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The Visual Analog Scale detects exercise-induced bronchoconstriction in children with asthma

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ABSTRACT

Objective: Exercise-induced bronchoconstriction (EIB) is a specific morbidity of childhood asthma and an important sign of uncontrolled asthma. The occurrence of EIB is insufficiently identified by the Childhood Asthma Control Test (C-ACT) and Asthma Control Test (ACT). This study aimed to (1) evaluate the Visual Analog Scale (VAS) for dyspnea as a tool to detect EIB in asthmatic children and (2) assess the value of combining (C-)ACT outcomes with VAS scores. **Methods:** We measured EIB in 75 asthmatic children (mean age 10.8 years) with a standardized exercise challenge test (ECT) performed in cold and dry air. Children and parents reported VAS dyspnea scores before and after the ECT. Asthma control was assessed by the (C-)ACT. **Results:** Changes in VAS scores (Δ VAS) of children and parents correlated moderately with fall in forced expiratory volume in 1 second (FEV_1), respectively $r_s=0.57$ ($p<.001$) and $r_s=0.58$ ($p<.001$). At a Δ VAS cutoff value of ≥ 3 in children, sensitivity and specificity for EIB were 80% and 79% (AUC 0.82). Out of 38 children diagnosed with EIB, 37 had a (C-)ACT score of ≤ 19 and/or a Δ VAS of ≥ 3 , corresponding with a sensitivity of 97% and a negative predictive value of 96%. **Conclusion:** This study shows that the VAS could be an effective additional tool for diagnosing EIB in children. A reported difference in VAS scores of ≥ 3 after a standardized ECT combined with low (C-)ACT scores was highly effective in detecting and excluding EIB.

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Exercise-induced asthma; childhood asthma; dyspnea perception; Asthma Control Test; asthma control

Introduction

Exercise-induced bronchoconstriction (EIB) is a common and highly specific morbidity of childhood asthma. It has a major impact on the quality of life in children, especially on the physical dimensions where it reduces participation in sports and play (1,2). In a study by Rabe et al. (3), not even 1 in 5 children with asthma had a normal physical activity pattern.

Although EIB reflects airway inflammation and is an important sign of uncontrolled asthma (4), it can also occur in children who have no other symptoms of asthma (5). It is officially diagnosed and monitored based on changes in lung function after a standardized exercise challenge test (ECT) (6). In daily practice, not all physicians have direct access to testing facilities and therefore have to rely on exercise-related

respiratory symptoms to assess EIB and asthma control. However, these self-reported symptoms are inconsistent with both the occurrence and severity of EIB when measured with an ECT (7–10). For a structured approach of respiratory symptoms, questionnaires such as the Childhood Asthma Control Test (C-ACT) and Asthma Control Test (ACT) are commonly used. These validated questionnaires are self-administered and evaluate asthma control over the previous 4 weeks (11). Prior studies have shown an inability of these questionnaires to predict results of pulmonary function tests and EIB in asthmatic children (12–14). This warrants the need for an additional tool for asthmatic children to report EIB symptoms.

A well-established tool for the assessment of dyspnea in adults is the Visual Analog Scale (VAS) (15).

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The VAS was first described in 1969 by Aitken (16) and is an effective tool to evaluate different sensations, such as pain and dyspnea (17). The VAS is a closed scale, usually consisting of a horizontal or vertical line with at both ends a picture or verbal description of a sensation. One end represents the absence of the sensation and the other the maximum intensity of the sensation (18). The tool is simple and time-efficient, which makes it specifically suitable for children. Few studies evaluated the VAS as a tool to assess EIB in asthmatic children so far. Tosca et al. (19) and Lima et al. (20) found a clinical significant relationship between increase in VAS scores and the fall in FEV₁ after an ECT. However, Panditi and Silverman (21) only found a weak correlation between fall in FEV₁ and the VAS scores of children. In these previous studies, asthma control was not assessed with questionnaires.

This study aimed to evaluate the VAS for dyspnea as a tool to detect EIB in children and to assess the value of combining (C-)ACT outcomes with VAS scores.

