

Patients With Adrenal Insufficiency Hate Their Medication: Concerns and Stronger Beliefs About the Necessity of Hydrocortisone Intake Are Associated With More Negative Illness Perceptions

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Context: Patients with adrenal insufficiency (AI) require daily and life-long hydrocortisone substitution with risks of under- and overreplacement, the necessity to adjust the dose in stressful situations, and a lack of clinical and biochemical parameters to assess optimal dosing. The spectrum of medication beliefs in patients with AI is currently unknown.

Objective: The objective of the study was to examine the possible association between illness perceptions and medication beliefs about hydrocortisone (HC) in patients with AI.

Design and Subjects: This was a cross-sectional evaluation of illness perceptions and medication beliefs in 107 patients with primary AI ($n = 49$), secondary AI after the treatment of Cushing's syndrome ($n = 29$), or treatment of nonfunctioning pituitary adenoma ($n = 29$). The Illness Perception Questionnaire-Revised and the Beliefs about Medicines Questionnaire were used for the assessment.

Results: Stronger beliefs about the necessity of HC and stronger concerns about the adverse effects of HC were associated with attribution of more symptoms to AI, to the perception of AI being more cyclical, to the perception of more negative consequences of AI, and to the presence of stronger emotional representations (all $P < .05$). Furthermore, stronger beliefs about the necessity of HC intake were associated with feelings of less personal control over AI ($P < .05$). Stronger concerns about the adverse effects of HC were associated with lower perceived treatment control and lower illness coherence (both $P < .05$). In addition, patients with Cushing's syndrome reported stronger beliefs regarding the necessity of taking HC, compared with patients with Addison's disease ($P = .039$) or nonfunctioning pituitary adenoma ($P < .001$).

Conclusion: Specific beliefs about the necessity of hydrocortisone replacement and concerns about its adverse effects were strongly associated with more negative illness perceptions. These specific beliefs differed, depending on the etiology of AI. These results need to be taken into account in the treatment of patients with AI and may serve to enable the development of psychosocial education/self-management programs aiming at improving quality of life. (*J Clin Endocrinol Metab* 99: 3668–3676, 2014)

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Abbreviations: AI, adrenal insufficiency; BMQ, Beliefs about Medicines Questionnaire; CSM, Common-Sense Model of self-regulation; HC, hydrocortisone; IPQ-R, Illness Perception Questionnaire-Revised; NFA, nonfunctioning pituitary adenoma; QoL, quality of life.

Patients with adrenal insufficiency (AI) require daily and life-long substitution with hydrocortisone (HC). AI can be caused by adrenal diseases, usually due to autoimmunity or bilateral adrenalectomy for other causes (primary adrenal insufficiency) or by (hypothalamo) pituitary disease due to pituitary tumors or their treatment (secondary adrenal insufficiency). Patients with AI report impairments in quality of life (QoL), with persistent physical and psychological complaints (1, 2), which have been attributed, at least in part, to intrinsic imperfections of hormone replacement therapy (3). The conventional HC replacement dose currently is approximately 20 mg/d, divided into three doses (10 mg in the morning, 5 mg in the afternoon, and 5 mg in the evening) to mimic to some extent the natural circadian profile of plasma cortisol levels. In case of stressful situations, like fever or stressful life events, the dose needs to be adjusted for the increased demand. There are evident risks of under- and overreplacement, ie, acute Addisonian crises on the one hand and weight gain and steroid induced osteoporosis on the other hand. Although some practical guidelines are available, individual variations in HC demands are large and optimal timing is crucial, whereas there are no reliable and sensitive biochemical parameters for a delicate substitution strategy. In view of the chronic character of AI and the life-long requirement of HC, patients need to develop and maintain self-management strategies directed toward optimal management of their HC intake and coping behavior.

