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Long-term adherence to inhaled corticosteroids in children with asthma: Observational study

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ABSTRACT

Introduction: Non-adherence to daily controller medication in childhood asthma is strongly dependent on potentially modifiable factors such as parental illness perceptions and medication beliefs. The extent to which adherence in children can be improved by addressing modifiable determinants of non-adherence has not been studied to date, however. We assessed long-term adherence and its determinants in children with asthma enrolled in a comprehensive asthma care program employing shared decision making with parents.

Methods: Observational study in 135 children 2–12 years of age with asthma attending a hospital-based outpatient clinic. One-year adherence to inhaled corticosteroids was measured by electronic devices. Parental illness perceptions and medication beliefs, and asthma control were assessed by validated questionnaires.

Results: Median (interquartile range) adherence was 84% (70–92%). 55 children (41%) did not achieve the pre-defined level of good adherence (≥80%) and this was associated with poorer asthma control. Parental perceived medication necessity was high, with a median (interquartile range) BMQ necessity score of 17 (16–20). Parents' replies to the five key questions on the core issues of the program showed high concordance of their illness perceptions and medication beliefs with the medical model of asthma and its treatment. Differences in these perceptions between adherent and non-adherent families were small and non-significant.

Conclusions: Poor adherence may persist in children despite a high level of concordance between medical team and parents on illness perceptions and medication beliefs, even in the absence of socio-economic barriers to good adherence. Achieving good adherence in all children is a complex task, requiring interventions not covered in current guidelines of managing asthma in children.

1. Introduction

Adherence to daily medication is of critical importance in determining the success of treating chronic conditions such as childhood asthma [1–3]. Poor adherence to maintenance medication is the rule rather than the exception, however [2,4]. This may be the result of patients and their parents not understanding the rationale for treatment (unwitting non-adherence) [5,6], which should be remediable by health care professionals providing information on the mechanisms of disease, the beneficial effects of medication, and the importance of daily use of controller medication. Studies, however, have shown that such education alone is insufficient to improve adherence [4,7], indicating that other factors are more important in driving non-adherence. These have been divided into two groups. Unplanned non-adherence relates to disorganized family (medicine taking) routines and child raising issues [6,8,9], and intentional non-adherence refers to patients (or their parents) who deliberately choose not to follow the doctor's

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recommendations [5,6]. Intentional non-adherence, strongly driven by illness perceptions and medication beliefs, has been proposed as the most important form of non-adherence, both in qualitative and quantitative studies [10,11].

Because of the accumulating evidence on the behaviors responsible for medication taking, non-adherence is now increasingly being viewed as 'a condition that can be diagnosed and treated' [12]. The extent to which adherence in children can be improved by addressing modifiable determinants of non-adherence has not been studied to date, however. If parental illness perceptions and medication beliefs are indeed the strongest determinants of adherence, excellent adherence should be expected in patients whose parents express beliefs concordant to the medical model of asthma.

We previously reported a very high median level of adherence to inhaled corticosteroids (ICS) over 3 months in 2–6 year old children with asthma enrolled in a comprehensive, guideline-based asthma management program [13]. Even in this group with high median adherence levels, the degree of adherence was strongly related to medication beliefs [13].

The aim of the present study was to assess one-year adherence to ICS and its determinants in 2–12 year old children with asthma. We focused on the role of illness perceptions and medication beliefs, hypothesizing that these would be different between families with high and those with lower levels of adherence.

2. Methods

2.1. Design and setting

This was an observational study with one year follow-up of asthmatic children aged 2–12 years, receiving asthma care in our hospital-based outpatient center with comprehensive self-management education and close follow-up. Details of our asthma management program have been described previously [13,14]. Briefly, children with troublesome or difficult to control asthma symptoms can be referred to our center by their primary care physician (which, in the Netherlands, is always a family physician). Our center is situated in a large secondary care general teaching hospital serving a mixed urban-rural population of approximately 350,000 inhabitants. Our strategy is to reach consensus with patients and parents on the treatment plan including daily use of ICS controller therapy through shared decision making [15]. We aim to achieve this by providing comprehensive self-management education and counseling, specifically eliciting, addressing and discussing parental illness perceptions and medication beliefs, instructing and checking correct inhalation technique, and providing scheduled close follow-up, with low-threshold accessibility to both pediatricians and asthma nurses for questions, concerns, and check-ups [14,15]. All children referred to our center in whom the diagnosis of persistent asthma is made are being prescribed daily ICS therapy. Patients are being seen at the center at least quarterly during the first year of the program, and at least twice a year afterwards (at least once a year by the attending pediatrician, and at least once a year by the pediatric asthma nurse).