Methods

Study design and patients

This study had a cross-sectional design. Children 4–17 years with a physicians' diagnosis of asthma were recruited from the outpatient clinic of the pediatric department of Medisch Spectrum Twente, Enschede, the Netherlands. From May 2015 to July 2018, 76 children were included. Children with spirometry-induced bronchoconstriction, exercise-induced laryngeal obstruction or severe airflow limitation in baseline spirometry (FEV₁ < 60% of predicted) were excluded. None were taking shortacting or longacting bronchodilators for at least 24 h prior to testing. Children with other pulmonary or cardiac disorders were excluded. This study was approved by the Medical Ethics Review Board Twente.

Exercise challenge test

The ECT's were performed in a climate chamber with dry, cold air (10.0–12.0 °C) following standard protocol (6). Children aged 8–17 years performed the ECT on a treadmill (H/P-Cosmos Quasar 4.0) for 6 min with submaximal exercise load and their nose clipped. The inclination of the treadmill was 10%. The speed of the treadmill was accelerated in a time period of 2 min until a steady-state heart rate was achieved around 85% of the maximal heart rate (220 – age). Heart rate was continuously measured by a radiographic ECG-device (Custo cardio 100 BT or polar-band). Children aged 4–7 years old performed the ECT on a jumping castle during 6 min. Van Leeuwen et al. showed that an age-adjusted ECT is preferable in younger children and that a jumping castle is a feasible method to assess and diagnose EIB in young children (22). A MicroLoop[®] MK 8 hand-held spirometer (ML3535) was used to measure pulmonary function, using standard ERS protocol (23). Baseline spirometry was measured in duplicate prior to exercise. Post-exercise flow volume curves were performed at 1, 3, 6, 9, 12, and 15 min and repeated in duplex. Next, two salbutamol inhalations of 200 µg were given and after 5 min reversibility was measured.

When patients experienced severe bronchoconstriction or a fall of $\geq 60\%$ in FEV₁ post-exercise before completing the protocol, salbutamol was administered to reverse bronchoconstriction. Children with a fall of $\geq 10\%$ in FEV₁ post-exercise were considered to have EIB (24).

Visual Analog Scale

The VAS for dyspnea used in this study consisted of a horizontal line of 10 cm with at both ends a picture; one representing the absence of dyspnea perception and one the maximum intensity (Figure 1). No interval markers were visible on the line. Children and their parents were asked to mark the point on the scale that corresponded with their perception of

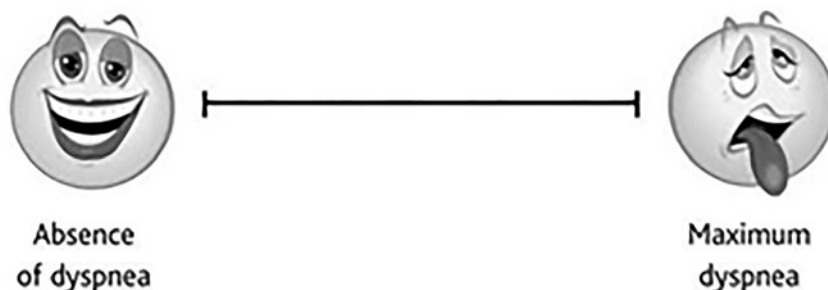


Figure 1. Visual Analog Scale (VAS). From (16).

dyspnea severity before exercise and just before post-exercise spirometry at $t = 3$ min. Children and parents completed the VAS scores simultaneously with the explicit instruction not to look at each other's scores.

Asthma Control Test

All children completed Dutch versions of the ACT or C-ACT, translated and linguistically validated by the MAPI-research institute in Lyon, before the ECT.

The ACT and C-ACT have been validated against spirometry and the rating of asthma control by specialists (11,25,26). Children ≥ 12 years filled in the ACT, which consisted of 5 items assessing asthma symptoms (daytime and nocturnal), use of rescue medications and the effect of asthma on daily functioning. Each item included 5 response options corresponding to a 5-point Likert-type rating scale. Responses for each of the 5 items were summed to yield a score ranging from 5 (poor control of asthma) to 25 (complete control of asthma). A cutoff score of 19 or less was used to identify patients with poorly controlled asthma (25).

