Psychological characteristics associated with the onset and course of asthma in children and adolescents: A systematic review of longitudinal effects

Marijke M. Tibosch a,b,*, Christianne M. Verhaak a, Peter J.F.M. Merkus b

Objective: To systematically review all available studies that investigated the longitudinal relationships between the psychological characteristics of children and adolescents suffering from asthma and those of their caregivers, and the onset and course of the asthma.

Methods: Relevant studies were identified using Medline, PubMed, and PsychINFO between 1970 and September 2009.

Results: Twenty studies matching inclusion criteria were reviewed. Six studies focused on child-specific psychological characteristics in relation to the onset and course of asthma. No compelling evidence was found for an association with asthma onset, but there was some evidence that the child's psychological characteristics can contribute to the subsequent course of asthma. Fourteen studies considered the effects of the psychological characteristics of the caregivers. Eleven studies found significant relationships between the psychological problems of caregivers and the subsequent onset and unfavorable course of the asthma in the child. Conclusion: In pediatric asthma both the psychological characteristics of the affected children and their caregivers appear to contribute to the course and possibly also to the onset of the condition.

Keywords: Asthma; Child; Adolescent; Parent; Caregiver; Psychological characteristics; Systematic review.

1. Introduction

With approximately 300 million persons currently suffering from asthma worldwide, this condition is one of the most common chronic diseases, especially in childhood [1]. Mean worldwide 'current wheeze' prevalence rates in the last 12 months range from 11.6% in 6–7-year age children to 13.7% in 13–14-year olds, according to phase III of the International Study of Asthma and Allergies in Children [2].

Recent epidemiological studies assessed the effects of psychosocial characteristics on the expression of atopic disorders. Besides studies on childhood asthma, Chida and colleagues reviewed the research on various other atopic disorders (e.g., allergic rhinitis, atopic dermatitis and food allergies) in both children and adults. They found robust, positive, and bidirectional associations between psychosocial factors and both the onset and prognosis of the conditions studied [3]. They, however, did not explicitly address the possible differential role that the characteristics of the children and parents or caregivers may play in the onset and course of asthma episodes in childhood and adolescence.

It is important to differentiate between the child’s and caregiver’s psychological characteristics, because it is still not known how these factors are related which each other in the case of childhood asthma. Moreover, children and caregivers tend to have different perceptions of to what constitutes severe asthma [4]. In addition, differences between their personal characteristics may yield valuable information about the direction interventions should take, i.e., whether the treatment should focus more on the child or on the caregiver(s). It is also important to differentiate between different aspects of mental health. Depression, anxiety or stressful events require other interventions.

Abbreviations: AE, allergen exposure; AL, caregiver alcohol use; BF, breast feeding; BM, baseline morbidity; BSI, Brief Symptom Inventory; BQ, Behavior Screening Questionnaire; BW, birth weight; CBCL, Child Behavior Checklist; CCEI, Crown-Crisp Experiential Index; CES-D, Center for Epidemiological Studies Depression Scale; CI, confidence interval; ECBI, Eyberg Child Behavior Inventory; ED, Emergency department; FHA, family history of asthma; GHQ, General Health Questionnaire; HAD, Hospital Anxiety and Depression Scale; HRI, history of respiratory infections; ICD, International Classification of Diseases; IgE, immunoglobulin E; IL, interleukin; INF, interferon; MH, mental health; OR, odds ratio; PACE, Psychosocial Assessment of Childhood Experiences; PP, parenting practices; PRS, Parenting Risk Scale; PSS, Perceived Stress Scale; RR, relative risk; SC, Spearman correlation; SES, socioeconomic status; SS, social support; TNF, tumor necrosis factor; UCLALSI-CV, University of California Los Angeles Life Stress Interview—Child Version.