2.2. Inclusion

Inclusion criteria for this study were a diagnosis of asthma made by the attending pediatrician based on national Dutch guidelines for the diagnosis and management of asthma (which are comparable to international guidelines) [16], and use of ICS for at least three months. Exclusion criteria comprised limited knowledge of the Dutch language, severe comorbidity and a sibling participating in the study.

Over a one-year period, parents of all 2–12 year old children with asthma visiting our outpatient clinic for a scheduled follow-up visit were asked to participate in the study. We aimed to include at least 100 patients to allow analysis of determinants of adherence, as a representative sample of all patients visiting our hospital-based secondary care pediatric asthma clinic, as previously reported [13].

2.3. Follow-up and assessment of adherence to ICS

Throughout the 12-months follow-up, adherence was monitored by electronic devices logging date and time of each ICS actuation: Smartinhaler® for MDI/spacer combination, SmartTracker® for MDI with dose counter, and SmartDisk® for Diskus/Accuhaler [13,17]. At each follow-up visit, or during home visits when time to the next scheduled follow-up visit exceeded 5 months, data recorded by the electronic devices where uploaded and proper recording function checked. Adherence was calculated as the number of electronically recorded inhaled doses expressed as a percentage of the number of doses prescribed, censored at 100% of the prescribed dose. Adherence data were not fed back to patients and parents, and remained unknown to the attending physician. To assess physicians' ability to recognize their non-adherent patients, the attending pediatrician was requested at each follow-up visit to estimate the patient's adherence on a visual analogue scale ranging from 0% to 100%. The primary investigator (TK) was the only person with access to the adherence data, and he was not involved in the medical care of study patients.

2.4. Putative determinants of adherence

We collected information on a range of putative determinants of adherence in all participating children. A complete list of these determinants is presented in e-Table 1 in the online repository. Briefly, the following determinants were assessed.

- *Clinical and demographic data* were collected by structured interview and chart review. At baseline, lung function was assessed before and after inhaling salbutamol 400 μg: flow–volume curves in children 5 years of age and older, and respiratory resistance (Rint) by MicrorintR in children < 5 years of age (MicrorintR; Micro Medical Ltd, Rochester, UK), following international guidelines [18,19]. Results were expressed as Z-scores [20].
- *Parental illness perceptions and medication beliefs* were assessed upon entry into the study by a number of validated questionnaires: the Brief Illness Perception Questionnaire (B-IPQ) [21], the Beliefs about Medicines Questionnaire (BMQ) [22], and the Treatment Satisfaction Questionnaire for Medication (TSQM) [23]. In addition, we applied the 'I Worry scale' (scoring parental worries about their child having asthma and using daily ICS) [24], and a locally developed asthma knowledge questionnaire to assess parental knowledge about the use of medication. The BMQ consists of 10 questions measured on a 5-point Likert-scale, five on necessity and five on concerns about ICS (sum scores of both items 5 to 25). The balance between these parent-perceived necessity and concerns can be calculated by subtracting the individuals' concerns score from the individuals' necessity score leading to a range of −20 to 20. Higher scores indicate stronger perceived necessity and/or lower concerns towards ICS use.
- To assess the *effectiveness of our asthma self-management program and the achieved concordance with parents* through shared decision making, the members of our asthma team a priori identified the five key questions from these questionnaires reflecting the core issues of the program (Table 2). Parents

whose responses to at least 4 of these 5 questions were in agreement with the medical model of asthma presented in our self-management education program were considered to show optimal concordance with the medical team.

- *Childrens' illness perceptions and medication beliefs* were assessed in participating children aged 8–12 years, who completed children's versions of each questionnaire, without input from their parents, under supervision of the investigator (TK).
- *Quality of asthma care*: we asked the parents to assess the degree of patient centeredness the physician had employed during the study period with a previously published questionnaire focusing on physician's exploration of parental views and concerns about the illness and the medication and on achieving mutual agreement about treatment [25]. In addition parents completed the Satisfaction with Information about Medicines Scale (SIMS) [26].
- At baseline and after 6 and 12 months of follow-up, *asthma control and parental quality of life* were assessed by parent-completed Asthma Control Questionnaire (ACQ) and the Pediatric Asthma Caregiver Quality Of Life questionnaire (PACQOL), respectively [27,28].