A valuable model that specifies determinants of self-management behavior is the Common-Sense Model of self-regulation (CSM) (4). This model describes how individuals come to understand their illness and how they

develop strategies to manage their illness. The model comprises three stages. Stage 1 is the identification of illness perceptions. These perceptions can be organized into five categories: identity, cause, time line, consequences, and cure/control. In the second stage, these illness perceptions determine coping strategies; the third stage comprises the appraisal of these coping strategies. In an extended CSM, beliefs about medicines are included, and it was demonstrated in patients with asthma that illness perceptions are correlated with beliefs about medicines (5). Furthermore, beliefs about medicines have been found to be predictive of medication adherence (6, 7), an important aspect of self-management behavior.

Beliefs about medicines are mostly assessed with the Beliefs about Medicines Questionnaire (BMQ) (8). The BMQ focuses on beliefs about necessity and concerns of taking a specific medicine. Furthermore, it focuses on the beliefs about the use of medicines in general, such as whether medication use is harmful and whether it is overused. See Table 1 for an overview of the psychological constructs mentioned above.

The aim of the present study was to explore possible associations between illness perceptions and medication beliefs about HC in patients with AI treated with HC replacement therapy. In accordance with previous studies, we hypothesized that illness perceptions are correlated with medication beliefs. Furthermore, we aimed to examine potential differences in beliefs about HC replacement therapy in patients with AI, due to Addison's disease, Cushing's syndrome, or nonfunctioning pituitary adenoma (NFA). The authors of the BMQ stated that the BMQ-specific subscale could discriminate between patients with different diagnoses (6). AI-

Table 1. Psychological Constructs

Psychological Construct	Explanation
Self-management behavior	The individual's ability to manage the symptoms, treatment, physical and psychosocial consequences, and lifestyle changes inherent in living with a chronic condition. Efficacious self-management encompasses the ability to monitor one's condition and to affect the cognitive, behavioral, and emotional responses necessary to maintain a satisfactory quality of life (26).
CSM of self-regulation	This model describes how individuals come to understand their illness and how they develop strategies to manage their illness. The model comprises three stages. Stage 1 is the identification of illness perceptions. These perceptions can be organized into five categories: identity, cause, time line, consequences, and cure/control. In the second stage, these illness perceptions determine coping strategies; the third stage comprises the appraisal of these coping strategies.
Extended CSM	In the extended CSM, beliefs about medicines are included.
Illness perceptions	The cognitive and emotional representations/perceptions of illness. These perceptions can be organized into five categories: identity, cause, time line, consequences, and cure/control.
IP: identity	The label used by patients to describe their illness
IP: cause	The perceived cause(s) of the illness
IP: time line	The perceived duration of the illness (acute vs chronic illness, and cyclical vs stable illness)
IP: consequences	Perceived negative consequences of the illness
IP: cure/control	The perceived degree to which the illness can be cured or controlled
Coping strategies	The way someone reacts to and deals with problems/situations
Beliefs about medicine	Beliefs about the necessity and concerns of taking a specific medicine

Abbreviation: IP, illness perception.

though AI is due to different causes in our cohort (Cushing's syndrome, Addison's disease, NFA), all patients were diagnosed with AI and were treated with HC replacement therapy. Therefore, we hypothesized that patients would not differ on the specific subscales of the BMQ. Providing information about the medication beliefs of patients treated with HC and the possible correlation with illness perceptions can be helpful for the development of a self-management intervention, aiming to improve QoL.

Patients and Methods

Design

A cross-sectional study was conducted in which patients with AI treated at our center were invited to fill out questionnaires on medication beliefs and illness perceptions. Patients were asked to complete the questionnaires at home and return these in a pre-paid envelope. Inclusion criteria were adult patients (aged > 18 y) and treatment for AI. The institutional Medical Ethics Committee approved the protocol.

Patients

Patients with AI were invited to participate in the current study. These patients received hydrocortisone replacement either for Addison's disease (n = 49) or after treatment for Cushing's syndrome (n = 29) or nonfunctioning pituitary adenomas (n = 29).

Cushing's syndrome

A clinical chart review of 77 patients who had been treated by transsphenoidal or adrenal surgery, if necessary, followed by repeated surgery and/or postoperative radiotherapy, was performed. Nine patients refused to participate for several reasons including old age and/or debilitating disease. For the present analysis, we included only patients with AI. Twenty-nine patients with AI participated in the current study and completed the questionnaires.