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In their meta-analysis of the data of nearly 5000 children suffering from asthma, McQuaid et al. found that these children had more psychological problems, especially internalizing problems, than their healthy peers [5]. The majority of the analyzed studies were cross-sectional, which therefore does not allow any conclusions to be drawn about causality. Several theories have been proposed to explain the mechanisms that relate psychological characteristics to asthma onset. As a result genetic, immunological, neural, endocrine, and behavioral pathways have been suggested as linking psychological characteristics to asthma onset, severity, and course. These pathways continue to be investigated [6–8]. Behavioral pathways include problems with treatment adherence and the effects of psychological problems on the perceptions and management of asthma by different informants.

It is important to ensure that psychological problems are detected early in asthmatic children, because there is evidence to suggest that such problems negatively affect the children's treatment adherence, which is already notoriously low in this population [9,10]. This may result in reduced physical and psychosocial health, and increased health care utilization and costs.

Moreover, besides the children's own psychological characteristics, psychological problems of their caregivers also tend to increase the risk of asthma onset or have a negative effect on the course of asthma [11–13]. If we are to improve psychosocial interventions that help enhance the children's overall health status and reduce the burden of asthma on the patients and their families as well as on society, knowledge of the interrelationship between these personal characteristics of children and their caretakers and asthma outcome is crucial. In order to compile an overview of the insights to date, we conducted a systematic review of the available empirical research on the longitudinal relationship between specific psychological characteristics of healthy and asthmatic children or teenagers and their caregivers, and the onset and course of asthma. In our report we consider the psychological characteristics of both parties in terms of anxiety, depression or exposure to stressful events, which also includes parenting stress.

2. Method

2.1. Selection of relevant studies

In this systematic review we evaluate reports published in peer-reviewed journals in English, German, French, and Dutch. The electronic databases of Medline, PubMed, and PsychINFO (between 1970 until the end of September 2009) were used to identify relevant publications. In order to identify publications on the subject of psychological characteristics and asthma in children and adolescents, we used the search terms: (asthma) AND (psych* OR emotion* OR distress* OR depress* OR mental* OR adjustment* OR anxiety OR behavior* OR quality of life). We limited our review to studies that included participants ≤18 years old. Since we were interested in longitudinal relationships between the psychological characteristics and the onset and course of asthma, we merely considered prospective (longitudinal) studies. We searched the reference lists of the studies in order to identify additional relevant studies, which we had not found with initial search strategies (snowball method).

2.2. Assessment of study quality

Study quality was determined based on the protocols of the Cochrane Database of Systematic Reviews [14]. The inclusion criteria were adjusted to fit the research questions of our review:

i. Database: English, German, French or Dutch language full-length publication in a peer-reviewed journal and abstract available in an electronic database.

ii. Selection of subjects: the participants in the study should be ≤18 years old and selected randomly or consecutively.

iii. Psychological characteristics (in children, adolescents or caregivers) such as anxiety, depression, behavior adjustment or general distress should be addressed through questionnaires or clinical interviews with proven reliability and validity, and should be compared with reference populations.

iv. Outcome measures associated with asthma should concern asthma onset or asthma course and assessed by well-expressed child or parental reports, physical parameters or physician's diagnosis.

v. Study design: Studies should have a prospective design investigating a longitudinal association between psychological characteristics of children or caregivers and the subsequent onset and/or course of asthma.

vi. All studies were required to have reported statistics (e.g., means and standard deviations, t, F).

Study inclusion and data extraction were conducted by the first author (MT) and verified by the second (CV).

2.3. Presentation of the results

We divided the relevant literature into prospective studies that investigated the child's asthma manifestations in relation to the child's psychological characteristics and those that examined them in relation to the caregiver's characteristics. If one publication addressed both research questions, it was considered as two separate studies.

3. Results

Our search strategy yielded 711 publications that addressed a wide range of topics related to psychology and asthma. The first author (M.T.) initially screened the titles and abstracts against the content and methodological criteria for review, which resulted in the exclusion of 643 articles. Table 1 shows the reasons for exclusion in this first round.

The remaining 68 publications (10%) subsequently underwent a more detailed, second evaluation of their content and methodological criteria, after which 53 publications were excluded. The reasons for this exclusion are detailed in Table 2. The flowchart in Fig. 1 provides an overview of the inclusion and exclusion process.