2.5. Analysis

We assessed the association of ICS adherence to all putative determinants, as defined a priori with a focus on parental perceptions about illness and medication, and on concordance between parents and medical team on the core issues of the program. Adherence was analyzed both as a continuous variable and dichotomized as good (≥80%) and poor (<80%) adherence because previous studies have shown that adherence > 80% is associated with good asthma control [1,2]. Because the distribution of adherence was highly skewed, nonparametric analyses were used throughout. The relationship of adherence to determinants with an ordinal distribution was assessed by Spearman's rank correlation coefficient (ρ), and its association to binary determinants with the Mann–Whitney U test. Additional analyses of the relationship between determinants and adherence were performed after adherence was dichotomized as >80% (good adherence) or < 80% (poor adherence). The relationship of dichotomized adherence to determinants with an ordinal distribution was assessed by the Mann–Whitney U test, and its association to binary determinants with the Fisher's exact test.

We chose to refrain from adjustments for multiple comparisons and from multivariate analysis because of the exploratory and observational nature of our study. All analyses were performed using SPSS version 17.0.

2.6. Ethical considerations

This study was approved by the hospital ethics review board; all parents provided written informed consent.

3. Results

3.1. Patient recruitment and follow-up

The recruitment and follow-up of children is presented schematically in Fig. 1. The 135 children recruited for long-term adherence monitoring were similar to the root population of eligible patients in demographic and clinical characteristics (data not shown). Of the 135 children (92% of those enrolled) who completed the study, 125 (93%) were followed for 1 year. In the remaining 10 children, ICS were stopped by mutual agreement between pediatrician and parents because the child was in apparent clinical remission (complete asthma control without the need for on-demand bronchodilator use, no exacerbations and no limitations in activities of daily life, sports and play for at least 12 months). For these patients, adherence data were being used if they had participated for at least 3 months in the study (Fig. 1).

Clinical and demographic characteristics are presented in Table 1. This was, on average, a middle-class Caucasian population. Most children had well-controlled asthma during maintenance treatment with only low-to moderate-dose ICS (Table 1). 15 patients (11%) had an exacerbation requiring a course of oral corticosteroids, two of whom (1.5% of total population) were hospitalized for asthma during the study period.

3.2. Adherence rates

Overall adherence was high, with median (interquartile range, IQR) adherence of 84% (70–92%). Of the 55 children (41%) with poor adherence (<80%), 21 (16% of the study population) had overall adherence < 50% of prescribed doses. Twenty-seven children (20%) received no ICS on ≥ 20% of study days. The attending physicians estimated an adherence level below 80% in 25 (45%) of the 55 children with poor adherence and in 9 (11%) of the 80 children with good adherence.

3.3. Parental illness perceptions and medication beliefs

Parental perceived ICS necessity was high, with a median (IQR) BMQ necessity score of 17 (16–20). ICS concerns exceeded necessity in 5 families (6%) with good adherence and 5 families (9%) with poor adherence ($p = 0.740$). The median (IQR) necessity-concerns differential was 5.5 (3.2–10.8). Parents who viewed daily ICS administration as convenient, and who expected little harm of medicines in general had higher ICS adherence rates (rank correlation coefficient between independent variables and adherence 0.26 [$p = 0.003$] and 0.19 [$p = 0.031$], respectively). None of the other items in the questionnaires showed statistically significant differences in parental perceptions and beliefs between adherent and non-adherent families.

Parents' replies to the five key questions on the core issues of the program showed high concordance of their illness perceptions and medication beliefs with the medical model of asthma and its treatment. Differences in these perceptions between adherent and non-adherent families were small and almost universally non-significant (Table 2). Forty-eight non-adherent families (87%) had illness perceptions and medication beliefs concordant with the medical model of asthma (Table 2).

3.4. Determinants of adherence

Of all other putative determinants of adherence, only better asthma control at 12 months follow-up as assessed by the ACQ was statistically significantly related to higher adherence (both when analyzed as a continuous variable and dichotomized as good (≥80%) and poor (<80%) adherence). Asthma control at study entry and at 6 months was also related to adherence. In the 28 completed questionnaires by children aged 8–12 years, only children's global satisfaction of daily ICS use was related to adherence when analyzed as a continuous variable ($\rho = 0.51$, $p = 0.006$). No other characteristics of children, including age, were related to adherence.

