Asthma Flare-up Diary for Young Children to monitor the severity of exacerbations

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Background: Few instruments exist to ascertain the severity of a preschool-aged child's asthma exacerbations managed at home.
Objective: We sought to develop and validate a functional status instrument to assess asthma exacerbation severity in preschoolers.
Methods: The parent-completed Asthma Flare-up Diary for Young Children (ADYC), which was developed systematically, comprises 17 items, each scored from 1 (best) to 7 (worst). The ADYC was completed daily from the onset of an upper respiratory tract infection (URTI) until asthma symptom resolution; the cumulative daily score was reported. The ADYC was examined for key psychometric properties in a randomized placebo-controlled trial of pre-emptive high-dose fluticasone in preschoolers with URTI-induced asthma.
Results: In 121 children aged 2.7 ± 1.1 years (59.5% male), the ADYC's internal consistency (Cronbach $\alpha = .97$), feasibility (97% completion), and test-retest reliability ($r = 0.71$; 95% CI, 0.59-0.80) were demonstrated. The ADYC was responsive to change between 2 consecutive days (Guyatt statistic = 0.77) with a minimal important difference of 0.22 (0.17-0.27). Of 871 episodes, the cumulative ADYC score was significantly higher during exacerbations than during URTIs (mean difference [MD], 7.6; 95% CI, 6.4-8.9) and for exacerbations with an acute-care visit (MD, 9.1; 95% CI, 7.6-10.7), systemic corticosteroids (MD, 10.1; 95% CI, 8.3-12.0), and hospitalization (MD, 6.8; 95% CI, 2.9-10.7) versus those without. In children receiving fluticasone, the ADYC score was significantly lower versus that in the placebo group (MD, 5.1; 95% CI, 1.8-8.3).
Conclusions: The 17-item ADYC proved feasible, responsive to day-to-day changes, and discriminative across exacerbations of different severities. In a trial testing effective therapy in preschoolers, it identified a significant reduction in asthma exacerbation severity. (J Allergy Clin Immunol 2016;137:744-9.)

Key words: *Asthma, discrimination, preschool child, questionnaire design, randomized controlled trial, reliability and validity*

Preschool-aged children experience more emergency department visits and hospitalizations for asthma than any other pediatric age groups.[1] Therapeutic advances are hampered by the lack of discriminative and responsive health outcomes applicable to this young age group. Indeed, clinical trials testing pre-emptive therapy to prevent exacerbations or treatment initiated on discharge from the emergency department are heavily weighted toward health care (eg, acute care visits) or medication use (eg, systemic corticosteroids). Yet asthma symptoms can persist for several days to weeks, with management occurring largely in the home before, after, or without seeking health care.[2,3] In fact, between 40% and 75% of preschool asthma exacerbations do not result in an acute care visit[4] or use of rescue systemic corticosteroids.[5-7] Use of rescue short-acting β_2-agonists (SABAs) provides useful information, but it hinges on the parental perception of needs and interpretation of symptom severity, which can vary between caregivers, even for the same symptom severity.[8,9] A valid measure to document the overall burden of an asthma exacerbation on the functional status of preschoolers would provide an important and complementary outcome to assess response to therapy.

Three main criteria limit the availability of asthma-specific tools for use in preschoolers in the context of an exacerbation, namely age group, short timeframe, and focus on an asthma flare-up. The 2 instruments specific to preschoolers with asthma or symptoms consistent with asthma include the 5-item Test for Respiratory and Asthma Control in Kids,[10] with a reporting period of 4 weeks, 3 months, and 1 year according to each item, and the 10-item Pediatric Asthma Caregiver Diary,[11] which was developed as a twice-daily diary with a reporting period of 12 hours. Seven published instruments pertain to both preschool- and school-aged children[12-18]; most have a retrospective reporting period of 4 weeks. None of the above-mentioned instruments[10-18] were applied specifically to the context of an acute

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We acknowledge the support of the funds from George Hogg Family Foundation and the Fonds de la recherche en santé du Québec for the infrastructure support provided to the Research Centre of the participating centers, namely the Centre hospitalier universitaire Ste-Justine (CHU Sainte-Justine), McGill University Health Centre (MUHC), Centre hospitalier universitaire de Sherbrooke (CHUS), and the Hôpital Maisonneuve-Rosemont. F.M.D. and R.P. were awarded the Bourse de Chercheur National (National Scholarship) of the FRSQ.