Table 1

<table>
<thead>
<tr>
<th>Reason for exclusion</th>
<th>Total</th>
<th>%</th>
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<tbody>
<tr>
<td>Main focus on medical aspects</td>
<td>230</td>
<td>32</td>
</tr>
<tr>
<td>Main focus on other diseases than asthma</td>
<td>128</td>
<td>18</td>
</tr>
<tr>
<td>Main focus on interventions</td>
<td>77</td>
<td>11</td>
</tr>
<tr>
<td>Main focus on sociodemographic, lifestyle or economic/epidemiological aspects</td>
<td>41</td>
<td>6</td>
</tr>
<tr>
<td>Psychometric properties of questionnaires insufficient</td>
<td>38</td>
<td>5</td>
</tr>
<tr>
<td>Participants older than 18 years</td>
<td>26</td>
<td>4</td>
</tr>
<tr>
<td>Main focus on smoking behavior/exposure</td>
<td>27</td>
<td>4</td>
</tr>
<tr>
<td>Main focus on association asthma and body weight</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>Non-prospective (non-longitudinal) design</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Review</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>No abstract available or not published in one of the target languages in a peer-reviewed journal</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Other (no focus on association between psychological characteristics and asthma)</td>
<td>34</td>
<td>5</td>
</tr>
<tr>
<td>Potentially relevant articles*</td>
<td>68</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>711</td>
<td>100</td>
</tr>
</tbody>
</table>

* Publications meeting the criteria for review as based on abstract content.
Ultimately 15 publications were included for review. They addressed 20 separate research questions pertaining to the association between psychological characteristics and the onset and course of asthma in the child [11–13,15–26]. Different psychological inventories were used to assess various psychological characteristics [27–39]. The details of the studies reviewed are summarized in Tables 3 and 4 and discussed in the following paragraphs.

3.1. Relationships with the child’s psychological characteristics

Six studies examined associations between the child’s psychological characteristics and the onset and course of their asthma (Table 3) using various psychological inventories, with sample sizes ranging from 71 to 3575 and follow-up times from two weeks to nine years. Psychological factors differed from internalizing problems and externalizing problems (such as behavior problems) to acute stress in terms of stressful events. Development or diagnosis of wheezing/asthma was only assessed by parental reports (no physicians’ diagnoses). One study based asthma course on peak-flow diaries [22] and one study assessed immune changes in the child’s blood [19].

3.1.1. Associations with asthma onset

Three studies focused on the child’s psychological characteristics in relation to asthma onset [11,15,23]. One was a large-scale study examining 3575 healthy 5-year olds. It concluded that internalizing problems (as measured by the Child Behavior Checklist) were not associated with the onset of asthma nine years later [15]. The study recoded internalizing symptoms into normal and abnormal symptoms using a cut-off score. The other two studies, which also used cut-off scores, concluded that externalizing problems (behavior problems as assessed with the Eyberg Child Behavior Inventory and Behavior Screening Questionnaire) were associated with the subsequent onset of wheezing or asthma [11,23]. However, both were smaller scale studies with shorter follow-up times (18 months and two years, respectively). Assessing 411 healthy children Calam et al. found externalizing problems to precede the onset of wheezing with an odds ratio of 8.95 [11]. Investigating the effect of externalizing problems in 265 children with atopic dermatitis Stevenson et al. found a small but significant odds ratio (1.15) between initial externalizing problems and the subsequent onset of asthma [23].

3.1.2. Associations with the course of asthma

Three studies investigated children’s psychological characteristics in relation to the course of their asthma. They all concluded that psychological problems and exposure to severely stressful events increased asthma severity over time [19,22,24]. One study examined the effects of exposure to acute and chronic stress (as measured by the Psychosocial Assessment of Childhood Experiences) on asthma severity in the following weeks (as based on peak-flow diaries) in 90 children (aged 6–13 years) [22]. The combination of high chronic stress with acute stress correlated positively with the subsequent increased risk of new asthma attacks. This result is in agreement with the finding of a recent
### Table 3
Prospective studies investigating relationships between child-specific psychological characteristics and the onset and course of asthma (*n*= 6).