4. Discussion

In this cohort of children with asthma receiving comprehensive asthma care, we recorded a high median adherence to ICS of 84% of prescribed doses. Their parents, mostly from Caucasian middle

Table 1
Characteristics of study patients, their parents and parental assessment of asthma care (n = 135).

Patients		
Age (mean; range; yrs)		6 (2–12)
Maintenance medication:	-inhaled corticosteroids (ICS)	90%
	-ICS and long-acting bronchodilators (%)	10%
	-ICS dose (fluticasone®; mean; range; μg)	250 (125–500)
Nr of children hospitalized in year before study (%)		37 (27%)
ACQ baseline (<0.75 = well-controlled asthma, >1.5 = not well-controlled asthma)		0.50 (0. 17–1.17)
ACQ at 6 months (n = 122)		0.33 (0 .00–1.00)
ACQ at 12 months (n = 107)		0.50 (0 .00–1.17)
Positive specific IgE to common inhalant allergens (%, n = 126)		61%
FEV_1 baseline (z-score, n = 79)		0.27 ± 1.2
Rint baseline (z-score, n = 33)		1.90 ± 2.8
Parents		
Educational level of mother (1 = low and 7 = high, n = 131)		5 (5–6)
Parental diagnosis of asthma (n = 133)		40%
Smoking (n = 133)		30%
PACQOL (1 = low and 7 = high quality of life)		6.3 (5.5 to 6.9)
PACQOL at 6 months (n = 118)		6.7 (6.1–6.9)
PACQOL at 12 months (n = 105)		6.7 (6.3–6.9)
Asthma care		
Duration of outpatient clinic asthma care before study (months)		18 (8–36)
Scheduled visits to outpatient clinic in year before study		4 (3–6)
SIMS (0 = low and 9 = high level of satisfaction)		9 (7–9)
Patient-centeredness questionnaire (1 = low and 5 = high, n = 107)		4.0 (3.4–4.6)

Data are presented as mean ± SD, or as median (interquartile range) unless otherwise stated; ACQ: Asthma Control Questionnaire [28]; Ig: immunoglobin; FEV1: forced expiratory volume in 1 s; Rint: respiratory resistance by the interrupter technique; PACQOL: pediatric asthma caregiver quality of life questionnaire [27]; SIMS: Satisfaction with Information about Medicines Scale [26].

Table 2
Key questions from the applied questionnaires, reflecting core educational aims of the self-management team and the level of achieved concordance.

	Score[a] and % concordance[b] of parents with adherence >80%		Score and % concordance of parents with adherence <80%		p-value
BMQ: 1 strongly agree – 5 strongly disagree					
My child's health at present, depends on the medicines	2 (2–2)	92%	2 (2–2)	76%	0004
My child's medicines protect him/her from becoming worse	2 (1–2)	96%	2 (2–2)	89%	0223
Brief IPQ: 1 not at all – 10 extremely helpful					
How much do you think the treatment can help your child's illness	8 (8–9)	94%	8 (7–9)	93%	0040
Asthma knowledge questionnaire: 1 = true, 2 = false, 3 = I don't know					
My child needs medication only when having symptoms.	2 (2–2)	96%	2 (2–2)	95%	0397
TSQM: 1 = Extremely satisfied – 7 = Extremely dissatisfied					
Overall, how confident are you that taking this medication is a good thing for your child?	2 (1–2)	92%	2 (1–3)	82%	0075
≥ 4 of the 5 parental replies concordant with the asthma team (%)		92%		87%	0337

BMQ: Beliefs about medicines questionnaire [22]; IPQ: Illness perceptions questionnaire-brief version [21]; TSQM: Treatment Satisfaction Questionnaire for Medication [23].
[a] Score presented as median and inter quartile range.
[b] Concordance defined as parental answers in agreement with the self-management education.

class, assessed the asthma care as patient-centered. Concordance (agreement with the medical team on the necessity of daily ICS use) was achieved with most parents. Despite the high median adherence rate and the high level of concordance, 55 children (40%) in our study failed to achieve the predefined threshold for good adherence of 80%, of whom only 25 children (45%) were correctly identified by their attending physician as non-adherent. Children with poor adherence had lower levels of asthma control. Adherence was not associated with the child's age.