Children 4–11 years filled in the C-ACT together with their parents. The C-ACT consisted of 7 questions, 4 aimed at children and 3 at their parents, corresponding to a 3-point and 5-point Likert-type rating scale respectively. The scores were summed to yield a score ranging from 0 (very poor control of asthma) to 27 (complete asthma control). Similar to the ACT, a score of ≤ 19 was used to indicate poor asthma control (26).

Statistical analyses

The maximum fall in FEV₁ (%) was calculated and used for statistical analyses. Results were expressed as mean values $\pm$ standard deviation (SD) for the normally distributed data and as median $\pm$ interquartile range (IQR) for not-normally distributed data. For nominal or ordinal data, numbers with corresponding percentages were used.

Differences between different groups (EIB yes/no, (C-)ACT controlled/uncontrolled, Δ VAS $<3/\geq 3$) were calculated with the Chi-Square test.

Correlations between the difference in VAS scores before exercise and 3 min after exercise (Δ VAS) and the fall in FEV₁ were calculated with Spearman's rho for non-normally distributed continuous variables. Correlations between continuous (C-)ACT scores and fall in FEV₁ were also calculated with Spearman's rho. Correlation coefficients were considered as follows:

Table 1. Characteristics of the study sample ($n = 75$).^a

Variables	
Sex ^b	
Female	22 (29.3%)
Male	53 (70.7%)
Age, years	10.8 (3.5)
BMI (kg/m ²)	18.9 (3.8)
Medication use ^b	
SABA	56 (74.7%)
LABA	10 (13.3%)
ICS	52 (69.3%)
NCS	24 (32.0%)
LTRA	11 (14.7%)
Atopy ^b	
C-ACT score	20.3 (5.2)
ACT score	18.4 (3.3)
FEV ₁ predicted (%)	91.2 (15.3)
Exercise challenge test	
Fall in FEV ₁ ^c (%)	14.4 (6.8–25.0)
Exercise-induced asthma ^b	41 (54.7%)
Δ VAS children	3.6 (2.8)
Δ VAS parents	2.7 (2.4)

^aValues are presented as mean (SD), except when indicated otherwise.

^bValue is presented as n (%).

^cValue is presented as median (IQR). BMI: Body Mass Index (kg/m²). C-ACT: Childhood Asthma Control Test. ACT: Asthma Control Test. FEV₁: Forced Expiratory Volume in 1 s. Δ VAS: change in Visual Analog Scale after exercise.

>0.81 = almost perfect agreement; 0.61 – 0.80 = substantial; 0.41 – 0.60 moderate; 0.21 – 0.40 fair; ≤ 0.20 slight (27).

Sensitivity, specificity, positive predicted values (PPV), negative predicted values (NPV), and the area under the curve (AUC) were calculated at various cut-off points of the Δ VAS dyspnea scores from children to detect EIB. A two-sided p values of less than .05 was considered statistically significant. All data analyses were performed with SPSS[®] Statistics, version 23.0.

Results

Eighty-six children with a physicians' diagnosis of asthma performed an exercise challenge test. Four children were excluded because of spirometry-induced bronchoconstriction and three because of exercise-induced laryngeal obstruction. Four children showed severe bronchoconstriction during the exercise challenge test, leading to a premature termination of the test. Seventy-five children were included for statistical analyses. Of these children, 72 completed the (C-)ACT successfully and 74 filled in all VAS scores.

Characteristics of the study population and exercise challenge test

Baseline characteristics of the study sample (53 boys, 70.7%) and the results of the ECT are shown in Table 1.