Addison's disease

Patients with Addison's disease (ie, primary adrenal insufficiency) were recruited via the outpatient clinic of the Department Endocrinology of the Leiden University Medical Centre and via the Dutch Adrenal Patient Society for Addison and Cushing Patients. The Dutch Adrenal Patient Society for Addison and Cushing Patients approached their own members; therefore, the actual number of patients invited in this study is unknown. A total of 49 patients participated in the current study and completed the questionnaires.

Nonfunctioning pituitary adenoma

A clinical chart review of 100 patients treated for NFA was performed. Twenty-five patients refused to participate, and for the present study, we included only patients with AI. Twenty-nine patients with NFA participated in the current study and completed all the questionnaires.

Treatment and follow-up

Cushing's syndrome

These patients had been diagnosed based on internationally agreed guidelines, ie, the clinical manifestations and positive biochemical tests including increased urinary excretion rates of free cortisol, decreased overnight suppression by dexamethasone (1 mg) and, since 2004, elevated midnight salivary cortisol values in addition to nonsuppressed ACTH levels. All patients had been treated by transsphenoidal or adrenal surgery, if necessary, followed by repeated surgery and/or postoperative radiotherapy. Cure was defined by normal overnight suppression of plasma cortisol levels (<50 nmol/L) after administration of dexamethasone (1 mg) and normal 24-hour urinary excretion rates of cortisol (<220 nmol per 24 h). Adrenal insufficiency was diagnosed when cortisol responses to CRH or insulin tolerance test were below the reference range of normal. At the time of the current study, all patients were in remission.

Addison's disease

Addison's disease had been diagnosed based on the classical clinical symptoms and biochemical confirmation of adrenal insufficiency in the presence of increased ACTH concentrations. Adrenal insufficiency was diagnosed when cortisol concentrations were below the reference range of normal with or without stimulation with ACTH. Thirty-nine patients (80%) were diagnosed with Addison's disease due to an autoimmune disease, five patients (10%) were diagnosed with Addison's disease due to nonautoimmune causes, and two patients (4%) were treated with bilateral adrenalectomy.

Nonfunctioning pituitary adenoma

Patients after surgical treatment for NFA, which was histopathologically confirmed, were included. Surgical treatment was performed in case of visual field defects in most patients. Postoperatively, magnetic resonance imaging scans were performed to detect tumor recurrence or regrowth. In case of progression, patients were either referred for radiotherapy or an expectative management was chosen. Adrenal insufficiency was diagnosed when postsurgical cortisol responses to CRH or insulin tolerance test were below the reference range of normal. At the time of the current study, all patients were free of recurrence.

Clinical follow-up

Patients were followed up at our outpatient department. Patients were monitored for (recurrence of) disease, according to appropriate dynamic tests in patients with Cushing's syndrome and magnetic resonance imaging scans in patients with nonfunctioning adenoma. In patients with pituitary diseases, pituitary function was monitored and pituitary hormone replacement was prescribed dependent on the results of the yearly evaluation of pituitary functions. The average dose of hydrocortisone was 20 mg/d divided into two to three dosages. Evaluation of GH deficiency was performed by insulin tolerance test and/or GHRH-arginine test, only in patients under the age of 70 years and only after at least 2 years of remission. In case of severe GH deficiency, treatment with recombinant human GH replacement was initiated, and the dose was titrated upon an IGF-1 concentration in the normal range for age. In addition, free T₄ and testosterone (T) levels (in male patients) were assessed. If results were below the

lower limit of the respective reference ranges, substitution with levothyroxine and/or T was prescribed. In case of amenorrhea and low estradiol levels in premenopausal women, estrogen replacement was provided. Patients with primary AI were treated with a combination of HC and mineralocorticoids. Concomitant hypothyroidism was treated with levothyroxine.

Methods

Beliefs about Medicine Questionnaire

The BMQ aims to assess cognitive and emotional representations of medication and comprises two sections (ie, BMQ Specific, BMQ General), each divided into two subscales. All subscales are described in detail in Table 2.