4.1. High median adherence

To our knowledge, this study reports the highest long-term adherence rate ever recorded in children or adults. Previous adherence studies using electronic measurement of daily ICS use in children with asthma reported adherence rates ranging from 34% to 77% [2]. No study assessing adherence for a time period of more than 6 months ever reported adherence levels exceeding 60% [2]. The most likely cause for the exceptionally high adherence rate we observed is the focus on achieving concordance with parents in our comprehensive asthma program through shared decision making. In addition, the prevalence of other known barriers to adherence, such as poverty and poor access to health care, was low in our study population. Remarkably, despite the high overall adherence, 40% of the study population showed poor adherence associated with lower levels of asthma control [1,13].

4.2. Illness perceptions and medication beliefs

A considerable body of evidence from a wide range of chronic conditions in adults and children shows that illness perceptions and medication beliefs are the strongest determinants of (non)-adherence to long-term therapy [10]. A previous Dutch study showed high prevalence of concerns about long-term ICS use in children with asthma, outweighing the perceived necessity of daily ICS use in many children [29]. This was also found in a previous focus group study among parents of children with asthma treated in primary care practices referring their patients to our outpatient clinic [30]. Apparently, most parents of asthmatic children have illness perceptions about asthma and medication beliefs about its

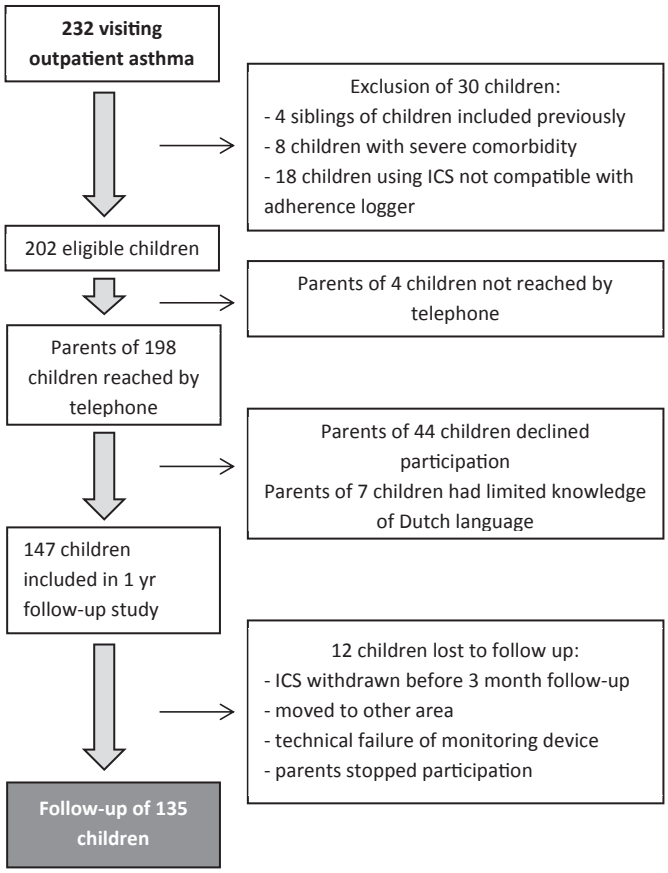

Fig. 1. patient flow chart.

treatment which do not agree with the medical model of asthma expressed in asthma guidelines. By contrast, the large majority of parents in our study expressed illness perceptions and medication beliefs in agreement with this medical model of asthma, with ICS necessity exceeding concerns in 91% of parents. We previously argued that this is likely to be the result of our comprehensive asthma care program focusing on achieving concordance with parents through shared decision making [13,30]. Interestingly, however, such illness perceptions and medication beliefs in accordance with the medical model of asthma were also observed in most parents with poor adherence in the present study. Intensifying self-management education aimed at modifying parental illness perceptions and medication beliefs is therefore unlikely to achieve the desired improvement in adherence in the 40% of families with poor adherence (<80%). For these families, other barriers of adherence need to be considered, therefore.