The mean baseline FEV₁ was 91.2% (SD 15.3) of predicted, with a median fall in FEV₁ after exercise of

14.4% (IQR 6.8–25.0). Forty-one children showed EIB. From these 41 children, 38 successfully completed the (C-)ACT. The mean increase of the VAS dyspnea score after exercise (Δ VAS) was 3.6 (SD 2.8) as reported by children and 2.7 (SD 2.4) as reported by parents. The mean C-ACT and ACT scores were 20.3 (SD 5.2) and 18.4 (3.3), respectively.

Asthma Control Test and EIB

There was no correlation between continuous C-ACT and ACT scores and fall in $FEV_{1\text{}}$, respectively $r_s = -0.23$ ($p = .67$) and $r_s = -0.07$ ($p = .36$). Using the customary cutoff point ≤ 19 for uncontrolled asthma, 31 out of 72 children were classified as having uncontrolled asthma (Table 2). There was a significant difference between the controlled and uncontrolled group and EIB diagnosis yes or no. The (C-)ACT had a sensitivity of 58%, a specificity of 75%, a PPV of 74% and NPV of 59% for EIB (Table 3).

Visual Analog Score and EIB

The Δ VAS dyspnea scores of children and parents were moderately correlated ($r = 0.54$, $p < .001$). The fall in $FEV_{1\text{}}$ after exercise was moderately correlated with the Δ VAS of both children and parents, respectively $r_s = 0.57$ ($p < .001$) and $r_s = 0.58$ ($p < .001$) (Figure 2). At a cutoff value of Δ VAS from children of ≥ 3 , the sensitivity for EIB was 80% and the specificity 79% (AUC 0.82, Figure 3). The PPV and NPV were 82% and 77% respectively (Table 3).

Table 2. (C-)ACT and VAS outcomes in EIB-cases and non-cases.^a

	EIB		Total	<i>p</i> value
	Yes	No		
(C-)ACT controlled	17	24	41	.011
(C-)ACT uncontrolled	23	8	31	
Total	40	32	72	
Δ VAS ≥ 3	32	7	39	.000
Δ VAS < 3	8	27	35	
Total	40	34	74	

^aEIB: exercise-induced bronchoconstriction. (C-)ACT: (Childhood) Asthma Control Test; uncontrolled = score ≤ 19 ; controlled = score > 19 . Δ VAS: change in Visual Analog Scale after exercise.

There were no significant differences in VAS scores between genders, children < 12 years and ≥ 12 years of age or between the use of different types of controller medication.

Combined Asthma Control Test and Visual Analog Scale

Out of 38 children with an EIB diagnosis 37 had a (C-)ACT score of ≤ 19 and/or a Δ VAS of ≥ 3 , corresponding with a sensitivity of 97% and a NPV of 96% for EIB. Specificity and PPV were 67% and 77%, respectively (Table 4).

Discussion

This study aimed to evaluate the VAS for dyspnea as a tool to detect EIB in children and to assess the value of combining (C-)ACT outcomes with VAS scores. In our cohort of 75 children, change in VAS dyspnea scores showed a clinical significant relationship with a fall in $FEV_{1\text{}}$ after exercise. In the ROC curve analysis of the childrens' VAS scores, the value of 3 was the optimal point for predicting EIB, with a sensitivity of 80% and a specificity of 79%. Since both an optimal sensitivity and specificity are clinically relevant for EIB, this cutoff value was used in our analysis. We found that the VAS was effective in detecting EIB in children with false-negative (C-)ACT outcomes. Combining the (C-)ACT with the VAS for dyspnea corresponded with a sensitivity of 97% and a NPV of 96% for EIB.

This is the first study that combined asthma control questionnaires with VAS dyspnea scores during a standardized exercise challenge test. We confirm the results of two previous studies (19,20) that found a similar clinical significant relationship between fall in $FEV_{1\text{}}$ and change in VAS scores in children with bronchial obstruction after an ECT. A study focusing on bronchodilatory response (28) also found a significant difference in VAS scores between children with and without bronchial reversibility. Panditi and Silverman (21) observed that children's VAS scores only related weakly to fall in $FEV_{1\text{}}$ after exercise, while parents' change in VAS was not related at all.