Illness Perception Questionnaire-Revised (IPQ-R)

The Illness Perception Questionnaire-Revised (IPQ-R) was used to measure cognitive and emotional representations of illness. The questionnaire was developed to assess the components of the illness representation of Leventhal's CSM and is frequently

used to study illness perceptions in chronic conditions (9–13). The IPQ-R is divided into three sections. These three sections are described in detail in Table 2.

Statistical analysis

Data were analyzed using PASW Statistics version 20 (SPSS Inc). All data were presented as mean \pm SD, unless mentioned otherwise. The primary analysis comprised the relationship between medication beliefs and illness perceptions. Partial correlation coefficients were calculated, correcting for the type of disease. Because of the exploratory nature of this primary analysis, adjustment of the level of significance for multiple testing was not performed, and the level of significance was set at $P \leq .05$.

The secondary analysis comprised a comparison of medication beliefs between the different patient groups (ie, Cushing's syndrome, Addison's disease, and NFA), using an ANOVA with a post hoc Bonferroni correction. To check the normality of data, the Kolmogorov-Smirnov test was used in addition to histograms and box plots. The level of significance was set at $P \leq .05$.

Table 2. Questionnaires: Purpose and Detailed Explanation

Questionnaire	Purpose and Detailed Explanation
BMQ	<p>The BMQ aims to assess cognitive and emotional representations of medication and comprises two sections (ie, BMQ specific, BMQ general), each divided into two subscales.</p> <ol style="list-style-type: none"> 1) The BMQ specific comprises two subscales assessing representations of medication prescribed for personal use: the specific-necessity subscale, which is focusing on the necessity of taking medications to remain healthy (ie, "My life would be impossible without my hydrocortisone"), and the specific concerns subscale, focusing on concerns about the adverse effects of taking medications (ie, "I sometimes worry about the long term effects of my hydrocortisone"). 2) The BMQ general comprises two 4-item subscales assessing beliefs about medicines in general: the general overuse subscale assesses beliefs that medicines are overprescribed (ie, "Doctors use too many medicines"), and the general harm subscale assesses beliefs about medicines as harmful, addictive, or poisonous (ie, "Medicines do more harm than good"). <p>All items were rated on a 5-point Likert scale ranging from 1 (strongly agree) to 5 (strongly disagree). The specific necessity subscale score ranged from 5 to 25 (midpoint = 15), the specific concerns subscale score ranged from 6 to 30 (midpoint = 18), and both general subscales scores ranged from 4 to 20. Higher scores indicate stronger beliefs. Among general medical patients, the Cronbach's α ranged from .51 to .86 (8).</p> <p>A differential score was calculated by subtracting the patient's concerns scores from the patient's necessity scores, leading to a range from -20 to 20 (6, 27).</p> <p>Higher scores on this differential indicate higher perceived necessity for the use of HC, relative to concerns about the use of HC.</p>
IPQ-R	<p>To measure cognitive and emotional representations of illness. The IPQ-R is divided into three sections.</p> <ol style="list-style-type: none"> 1) Illness identity dimension: a list of 14 general commonly occurring symptoms. These symptoms include pain, sore throat, nausea, breathlessness, weight loss, fatigue, stiff joints, sore eyes, wheeziness, headaches, upset stomach, sleep difficulties, dizziness, and loss of strength. Patients are asked to rate whether they experienced the symptoms and whether they believe the symptom to be related to their illness (yes/no). The summed yes-rated items of the disease-related symptoms are used in the analysis. 2) Illness perception dimensions: consists of 38 statements concerning views on the illness, scored on a 5-point Likert scale (from strongly disagree to strongly agree). The questions are transformed to seven dimensions: time line acute/chronic, time line cyclical, consequences, personal control, treatment control, emotional representations (the emotional responses generated by the illness, for example, getting upset or depressed when thinking about the illness or feeling angry, afraid, or anxious), and illness coherence. A higher score indicates a stronger belief in that particular dimension. 3) Causal attributions: this part of the questionnaire was not used in the analysis in the present study.