4.3. Other modifiable determinants of adherence

Apart from illness perceptions and medication beliefs, non-adherence may also be determined by a range of other modifiable and non-modifiable factors [31]. Previous studies have highlighted a number of barriers to optimal adherence including limited access to health care, limited health insurance, illiteracy, language barriers, and issues generating 'high levels of worry about competing household priorities', such as poverty [31,32]. These did not appear to play a role in our study population which was, on average, middle class, with good access to health care, mandatory health insurance covering reimbursement of maintenance medication use, and proper understanding of the Dutch language. In a previous study using in-depth interviews with parents whose children showed poor adherence revealed additional barriers to adherence, such as child-raising issues, relational issues, and transferring responsibility for daily medication use to the child at an inappropriately early age [33]. The present study shows that most of these non-adherent families were not recognized by the attending pediatrician, despite the extensive asthma care with frequent follow-up visits. These findings suggest that identifying non-adherence and its barriers is likely to require both actively and objectively monitoring of adherence [2], feedback of its results [34], and non-confrontational discussion of potential reasons for non-adherence [15]. Whether barriers identified in such a way can be modified through targeted interventions should be investigated in further studies.

4.4. Strengths and weaknesses

The main strengths of this study are the electronic assessment of adherence and the 12-months follow-up period. The main limitation of our study is its generalizability. Because most parents and children in our study population came from Caucasian middle-class families, the applicability of our findings to other social settings remains to be established. However, because many barriers such as limited access to health care were not prevalent in this population, this study highlights the difficulties in achieving optimal adherence in children with asthma and their families, even in the absence of socio-economic disadvantages.

5. Conclusion

In this middle class Caucasian population of families with children with asthma with good access to comprehensive asthma care, a high level of concordance regarding the daily use of ICS was achieved. Although this was associated with a high median adherence of 84% of prescribed doses, 40% of the children remained non-adherent. These children had lower levels of asthma control, and were poorly recognized by the medical team. It is unlikely that this type of non-adherence can be improved by additional education or focusing on illness perceptions and medication beliefs. Potential strategies required to improve adherence may need a tailor-made approach including objective assessment of adherence and a non-confrontational and detailed discussion of potential barriers to adherence.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.rmed.2015.07.016.

References

[1] T. Klok, A.A. Kaptein, E.J. Duiverman, P.L. Brand, It's the adherence, stupid (that determines asthma control in preschool children)!, Eur. Respir. J. 43 (2014) 783–791.
[2] R.W. Morton, M.L. Everard, H.E. Elphick, Adherence in childhood asthma: the elephant in the room, Arch. Dis. Child. 99 (2014) 949–953.
[3] N.S. Jentzsch, P. Camargos, E.S. Sarinho, J. Bousquet, Adherence rate to