Disclosure of potential conflict of interest: F. M. Ducharme has received research support from the Canadian Institutes of Health Research; has received consulting fees from Institut nationale d'excellence en soins et services de santé (INESSS), Boehringer Ingelheim, and GlaxoSmithKline; has received travel support from the Canadian Institutes of Health Research, the European Academy of Allergy and Clinical Immunology Congress, and the Canadian Thoracic Society Asthma Committee (Canadian Lung Association); has received donations from Takeda and Merck for the Paediatric asthma database and Biobank of the Sainte-Justine University Hospital Centre; is employed by CHU Sainte-Justine and the University of Montreal; and has received payment for development of educational presentations from the University of British Columbia, Children's Hospital of Ireland, and the University of Montreal. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication March 27, 2015; revised June 18, 2015; accepted for publication July 3, 2015.

Available online September 2, 2015.

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0091-6749/$36.00

http://dx.doi.org/10.1016/j.jaci.2015.07.028

Abbreviations used
ADYC: Asthma Flare-up Diary for Young Children
MD: Mean difference
SABA: Short-acting β_2-agonists
URTI: Upper respiratory tract infection

asthma exacerbation. Therefore a validated measure is needed to assess the severity of asthma exacerbations in preschool-aged children.

With a rigorous methodology, the objectives of this study were (1) to develop a parent-completed functional status instrument to ascertain the severity of an acute asthma exacerbation in children aged 1 to 6 years and (2) to ascertain its psychometric properties in the context of a therapeutic randomized controlled trial.

METHODS

In accordance with Kirshner and Guyatt's approach,[19] the questionnaire development involved 5 sequential tasks: (1) item generation, (2) item reduction, (3) item presentation and scaling, (4) pretesting for clarity, and (5) independent validation of psychometric properties. The institutional review board of the Montreal Children's Hospital (Montreal, Quebec, Canada) approved all phases of the study. Informed consent was obtained from parents or guardians of preschoolers. French and English versions of these instruments were simultaneously developed by using the back-translation technique[20] and underwent simultaneous and independent evaluations across each of the development phases.

The development phases are described in detail in the Methods section in this article's Online Repository at www.jacionline.org. Briefly, item generation involved a literature review to generate items to use as probes in an open-ended questionnaire, which was administered to caregivers of preschool-aged children recruited in the emergency department and short-stay hospitalization unit during an exacerbation. In the item-reduction phase an 84-item questionnaire was administered to a second group of caregivers, who were asked to endorse and rate the perceived importance of each item. Items were then eliminated based on the relevance, the product of endorsement and importance, the correlation coefficients, and principal component analysis. Item presentation and scaling involved grouping the 17 remaining items and formulating them into a statement of frequency or intensity coupled with a scaled response option from 1 (not at all) to 7 (all the time/extremely) with a "cannot answer" option. In pretesting for clarity, cognitive interviews with a third group of caregivers elicited feedback and verified understanding of each question and response option; the final 17-item instrument, called the Asthma Flare-up Diary for Young Children (ADYC), surpassed the requirement for 80% or greater clarity. Available in French and English, it has a sixth-grade reading level (Flesch-Kincaid), with each of the 17 items scored from 1 to 7 and a maximum average daily score of 7 (see Figs E1 and E2 in this article's Online Repository at www.jacionline.org).

