed at the time the second measurement of PA was performed. Median (IQR) FEV1%pred significantly improved from 88.0 (80–98) to 98.0 (90–106) ($p = 0.034$) in these patients. At both measurements eleven (42.3%) patients achieved an MVPA of approximately 60 min as recommended by WHO. Six of these patients achieved MVPA of 60 min at the time their asthma was uncontrolled and controlled. The median activity levels assessed by the accelerometer at the time of uncontrolled asthma appeared not to be significantly different from the time asthma was controlled (Table 2). MVPA increased (>10%) in 46.2% of the patients when asthma control was achieved, was comparable in 23.1% of the patients, and decreased (>10%) in 30.7% of the patients (Figure 2). In addition, self-reported PA was not significantly different (within 0.5 points lower or higher than baseline value) in 52.4% of the patients at the time of uncontrolled and controlled asthma (Table 2). In 19.0% and 28.6% of the patients the self-reported PA increased and decreased >0.5 points, respectively (Figure 3).

Discussion

Our findings demonstrate that improvement of asthma control was not associated with an increase in self-reported or accelerometer recorded PA in children during regular follow-up for asthma. Interestingly, an individual patient with improvement of asthma control could either have an increased, comparable, or decreased level of PA .

Although our findings suggest that it is not worthwhile to assess PA by means of extensive questionnaires or activity trackers during regular follow-up of children with asthma, it is beyond doubt that PA should be advocated for children with asthma. It is well known that uncontrolled asthma may trigger symptoms and result in premature termination of the activity or even prevent the child from starting PA (25). This underscores the need to inquire whether the child's participation in leisure activities, community sports and/or physical exercise lessons at school has changed over time

To this end, it may be sufficient to use validated questionnaires such as the asthma control questionnaire and childhood asthma control test to assess the level of PA.

To date, little is known about the effect of asthma control on PA. In cross sectional studies neither asthma status nor severity was associated with moderate vigorous PA measured by accelerometers (6, 10). Vahlkvist et al. demonstrated that improvement in asthma control was associated with an increase in objective PA in newly diagnosed untreated asthma from approximately 30 to 45 min per day after one year of treatment (11). We did not find an increase in MVPA as previously reported by Vahlkvist et al. but such an increase might be achieved only in children with untreated asthma (11).

Overall, our results may not be comparable to other studies not only due to the small sample size but the fact that we performed a real life study in contrast to cross sectional or studies with fixed study visits may also explain the discrepancies. The following limitations of our explorative study need to be addressed particularly. We recognize that subjective PA was based on recollection of PA in the week prior to the study visit as opposed to the objective measurement determined by an accelerometer in the week after the visit. However, both measurements did not demonstrate a significant change. Also, the period of assessment may have been too short to detect a significant impact on PA levels. Maybe monthly assessments would have yielded other results. On the other hand, in daily practice, frequent and/or demanding assessments are not likely to increase patient's adherence. This is reflected by the fact that some patients were not willing to wear the accelerometer, and/or did not fill in or complete the PA questionnaire for a second time. Although, adherence may have been improved if patients would have been invited for extra visits to the clinic, our aim was to determine whether it is useful to assess PA levels during regular follow-up. The awareness of participating in a study may have motivated the children to increase their PA after the initial visit. In addition, wearing an accelerometer may raise awareness of the need to be physically active, and not be representative of the usual PA behavior (26). This could have improved baseline PA levels measured by the accelerometer and thus reduce the change in PA measured between the two visits. In contrast, study participation could not have affected a potential change in self-reported PA level as this reflected the PA level in the week prior to the initial assessment. However, retrospectively reported PA may be subject to recall bias.