beclomethasone dipropionate and the level of asthma control, Respir. Med. 106 (2012) 338–343.
[4] S. van Dulmen, E. Sluijs, D.L. van, R.D. de, R. Heerdink, J. Bensing, Patient adherence to medical treatment: a review of reviews, BMC Health Serv. Res. 7 (2007) 55.
[5] A.G. Weinstein, The potential of asthma adherence management to enhance asthma guidelines, Ann. Allergy Asthma Immunol. 106 (2011) 283–291.
[6] B.G. Bokhour, E.S. Cohn, D.E. Cortes, et al., Patterns of concordance and non-concordance with clinician recommendations and parents' explanatory models in children with asthma, Patient Educ. Couns. 70 (2008) 376–385.
[7] A.J. Dean, J. Walters, A. Hall, A systematic review of interventions to enhance medication adherence in children and adolescents with chronic illness, Arch. Dis. Child. 95 (2010) 717–723.
[8] A. Schultz, P.D. Sly, G. Zhang, A. Venter, S.G. Devadason, P.N. Le Souef, Usefulness of parental response to questions about adherence to prescribed inhaled corticosteroids in young children, Arch. Dis. Child. 97 (2012) 1092–1096.
[9] B.H. Fiese, F.S. Wamboldt, R.D. Anbar, Family asthma management routines: connections to medical adherence and quality of life, J. Pediatr. 146 (2005) 171–176.
[10] A.A. Kaptein, T. Klok, R. Moss-Morris, P.L. Brand, Illness perceptions: impact on self-management and control in asthma, Curr. Opin. Allergy Clin. Immunol. 10 (2010) 194–199.
[11] R. Horne, S.C. Chapman, R. Parham, N. Freemantle, A. Forbes, V. Cooper, Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the necessity-concerns framework, PLoS One 8 (2013) e80633.
[12] Z.A. Marcum, M.A. Sevick, S.M. Handler, Medication nonadherence: a diagnosable and treatable medical condition, JAMA 309 (2013) 2105–2106.
[13] T. Klok, A.A. Kaptein, E.J. Duiverman, P.L. Brand, High inhaled corticosteroids adherence in childhood asthma: the role of medication beliefs, Eur. Respir. J. 40 (2012) 1149–1155.
[14] T. Klok, E.P. de Groot, A.F.J. Brouwer, P.L.P. Brand, Follow-up of children with asthma, Eur. Respir. Mon. 56 (2012) 210–223.
[15] P.L. Brand, T. Klok, A.A. Kaptein, Using communication skills to improve adherence in children with chronic disease: the adherence equation, Paediatr. Respir. Rev. 14 (2013) 219–223.
[16] N. Boluyt, B.L. Rottier, J.C. de Jongste, R. Riemsma, E.J. Vrijlandt, P.L. Brand, Assessment of controversial pediatric asthma management options using grade, Pediatrics 130 (2012) e658–e668.
[17] S.W. Burgess, S.S. Wilson, D.M. Cooper, P.D. Sly, S.G. Devadason, In vitro evaluation of an asthma dosing device: the smart-inhaler, Respir. Med. 100 (2006) 841–845.
[18] M.R. Miller, J. Hankinson, V. Brusasco, et al., Standardisation of spirometry, Eur. Respir. J. 26 (2005) 319–338.
[19] N. Beydon, C. M'buila, A. Bados, et al., Interrupter resistance short-term repeatability and bronchodilator response in preschool children, Respir. Med. 101 (2007) 2482–2487.
[20] S. Stanojevic, A. Wade, T.J. Cole, et al., Spirometry centile charts for young Caucasian children: the Asthma UK collaborative initiative source, Am. J. Respir. Crit. Care Med. 180 (2009) 547–552.
[21] E. Broadbent, K.P. Petrie, J. Weinman, The brief illness perception questionnaire, J. Psychosom. Res. 60 (2006) 631–637.
[22] R. Horne, J. Weinman, M. Hankins, The belief about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication, Psychol. Health 14 (1999) 1–24.
[23] M.J. Atkinson, A. Sinha, S.L. Hass, et al., Validation of a general measure of treatment satisfaction, the treatment satisfaction questionnaire for medication (TSQM), using a national panel study of chronic disease, Health Qual. Life Outcomes 2 (2004) 12.
[24] K.A. DeVet, H.T. Ireys, Psychometric properties of the maternal worry scale for children with chronic illness, J. Pediatr. Psychol. 23 (1998) 257–266.
[25] P. Little, H. Everitt, I. Williamson, et al., Observational study of effect of patient centredness and positive approach on outcomes of general practice consultations, BMJ 323 (2001) 908–911.
[26] R. Horne, M. Hankins, R. Jenkins, The Satisfaction with Information about Medicines Scale (SIMS): a new measurement tool for audit and research, Qual. Health Care 10 (2001) 135–140.
[27] E.F. Juniper, G.H. Guyatt, D.H. Feeny, P.J. Ferrie, L.E. Griffith, M. Townsend, Measuring quality of life in children with asthma, Qual. Life Res. 5 (1996) 35–46.
[28] E.F. Juniper, J. Bousquet, L. Abetz, E.D. Bateman, Identifying 'well-controlled' and 'not well-controlled' asthma using the asthma control questionnaire, Respir. Med. 100 (2006) 616–621.
[29] E.S. Koster, A.H. Wijga, G.H. Koppelman, et al., Uncontrolled asthma at age 8: the importance of parental perception towards medication, Pediatr. Allergy Immunol. 22 (2011) 462–468.
[30] T. Klok, P.L. Brand, H. Bomhof-Roordink, E.J. Duiverman, A.A. Kaptein, Parental illness perceptions and medication perceptions in childhood asthma, a focus group study, Acta Paediatr. 100 (2011) 248–252.
[31] D. Drotar, M.S. Bonner, Influences on adherence to pediatric asthma treatment: a review of correlates and predictors, J. Dev. Behav. Pediatr. 30 (2009) 574–582.
[32] L.A. Smith, B. Bokhour, K.H. Hohman, et al., Modifiable risk factors for suboptimal control and controller medication under use among children with asthma, Pediatrics 122 (2008) 760–769.
[33] T. Klok, S. Lubbers, A.A. Kaptein, P.L. Brand, Every parent tells a story: why non-adherence may persist in children receiving guideline-based comprehensive asthma care, J. Asthma 51 (2014) 106–112.
[34] S.W. Burgess, P.D. Sly, S.G. Devadason, Providing feedback on adherence increases use of preventive medication by asthmatic children, J. Asthma 47 (2010) 198–201.