<table>
<thead>
<tr>
<th>First author (year)</th>
<th>Cohort (Nation)</th>
<th>Mean age/age range</th>
<th>Follow-up</th>
<th>Psychological factor (instrument)</th>
<th>Asthma parameter (instrument)</th>
<th>Controlled covariates</th>
<th>Main conclusion(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alati [15] (2005)</td>
<td>3575 healthy children (2726 without and 849 with internalizing symptoms) (Australia)</td>
<td>5 years</td>
<td>9 years</td>
<td>Internalizing symptoms (CBCL)</td>
<td>Onset of asthma (maternal report)</td>
<td>Sex, SES, Anxiety &amp; Depression at 5 yrs.</td>
<td>Internalizing symptoms were not associated with the development of asthma (m, OR, 0.98; 95%CI, 0.69–1.38; f, OR, 1.13; 95%CI, 0.78–1.63)</td>
</tr>
<tr>
<td>Calam [11] (2005)</td>
<td>411 healthy children (UK)</td>
<td>3 years</td>
<td>2 years</td>
<td>Behavioral problems (ECBI)</td>
<td>Development of wheezing (parent report)</td>
<td>None (in univariate logistic regression analysis)</td>
<td>Behavior problems anteceded the development of wheezing (OR, 8.95; 95%CI, 2.29–34.93) Children with the combination of higher levels of chronic stress and acute stress showed increased IL-4 (β = 8.16, <em>p</em> &lt; 0.01), increased IL-5 (β = 43.74, <em>p</em> = 0.007), increased IFN-γ (β = 11334.98, <em>p</em> = 0.004) and more asthma symptoms (β = 0.41, <em>p</em> = 0.024)</td>
</tr>
<tr>
<td>Marin [19] (2009)</td>
<td>71 children with asthma</td>
<td>13 years</td>
<td>3 months</td>
<td>Acute and chronic stress (UCLALSI-CV)</td>
<td>Production of cytokine interleukin (IL-4, IL-5, IL-13), IFN-γ and asthma symptoms (self-report)</td>
<td>Asthma severity, medication, SES</td>
<td>Children with the combination of higher levels of chronic stress and acute stress showed increased IL-4 (β = 8.16, <em>p</em> = 0.01), increased IL-5 (β = 43.74, <em>p</em> = 0.007), increased IFN-γ (β = 11334.98, <em>p</em> = 0.004) and more asthma symptoms (β = 0.41, <em>p</em> = 0.024)</td>
</tr>
<tr>
<td>Sandberg [22] (2000)</td>
<td>90 children with asthma (20 exposed to high and 70 to low-to-moderate chronic stress) (Scotland)</td>
<td>6–13 years</td>
<td>1 day to 18 months</td>
<td>Acute and chronic psychological stress (PACE)</td>
<td>Asthma severity (peak-flow diary)</td>
<td>Age, sex, smoking, SES, BM</td>
<td>Severe acute stress accompanied by high chronic stress increased the risk of new asthma attacks within a fortnight (OR, 2.98; 95%CI, 1.2–7.38). Severe acute stress without accompanying chronic stress did not increase the risk of new asthma attacks until the second week with a peak around 4–6 weeks (OR, 2.17; 95%CI, 1.32–3.57). Behavior problems anteceded the onset of asthma (OR, 1.15; 95%CI, 1.02–1.29). Children with a lowered baseline mental health had more days of wheezing (SC, –12; <em>p</em> &lt; .01), a lower general functional status (SC, –13; <em>p</em> &lt; .01) and fewer hospitalizations (SC, –10; <em>p</em> &lt; .01). They did not have more unscheduled health visits (SC, .02; <em>p</em> &gt; .05).</td>
</tr>
<tr>
<td>Stevenson [23] (2003)</td>
<td>265 children with atopic dermatitis (UK)</td>
<td>2 years and 11 months</td>
<td>18 months</td>
<td>Behavior problems (BSQ)</td>
<td>Asthma onset (parent report)</td>
<td>IgE, treatment and severity of atopic dermatitis BM, age, sex, race, Research Centre, Caregiver’s MH, AL, Life events, PP, SS</td>
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</tbody>
</table>