Table 3. Sensitivity, specificity and predictive values for EIB.^a

	(C-)ACT uncontrolled	Δ VAS ≥ 3	(C-)ACT uncontrolled and/or Δ VAS ≥ 3
Sensitivity for EIB	58%	80%	97%
Specificity for EIB	75%	79%	67%
Positive predictive value for EIB	74%	82%	77%
Negative predictive value for EIB	59%	77%	96%

^a(C-)ACT: (Childhood) Asthma Control Test; uncontrolled: score ≤ 19 . Δ VAS: change in Visual Analog Scale. EIB: exercise-induced bronchoconstriction.

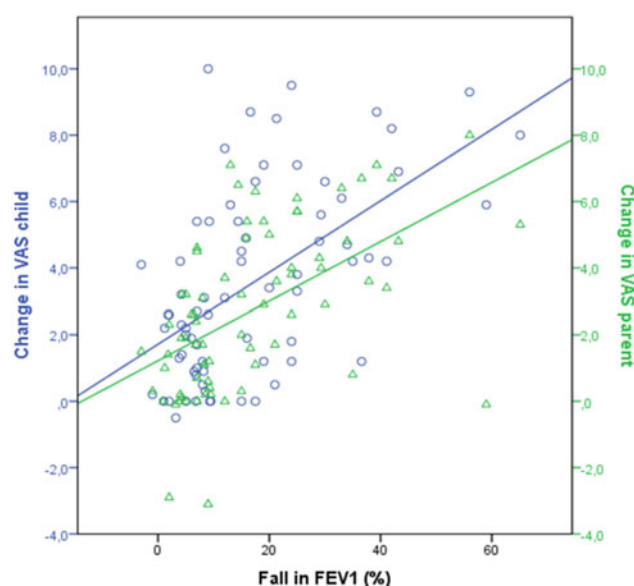


Figure 2. Relationship between fall in FEV₁ after exercise and change in VAS scores of children (○) and parents (Δ).

Most of these children however were managed in primary care, while most participants of the aforementioned studies and our study were treated in secondary care. It is known that children with undiagnosed asthma have worse perception of dyspnea than children with diagnosed asthma (29). Therefore it could be argued that children and parents treated in secondary care may have better symptom perception due to more intensive training and guidance.

We confirm the poor predictive value of the (C-)ACT for EIB. Our observed percentage of false-negative (C-)ACT's (24%) is in line with previous literature, where this ranges from 15% to 61% (25,30). A possible explanation for this notable high percentage and broad range of false-negative outcomes could be that these questionnaires are subject to recall-bias and the personal interpretation of the questions by children and parents, which can vary highly between individuals. Furthermore, the limited focus of the questions on bronchial hyperresponsiveness triggered by exercise may play a role; the C-ACT contains only one question related to exercise, while the ACT only focuses on other triggers of bronchial hyperreactivity.

We found that the VAS was effective in the detection of EIB and thus asthma control, as a Δ VAS of ≥ 3 was able to identify children with a false-negative (C-)ACT suffering from EIB. This can be explained by the fact that the VAS exclusively focuses on the dyspnea sensation in the immediate moment, avoiding recall-bias and reducing the influence of interpretational and linguistic issues. However, a reasonable capacity for abstract thinking is needed to understand