Also, the follow-up time may not have been long enough for some patients to be able to detect a significant difference in PA level. The time between the two assessments varied from 3 months to approximately one year for our patients. This does not imply that asthma control was not achieved earlier for the specific patients, however, regular follow-up visits were planned to reflect daily practice rather than fixed study visits. The patients in our study may also not be comparable to other group as they may differ in asthma severity or participation in community sports. Although the majority of the children participated in community sports we did not evaluate the frequency nor intensity of the sports. The number of children was too small to select for severity of asthma or children who were steroid naïve before inclusion. In addition, the children in our study all have access to regular follow-up asthma care. This may not be true for other populations. It will be interesting to evaluate these factors in future studies.

We conclude, that based on the results of this study, it may not be worthwhile to determine PA extensively during regular follow-up of children with asthma. Further studies are needed in a larger and more heterogeneous population before firm conclusions can be drawn. Nevertheless, it remains important to encourage children with asthma to participate in community sports or other activities.

Contributors statement

Arvid Kamps had primary responsibility for protocol development, and writing the manuscript.

Anne Clevering, Bram Nieuwdorp and Wouter de Weger had primary responsibility in enrolment, preliminary data analysis and contributed in writing of the manuscript.
Lidy van Lente had primary responsibility for protocol development, performed the final data analyses and contributed to the writing of the manuscript.
All authors read, and approved the final manuscript.

Conflict of Interest:

The authors declare that they have no conflict of interest.

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Table 1. Baseline characteristics of the included patients ($N = 30$).

Gender (boys/girls)	21/9
Age in years, mean (SD)	10.5 (2.9)
Length in cm, mean (SD)	146.8 (18.7)
Weight in kg, median (IQR)	35.0 (27.8 – 48.3)
BMI z-score, median (IQR)	0.29 (-0.6 – 0.9)
Rhinitis, N (%)	22 (73.3)
Eczema, N (%)	9 (30.0)
Sensitisation to one or more inhalant allergens, N (%)	24 (80.0)
Asthma duration in months, median (IQR)	21.0 (4.0 – 57.0)
Maintenance inhaled corticosteroids, N (%)	19 (63.3)
Duration of medication use in months, median (IQR)	13.0 (4.8 – 33.0)
Combination of inhaled corticosteroids and long acting beta agonist, N (%)	8 (26.7)
FEV ₁ % predicted	88.0 (80.0–98.0)
%Reversibility, median (IQR)	12.0 (6.0–18.0)
Exacerbation in previous 3 months, N (%)	16 (53.3)
Participation in community sports, N (%)	23 (76.7)

Table 2. Physical activity at the time of uncontrolled and controlled asthma*.

	Asthma uncontrolled	Asthma controlled	95% CI	p-value (95% CI)
PAQ [#]	7.4 (5.9 – 10.1)	7.2 (6.5 – 11.0)	(-0.27 – 0.42)	0.67*
Wear (days)	7.0 (7.0 – 8.0)	7.0 (4.8 – 7.0)	(-0.06 – 2.06)	0.064*
Weartime (min/day)	671 (621 – 659)	618 (569 – 691)	(4.0 – 86.5)	0.04**
Weartime (%)	46.6 (43.0 – 49.4)	42.9 (40.0 – 48.0)	(0.43 – 5.84)	0.046**
Sedentary (min/day)	351 (331-389)	339 (307-367)	(-11.9 – 49.4)	0.27**
Light (min/day)	242 (215-273)	224 (193-243)	(7.09 – 44.7)	0.017**
Moderate (min/day)	38 (32-48)	36 (27-43)	(-2.30 – 9.44)	0.17**
Vigorous (min/day)	17 (14-22)	15 (7-25)	(-5.30 – 5.15)	0.73**
MVPA [†] (min/day)	56 (43-66)	53 (35-63)	(-12.4 – 10.9)	0.77**

Data presented as median (interquartile range).

[#]PAQ = Physical Activity Questionnaire (score adjusted for age and gender) (17).

[†]MVPA = Moderate Vigorous Physical Activity.

*Paired t-test; **Wilcoxon matched pairs signed rank sum T test.