CBCL = Child Behavior Checklist, m = male, f = female, OR = odds ratio, CI = confidence interval, β = coefficient, IFN = interferon, ECBI = Eyberg Child Behavior Inventory, PACE = Psychosocial Assessment of Childhood Experiences, BSQ = Behavior Screening Questionnaire, SC = Spearman Correlations, Covariates; Sex = child’s sex, SES = socioeconomic status, Smoking = by caregiver, BM = baseline morbidity, MH = mental health, AL = caregiver alcohol use, PP = parenting practices, and SS = social support.
<table>
<thead>
<tr>
<th>First author (year)</th>
<th>Cohort (Nation)</th>
<th>Mean age/age range</th>
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<th>Controlled covariates</th>
<th>Main conclusion(s)</th>
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<tr>
<td>Bartlett [16] (2001)</td>
<td>158 children with asthma (USA)</td>
<td>7 years and 11 months</td>
<td>6 months</td>
<td>Maternal depression (CES-D)</td>
<td>Asthma morbidity (ED use, parent reported)</td>
<td>Child’s &amp; Caregiver’s Age, SES, Asthma morbidity</td>
<td>Mothers with high depression symptoms were more likely to take their asthmatic child to the ED (PR, 1.3; 95%CI, 1.1–5.0) Parental depression was not associated with the development of wheezing Parental anxiety was not associated with the development of wheezing Parental psychiatric disorder was not associated with the development of wheezing Maternal prenatal anxiety was associated with an increased risk of developing childhood asthma (OR, 1.64; 95% CI, 1.25–2.17) Parenting difficulties were associated with the onset of asthma in the 6–8-year-old children (OR, 2.1; 95% CI 1.15–3.71) Exposure to continued maternal distress from birth until age 7 was associated with an increased risk of developing childhood asthma (OR, 1.29; 95% CI, 1.01–1.55) An increase in wheezing and perceived parental stress levels showed a trend towards significance (OR, 1.18; 95% CI 0.99–1.42). Parental stress was associated with wheezing in boys without parental asthma (OR, 1.34; 95% CI 1.04–1.74), but not in girls or children with parental asthma. In the boys without parental asthma there was a strong dose-response relationship, with the top quartile of stress reaching an OR of 2.76 (95% CI 1.39–5.51) compared to the bottom quartile. Parenting difficulties were associated with the onset of asthma before age 3 (RR, 3.4; 95% CI 1.01–11.59) Children of caregivers with a lower baseline mental health had more hospitalizations (RC, .11; p &lt; .01), but unscheduled health visits (RC, .01; p &gt; .05), days of wheezing (RC, .03; p &gt; .05) and lower general functional status (RC, .02; p &gt; .05) were not elevated.</td>
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<tr>
<td>First author (year)</td>
<td>Cohort (Nation)</td>
<td>Mean age/age range</td>
<td>Follow-up</td>
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<tr>
<td>Wolf [13] (2008)</td>
<td>50 children with asthma and 33 healthy children (Canada)</td>
<td>8–18 years</td>
<td>7 months</td>
<td>Parental depression (CES-D)</td>
<td>Asthma-relevant inflammatory markers: eosinophil cationic protein (ECP) and stimulated interleukin-4 (IL-4)</td>
<td>Asthma severity and medication, Depressive symptoms or anxiety in child, Age, Sex</td>
<td>Higher levels of parental depression were associated with elevations in the child’s ECP over time ($\beta=.19$, $p=.046$), but IL-4 production remained more or less unchanged over time ($\beta=.16$, $p=.19$)</td>
</tr>
<tr>
<td>Wolf [13] (2008)</td>
<td>50 children with asthma and 33 healthy children (Canada)</td>
<td>8–18 years</td>
<td>7 months</td>
<td>Parent-perceived stress (PSS)</td>
<td>Asthma-relevant inflammatory markers: eosinophil cationic protein (ECP) and stimulated interleukin-4 (IL-4)</td>
<td>Asthma severity and medication, Depressive symptoms or anxiety in child, Age, Sex</td>
<td>Higher levels of perceived parental stress were associated with increased IL-4 production ($\beta=.29$, $p=.019$) and ECP release ($\beta=0.27$, $p=0.004$) in the children</td>
</tr>
<tr>
<td>Wright [25] (2002)</td>
<td>496 healthy infants with family history of atopy (USA)</td>
<td>2 months</td>
<td>1 year</td>
<td>Caregiver-perceived stress (PSS4)</td>
<td>Recurrent wheezing at age 14 months (parent report)</td>
<td>Smoking, BF, HRI, AE, Sex, SES, BW, FHA</td>
<td>Caregiver’s stress predicted the incidence of recurrent wheezing (RR, 1.4; 95% CI 1.1–1.9) In the first 6 months after birth caregiver’s stress was associated with increased lymphocyte proliferative response (for Dermatophagoides farina: OR, 1.5; 95%CI 1.0–2.3 and for cockroach: OR, 1.13; 95%CI 0.7–1.8). In the children aged 6 to 18 months higher caregiver stress was associated with a high total IgE level (OR, 2.03; 95%CI 1.1–3.6) as well as with increased cytokine expression (TNF-α).</td>
</tr>
<tr>
<td>Wright [26] (2004)</td>
<td>215 children with family history of atopy (USA)</td>
<td>2 months</td>
<td>2 years</td>
<td>Caregiver-perceived stress (PSS-4)</td>
<td>Asthma-relevant immune response markers (IgE expression, lymphocyte proliferative response and cytokine production)</td>
<td>Age, FHA, Sex, Cold status, AE at 2–3 months, Race</td>
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</tbody>
</table>
study by Marin et al., in which 71 children with asthma (mean age 13 years) were included [19]. Children who had higher levels of chronic family stress showed an increased production of IL-4, IL-5, and IFN-γ at times when they had experienced an acute stressful event in the past 3 months. They also reported more asthma symptoms. The third study included 1260 children (aged 4–9 years) with asthma. It found that children with psychological problems (internalizing as well as externalizing problems as assessed with the Child Behavior Checklist) had more days of wheezing and a lower general functional status in the following nine months [24]. However, they had fewer hospitalizations than their peers without psychological problems and a similar number of unscheduled visits as these peers.