Table 3. Clinical Characteristics of Patients After Long-Term Remission of Cushing's Syndrome

	Cushing's Syndrome (n = 29)
Gender, male/female	5/24
Age, y	53.59 (10.4)
Education, n	Low: 11 Medium: 9 High: 8 Unknown: 1
Pituitary adenoma, n, %	25 (86%)
Adrenal adenoma/carcinoma, n, %	4 (14%)
Transsphenoidal surgery, n, %	21 (72%)
Adrenal surgery, n, %	14 (50%)
Additional radiotherapy, n, %	10 (35%)
Duration of follow-up, y	18.38 (13.1), range 3–46
Hypopituitarism, n, %	GH: 21 (72%) LH/FSH: 13 (45%) TSH: 17 (59%)

Data are mean (SD) or number and percentage unless otherwise stated.

Results

Sociodemographic and clinical characteristics (Tables 3, 4, and 5)

Patients in remission of Cushing's syndrome

Sociodemographic and clinical characteristics are detailed in Table 3. A total of 29 patients in long-term remission of Cushing's syndrome were included. Eighty-six percent had been treated for ACTH producing pituitary adenomas, whereas 14% had been treated for cortisol producing adrenal adenomas. Seventy-two percent of the patients had been treated by transsphenoidal surgery, 50% by adrenalectomy, and 35% by additional radiotherapy. At the time of the current study, 72% of the patients were diagnosed with GH deficiency, 45% with LH/FSH deficiency, and 59% with TSH deficiency. The mean follow-up duration was 18 ± 13 years (range 3–46 y).

Patients with stable Addison's disease

A total of 49 patients with stable Addison's disease were included. All patients were on stable hydrocortisone and fludrocortisone replacement therapy for a mean duration of 9.60 ± 8.4 years (range 2–38 y). Eighty-two percent of the patients also used fludrocortisone in addition to hydrocortisone. Additional medical therapy included dehydroepiandrosterone (29% of patients), levothyroxine (45%), and antihypertensive agents (12%). The characteristics are displayed in Table 4.

Patients treated for NFA

Clinical and sociodemographic characteristics regarding patients treated for NFA are detailed in Table 5. A total of 29 patients were included in the present study. All patients had been treated by transsphenoidal surgery, and

Table 4. Clinical Characteristics of Patients With Stable Addison's Disease

	Addison's Disease (n = 49)
Gender, male/female	18/31
Age, y	49.02 (11.9)
Education, n	Low: 10 (20%) Medium: 17 (35%) High: 22 (45%)
PAI diagnosis	Autoimmune: 39 (80%) Nonautoimmune: 5 (10%) Bilateral adrenalectomy: 2 (4%) Unknown: 3 (6%)
Disease duration, y	9.60 (8.4), range 2–38
Hydrocortisone dose ^a	24.73 (7.4)
Florinef, n, %	40 (82%)
DHEA, n, %	14 (29%)
Levothyroxine, n, %	22 (45%)
Antihypertensives, n, %	6 (12%)

Abbreviations: DHEA, dehydroepiandrosterone; PAI, primary adrenal insufficiency. Data are mean (SD) or number and percentage.

^a Total dose per day.

38% by additional radiotherapy. In addition to adrenal insufficiency, multiple pituitary hormone deficiencies, as expected, were present in almost all patients (97% GH deficiency, 97% LH/FSH deficiency, and 83% TSH deficiency). The mean duration of follow-up was 16.5 ± 10 years (range 4–41 y).

Relationships between illness perceptions and medication beliefs in patients with adrenal insufficiency (Table 6 and Figure 1)

The relationships between beliefs about medicine and illness perceptions were explored for the entire sample of patients with adrenal insufficiency (ie, Cushing's syndrome, Addison's disease, and NFA). Table 7 shows the raw scores on the BMQ and IPQ-R per disease category and for the overall AI sample. The associations between the scores on the IPQ-R and BMQ are listed in Table 6. Specific necessity (ie, the necessity of taking hydrocorti-

Table 5. Clinical Characteristics of Patients After Treatment for NFA

	NFA (n = 29)
Gender, male/female	15/14
Age, y	59.43 (12.6)
Education, n	Low: 5 Medium: 10 High: 13
Transsphenoidal surgery, %	29 (100%)
Additional radiotherapy, %	11 (38%)
Duration of follow-up, y	16.52 (10.3)
Hypopituitarism, %	GH: 28 (97%) LH/FSH: 28 (97%) TSH: 24 (83%)

Data are mean (SD) or number and percentage unless otherwise stated.