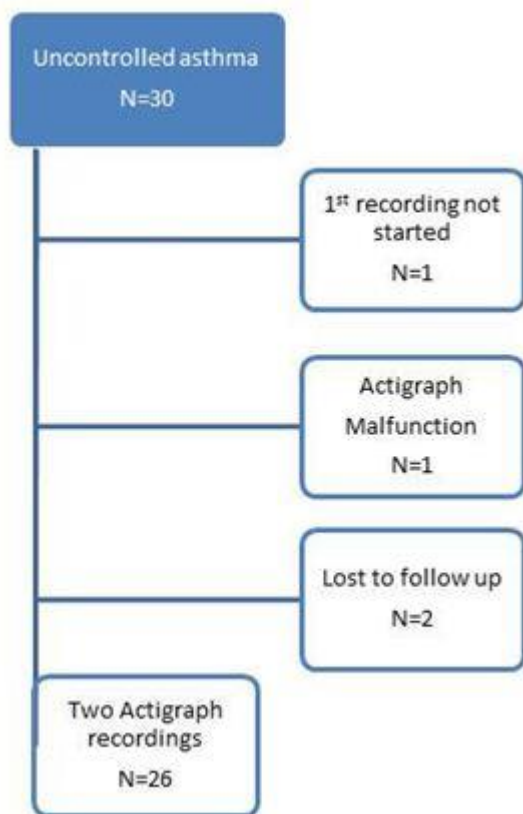


Figure 1. Flow chart of inclusion.

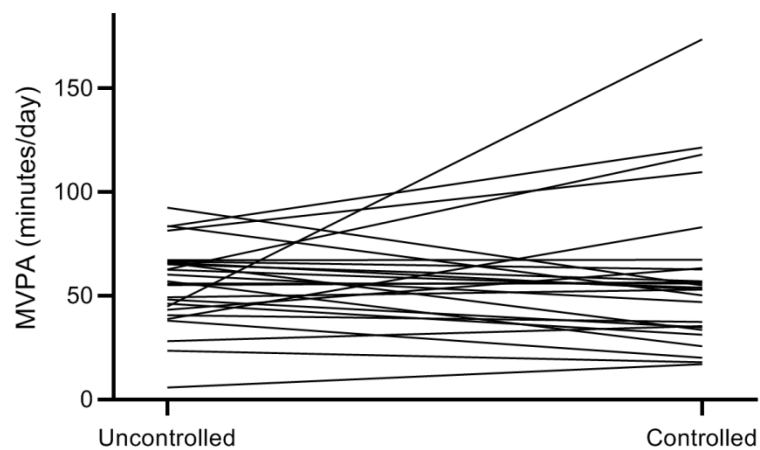


Figure 2. Moderate vigorous physical activity (minutes/day) for individual patients at the time of uncontrolled and controlled asthma.

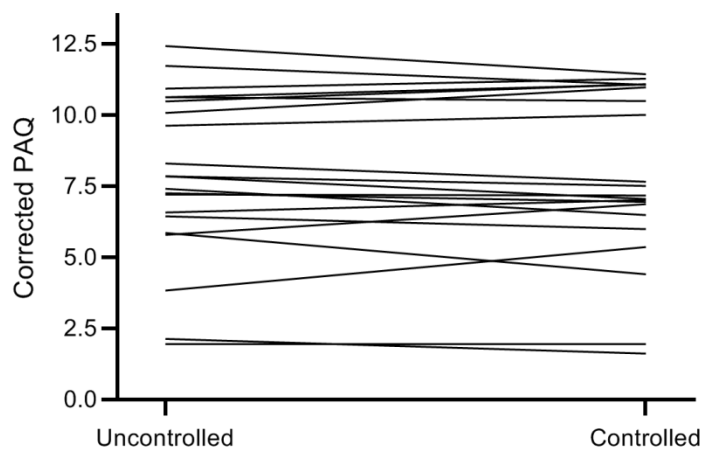


Figure 3. PAQ score, adjusted for age and gender, for individual patients at the time of uncontrolled and controlled asthma.