3.2. Relationships with the psychological characteristics of the child's caregiver

Eleven publications, which together address 14 research questions, reported on associations between the psychological characteristics of the child's principal caregiver and the onset or course of asthma (Table 4). Sample sizes ranged from 50 to 13,907 children and follow-up times ranged from 6 months to 8 years. Different psychological characteristics of the caregivers were assessed: anxiety and depression (Center for Epidemiological Studies Depression Scale, Hospital Anxiety and Depression Scale and the Crown-Crisp Experiential Index), exposure to different types of stress (Perceived Stress Scale and Parenting Risk Scale), and more general psychological characteristics (Brief Symptom Inventory, physician's diagnosis based on the International Classification of Diseases, and the General Health Questionnaire).

Half of the studies assessed asthma outcome using parental reports, while physicians were involved in five studies and asthma-relevant markers such as eosinophil cationic protein (ECP) release and interleukin-4 (IL-4) production were examined in the child's blood were assessed in three studies.

3.2.1. Associations with asthma onset in the child

Ten research questions (in eight publications) examined the psychological characteristics of the caregivers in relation to the onset of asthma in their children [11,12,17,18,20,21,25,26]. Investigating three aspects, Calam et al. found that parental or caregiver depression, anxiety and psychiatric disorder were not associated with the psychological characteristics of the caregiver in relation to the cause of the child's asthma, and all found significant associations [13,16,24]. Assessing the mothers of 158 8-year-old children with asthma Bartlett et al. found that the mothers with depressive symptoms were more likely to take their child to the emergency department in the following six months [16].