Table 6. Partial Correlations (Corrected for Disease Type) Between Medicine Beliefs and Illness Perceptions in Patients With Adrenal Insufficiency

	Specific Necessity	Specific Concerns	General Overuse	General Harm
Illness identity	0.260 ^a	0.351 ^a		
Time line (chronic/acute)				
Time line (cyclical)	0.269 ^a	0.322 ^a		0.294 ^a
Consequences	0.343 ^a	0.224 ^b		
Personal control	−0.225 ^b			
Treatment control		−0.197 ^b		
Emotional representations	0.399 ^a	0.365 ^a		0.272 ^a
Illness coherence		−0.271 ^a		

^a $P < .01$; ^b $P < .05$.

sone to remain healthy) was strongly associated with various illness perception subscales. There was a positive association between specific necessity and illness identity ($r = 0.260$, $P = .007$), cyclical time line ($r = 0.269$, $P = .006$), perceived negative consequences ($r = 0.343$, $P < .01$), and emotional representations ($r = 0.399$, $P < .01$). This indicates that stronger beliefs about the necessity of hydrocortisone to stay healthy are related to attributing more symptoms to adrenal insufficiency, perceiving AI is being more cyclical, perceiving more negative consequences, and having stronger emotional representations. Furthermore, specific necessity was negatively associated with perceived personal control ($r = -0.225$, $P = .021$), indicating that stronger beliefs about the necessity of hydrocortisone are associated with feelings of less personal control over AI.

The subscale specific concerns (ie, concerns about the adverse effects of taking hydrocortisone) was positively associated with illness identity ($r = 0.351$, $P < .01$), cyclical time line ($r = 0.322$, $P = .001$), perceived negative

consequences ($r = 0.224$, $P = .021$), and emotional representations ($r = 0.365$, $P < .01$). This indicates that stronger concerns about the adverse effects of hydrocortisone are related to attributing more symptoms to AI, perceiving AI is being more cyclical, perceiving more negative consequences, and having stronger emotional representations. Specific concerns was negatively associated with perceived treatment control ($r = -0.197$, $P = .044$) and illness coherence ($r = -0.271$, $P = .005$), indicating that stronger concerns about the adverse effects of hydrocortisone are associated with lower perceived treatment control and a lower illness coherence.

The subscale general harm (ie, beliefs about medicines in general being harmful, addictive, or poisonous) was positively associated with cyclical time line ($r = 0.294$, $P = .003$) and emotional representations ($r = 0.272$, $P = .005$), indicating that perceiving AI as being more cyclical and having stronger emotional representations is related to stronger beliefs about the harm of general medication. The subscale general overuse (ie, beliefs that medicines in general are overprescribed) was not associated with illness perceptions.

Beliefs about HC in patients with Cushing's syndrome, Addison's disease, or NFA (Table 7 and Figure 2)

All patients with Cushing's disease (100%) reported the need to use HC (scores below the midpoint on the specific necessity subscale). However, 72% of these patients reported concerns about the use of HC (scores above the midpoint of the specific concerns subscale). All patients with Addison's disease (100%) reported in the necessity of taking HC, and 65% of these patients had concerns about using it. Ninety-three percent of patients with NFA