Pretesting for psychometric properties

The psychometric properties of the ADYC were pretested in preschoolers enrolled in a multicenter randomized trial of pre-emptive high-dose fluticasone versus placebo initiated at the onset of an upper respiratory tract infection (URTI); as described previously, the intervention reduced by half the number of exacerbations requiring rescue oral corticosteroids (odds ratio, 0.49; 95% CI, 0.3-0.83).[4] Briefly, 129 participants aged 1 to 6 years with virus-induced asthma who recently required systemic corticosteroids were enrolled in the trial. From the first day of a URTI (ie, symptoms of runny or congested nose, sore throat, earache, and/or fever), parents were asked to initiate use of the study drug and complete the ADYC diary daily in the evening until 2 days without any asthma symptoms (ie, cough, whistling, or difficulty breathing). On the same page as the ADYC, parents documented their global assessment of the change in their child's status over the past 24 hours, the number of inhalations of rescue SABAs, and administration of rescue oral corticosteroids, if any. At randomization, the research personnel explained how, when, and how long to fill out the ADYC and asked parents to contact them at the first URTI to review the instructions for completion. If asthma symptoms developed, parents were instructed to start salbutamol at a dose of 2 to 4 puffs every 4 hours as needed and explained when to present to the emergency department in the case of a poor response. If asthma symptoms persisted for 10 days or more, parents were to contact the research nurse, who then reviewed the progress and could request a physician's office visit, if needed; such unscheduled medical assessments were not used in the validation process, although any referral to the emergency department, prescription of oral corticosteroids, or hospital admission were considered in the validation. During monthly telephone calls, the research nurse enquired about URTIs and health care resource use and reviewed the instructions for completion of the ADYC.

A priori diary definitions

A complete set of diaries for an episode was defined as 2 or more consecutive days, with no more than 1 missing or "cannot answer" item per day. A symptomatic day required at least 2 of 3 symptoms (cough, difficulty breathing, or wheezing). An asthma exacerbation was defined as 2 or more symptomatic days. The cumulative ADYC score was the sum of the total daily score from the first to last day during an episode.

Statistical methods

The applicability of the ADYC was explored based on the proportion of caregivers who answered each of the 17 items per day and per episode. With an average of 8 (range, 1022) URTI episodes per child,[4] we randomly selected 1 complete set of diaries (with no missing items) per patient for inclusion in a factor analysis. Using the target matrix for Procrustean transformation, the factor analysis served to validate domains of the ADYC. Final items were selected based on the combination of an eigenvalue of greater than 1 for each factor, a relevance score of greater than or equal to 0.4 for each item, and clinical relevance.[21] Allowing for no more than 1 missing or "cannot answer" item, the following analyses were conducted. Internal consistency was examined by using the Cronbach α value in 1 randomly selected symptomatic day per subject; missing items were imputed by their means. Randomly selecting 2 consecutive symptomatic days per patient in whom the parents' global assessment of change on the second day was deemed "unchanged" from the previous 24 hours (ie, rated -1, 0, or 1), we examined test-retest reliability using intraclass correlation. Conversely, randomly selecting 2 consecutive symptomatic days per patient in whom the parental global assessment of change on the second day indicated notable deterioration (-2 to -7) or improvement ($+2$ to $+7$) in the past 24 hours, we reported the within-subject change in daily score with 95% CIs and documented the responsiveness to change by using the Guyatt responsiveness statistic; that is, the mean change in those who changed divided by the SD of those who did not change.[22] The difference (95% CI) in cumulative ADYC scores during episodes was compared between the pre-emptive high-dose fluticasone and placebo groups, adjusting for individual clustering of episodes and sites and using random effects. Discriminative validity was examined by comparing the mean difference (MD; and 95% CI) in the cumulative score for dichotomous episodes that did or did not result in an (1) exacerbation, (2) emergency department visit, (3) rescue systemic corticosteroid use, and (4) hospitalization adjusted for individual clustering of episodes and sites and using random effects. Mean ADYC scores with SDs were also reported. The minimally important change in the daily ADYC score between 2 consecutive days was calculated on all pairs of consecutive days during which a parent's global assessment of change in his or her child's asthma status between the 2 days was rated -2, -3, $+2$, or $+3$; this analysis was adjusted for within-subject clustering of episodes. For all above analyses, language was offered as a candidate variable. The analyses were conducted with SAS 9.3 software (SAS Institute, Cary, NC).