In a large cohort of 1260 asthmatic children (aged 4–9 years) With et al. observed that psychological problems in caregivers were associated with more hospitalizations of the child in the following three to nine months, although the frequency of unscheduled visits, days of wheezing or lower general functioning status was not higher relative to those reported in the children of untroubled caregivers [24]. Wolf et al. found higher levels of parental depression (mean child's age was 13.3, n = 50) to be associated with increased eosinophil cationic protein (ECP) release six months later, although the interleukin-4 production had not increased. Higher levels of parental stress were associated with both an increased ECP release and an increased IL-4 production [13].

4. Discussion and conclusion

4.1. Discussion

In this systematic review we evaluated 15 publications that addressed 20 research questions pertaining to possible relationships between psychological characteristics and the onset or course of childhood asthma. Six of the research questions addressed associations with the child's psychological characteristics. The remaining 14 research questions addressed associations with the psychological characteristics of the child's principal caregiver.

Our evaluations showed that there was no compelling evidence that child psychological problems increased the risk of developing asthma. Results were conflicting and differences in the samples, assessment instruments and methods, follow-up times, and statistical analyses did not make it possible to draw firm conclusions about child characteristics contributing to asthma onset.

The fact that Alati et al. failed to find any correlations between internalizing psychological problems in the child and the onset of asthma is somewhat remarkable, in view of the fact that in their large meta-analysis McQuaid et al. concluded that children with asthma had in particular more internalizing than externalizing disorders [15,5]. A possible explanation could be that children who already suffer from asthma are at risk regarding the subsequent development of internalizing problems. Two other smaller studies concluded that externalizing problems preceded the onset of wheezing.

There was some evidence that child-specific psychological characteristics contributed to an unfavorable course of the asthma over time. Two studies found that the combination of current high chronic stress and acute stress correlated positively with the subsequent increased production of immune markers and risk of new asthma attacks [22,19]. Another study found that children with more psychological problems (internalizing as well as externalizing problems) had more days of wheezing and a lower
general functional status in the following nine months. However, they also reported that the number of hospitalizations was lower with these children than with their untroubled peers, while the number of unscheduled health visits was similar [24]. Differences in measurements of psychological characteristics and asthma course made it impossible to draw a firm overall conclusion.

The results for the onset of childhood asthma in relation to the psychological characteristics of the child's caregiver were more unambiguous: except for one study that investigated three caregiver aspects [11], all other studies found significant, positive correlations. The caregiver's self-reported stress and psychological problems appeared to be associated with a higher risk of asthma onset both in healthy children with a positive family history of asthma and in an overall healthy cohort [12,17,18,20,21,25,26]. In contrast, when Calam et al. tried to find associations between parental psychological problems and subsequent parent-reported onset of wheezing, they found none [11].

With regard to caregiver characteristics and the course of childhood asthma, three studies demonstrated that in children with asthma or children at risk of atopy, the caregiver's psychological problems and stress were associated with a higher risk of a less favorable course over time, as reflected in the higher number of emergency department visits [16] and elevated inflammatory and immunological markers in the children's peripheral blood [13]. Surprisingly, Well et al. found that, apart from more hospitalizations, the children of caregivers with psychological problems did not have more unscheduled health visits, days of wheezing or lower general functional status than the children with 'healthy' caregivers [24]. It was impossible to draw a firm, general conclusion again, because of major differences in study designs, psychological instruments, children's ages, follow-up times, controlled covariates, and data analyses the various studies addressing caregiver involvement. In particular the fact that the assessed psychological characteristics differed completely (in nature, focus, and time period), made it impossible to gain insight into which psychological characteristics are more or less important in this complex but intriguing interaction between asthma and psychology.