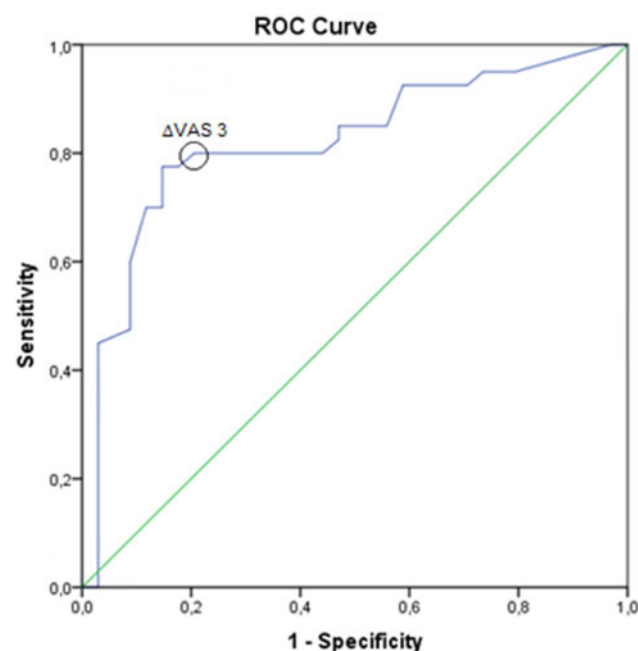


Figure 3. Receiver operator characteristic (ROC) curve analysis for the Visual Analog Scale (VAS) scores from children to diagnose exercise-induced broncho-constriction (EIB). The circle indicates an increase in VAS score of 3, associated with a sensitivity of 80% and a specificity of 80%.

Table 4. Combined (C-)ACT and VAS outcomes in EIB-cases and non-cases.^a

	EIB		Total
	Yes	No	
(C-)ACT uncontrolled and/or Δ VAS ≥ 3	37	11	48
(C-)ACT controlled and Δ VAS < 3	1	22	23
Total	38	33	71

^aEIB: exercise-induced bronchoconstriction. (C-)ACT: (Childhood) Asthma Control Test; uncontrolled = score ≤ 19 ; controlled = score > 19 . Δ VAS: change in Visual Analog Scale after exercise.

the VAS, and it has been suggested that this makes the tool less suitable for children (17). Our own experience is that the VAS is specifically suitable for children because of its practical and simple design. During our study, both children and parents had little trouble understanding the tool. If the VAS would prove to be a valid tool in a real-life setting, this could reduce the need for exercise challenge tests and advance e-health.

For this study, different bronchial provocation tests were considered for the evaluation of the VAS. Direct provocation tests using methacholine or histamine are sensitive tests since they directly stimulate the airway smooth-muscle cells. However, due to their low specificity (31) they were found to be less suitable for this study. Both mannitol and exercise can be used as indirect provocation tests, triggering the release of endogenous mediators that causes airway smooth

muscles to contract (32). Exercise provokes significant bronchoconstriction in 70–80% of asthmatic children. It leads to evaporative water loss of the airway mucosa, inducing both an increased airway osmolarity and cooling down followed by rapid rewarming of the airway epithelium, leading to smooth-muscle contraction (33). The inhalation of mannitol leads to the contraction of airway smooth-muscles cells by liberating mediators that stimulate inflammatory cells (34). A study by Barben et al. (35) showed that a mannitol challenge is feasible in children and is a suitable alternative for an exercise challenge testing in childhood. For this study, we used a standardized exercise challenge test because of the expertise of our team with these test, and because mannitol powder has not been approved in children under 12 years of age in all countries in the European Union. Furthermore, we found exercise to be a better reproduction of a dyspnoeic episode caused by playing sports in a real-life setting, creating possibilities for the use of the VAS implemented in e-health.

A major strength of this study is the way we performed the ECT's. A standardized test was performed in a climate chamber with dry and cold air, following standard protocol. Young asthmatic children (4–7 years old) performed the test on a jumping castle, a technique that has previously been validated by members of our study group (22). We measured the post-VAS 3 min after exercise when exercise-induced dyspnea, which can mimic EIB symptoms, had faded away. We anticipated this would provide sufficient time to prevent bias of exercise-induced dyspnea and yet would synchronize with the average maximum fall in lung function.

A limitation of our study is that we observed the relation between VAS and fall in FEV₁ only during a standardized ECT. Further research employing activity trackers, heart rate sensors and hand-held spirometers could validate the efficacy of VAS in real-life settings and improve perception in poor perceivers.

Conclusion

This study shows that the VAS could be an effective additional tool for diagnosing EIB in children. In our study, a reported difference in VAS scores of ≥ 3 after an ECT combined with low (C-)ACT scores was highly effective in detecting and excluding EIB.

Declaration of interest

The authors report no conflicts of interest.

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