Our review once more shows that asthma is a complex disease of multifactorial etiology, subject to a wide range of genetic and environmental influences (both biological and psychological), and interactions between these factors.

4.1.1. Strengths and weaknesses

To our knowledge this is the first systematic review to specifically evaluate the available evidence of longitudinal relationships between the psychological characteristics of healthy and asthmatic children and adolescents, and their parents or caregivers and the onset and course of childhood asthma. However, given the nature of reviews, a positive publication bias that may have affected our conclusions cannot be excluded.

Another point of concern is a methodological one: nearly all the studies we reviewed exclusively derived their information from self-report subjective questionnaires. This implies that the psychological problems of parents or caregivers may have affected their perceptions of illness and symptoms in the child in their care as well as their expectations concerning the child's health, almost certainly in cases where the child was at risk of developing atopy or asthma. This does not only apply to the questionnaires inquiring about their own psychological characteristics and those of the children, but also to their interpretations of respiratory symptoms and diagnoses of asthma. In order to overcome this problem, a recent review by Everhart et al. suggests that researchers should consider using an informant other than the child's parent when other parent-report measures are used in their studies [40]. Moreover, our review of the available results was hampered by the substantial differences in study designs and parameters. This obviously prevented us from basing a theoretical model on the likely underlying mechanisms, i.e. on how and especially which psychological characteristics interfere with the onset and course of childhood asthma. This means that we presently cannot answer the question whether we have to focus more on psychological problems (such as anxiety or depression) or on perceived stress. Because of the inconsistent reporting of statistics (and the many differences in designs, sample sizes, and parameters) in most included studies, we were not able to define effect sizes in an accurate way. For future reviews it would be useful to consider effect sizes and confidence intervals to strengthen methodological rigor and gain more knowledge of the magnitude of relationships between psychological characteristics and asthma outcome.

Finally, our evaluation was one-sided, although we believe that there is a reciprocal, bidirectional relationship between psychological characteristics and asthma. In order to gain more knowledge of this complex interaction, it is therefore important that future research broadens its scope in both directions and considers the interrelationships between the child's features and those of its parents or immediate caregivers in one design.

4.1.2. Research recommendations

Following the first research recommendations mentioned above, we believe future research should take the following points into consideration. First of all, asthma outcome should be optimized by including physicians' diagnoses of asthma (preferably on the basis of international guidelines). Secondly, reliable and validated self-report instruments to monitor asthma control and asthma-related quality of life should be used with records kept by both the caregiver and the child. Thirdly, a wide variety of medical parameters should be assessed (medication, unscheduled health, emergency department visits, hospitalizations, lung function tests, fractional exhaled nitric oxide or other inflammatory markers, and airway hyperresponsiveness). In addition, the psychological characteristics of children as well as of caregivers should be assessed through standardized, validated instruments in sufficiently large samples composed of patients of varying ages. The psychological characteristics of the caregivers should be clearly subdivided into different concepts such as anxiety versus depression and exposure to stress (acute versus chronic). In children it seems important to differentiate between internalizing and externalizing problems. Follow-up periods should be prolonged to allow children to be monitored from birth into adolescence. The interaction between genetic, biological and psychological features should be investigated in closer detail in order to gain a greater insight into this complex disease. Finally, associations between psychological characteristics and asthma merit reciprocal and bidirectional scrutiny.

We expect that such sophisticated investigations into childhood asthma will enhance our understanding of the complex interrelationship between the psychological characteristics of children and their caregiver(s) and the onset and course of asthma. Ultimately this will help us to improve holistic interventions to reduce the burden of asthma and improve the quality of life of families who have children with asthma.

4.2. Conclusion

The reviewed studies strongly suggest that various psychological problems in children and their caregivers have an effect on the course of childhood asthma, perceived asthmatic symptoms, objective markers of atopy and inflammation, and, possibly, also on the onset of asthma.
4.3. Practice implications

Since the underlying mechanisms are unknown as yet and require additional research, no practical implications or recommendations can be given at this moment.

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Conflict of interest

We have no conflict of interest.

References