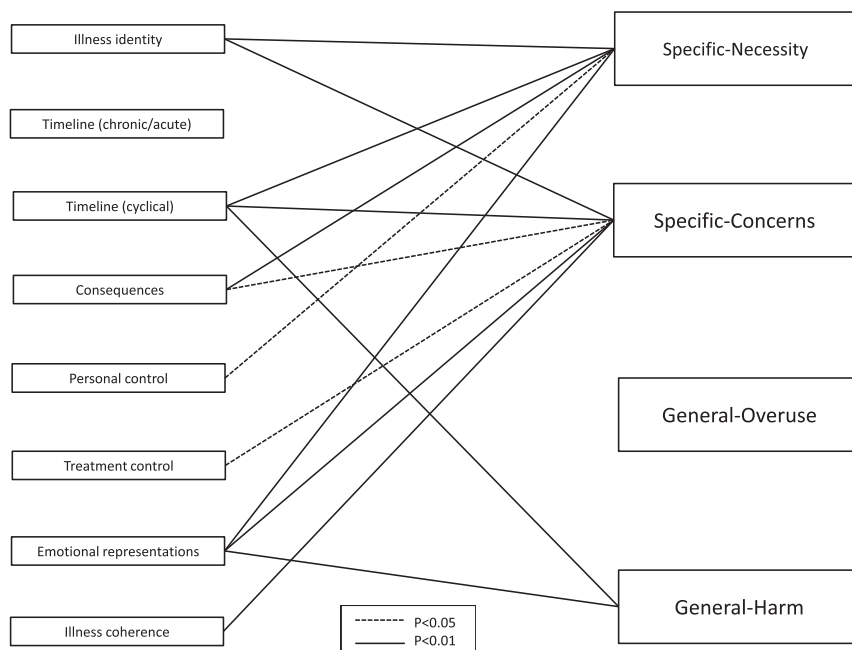


Figure 1. Observed correlations between illness perceptions and medication beliefs.

Table 7. Beliefs About Hydrocortisone and Illness Perceptions in Patients With AI

	Overall Sample of AI Patients (n = 107)	Cushing's Syndrome (n = 29)	Addison's Disease (n = 49)	NFA (n = 29)
BMQ				
Specific necessity	19.62 ± 2.43	20.90 ± 2.45	19.57 ± 2.05 ^a	18.41 ± 2.44 ^a
Specific concerns	18.39 ± 2.89	18.86 ± 3.48	18.25 ± 2.86	18.14 ± 2.28
General overuse	10.07 ± 2.71	9.97 ± 3.00	9.69 ± 2.17	10.79 ± 3.11
General harm	9.21 ± 2.78	9.48 ± 3.49	8.63 ± 2.28	9.90 ± 2.62
Differential (necessity concerns)	1.23 ± 3.03	2.03 ± 3.42	1.32 ± 2.71	0.28 ± 2.97
IPQ-R				
Illness identity	3.53 ± 3.02	4.59 ± 3.00	3.41 ± 2.97	2.64 ± 2.92
Time line (chronic/acute)	27.33 ± 3.27	26.57 ± 3.98	27.90 ± 2.72	27.10 ± 3.34
Time line (cyclical)	11.09 ± 4.08	13.10 ± 3.84	10.92 ± 4.16	9.29 ± 3.30
Consequences	18.58 ± 5.45	21.95 ± 4.82	17.73 ± 5.17	16.56 ± 5.13
Personal control	17.89 ± 5.36	16.64 ± 6.43	19.04 ± 4.57	17.18 ± 5.22
Treatment control	16.47 ± 3.88	16.59 ± 5.05	15.67 ± 3.50	17.75 ± 2.72
Emotional representations	13.45 ± 4.41	15.52 ± 5.46	12.86 ± 3.46	12.35 ± 4.13
Illness coherence	17.33 ± 2.75	17.07 ± 3.20	17.35 ± 2.60	17.57 ± 2.57

Raw scores per disease are also listed. Data are mean ± SD. Defined range per subscale on the BMQ are as follows: specific necessity (range 5–25), specific concerns (range 6–30), general overuse (range 4–20), and general harm (range 4–20). Defined range per subscale on the IPQ-R are as follows: illness identity (range 0–14), time line chronic/acute (range 6–30), time line cyclical (range 4–20), consequences (range 6–30), personal control (range 6–30), treatment control (range 5–25), emotional representations (range 6–30), and illness coherence (range 5–25).

^a Significantly different compared with Cushing's syndrome.

reported no doubts about the necessity of using hydrocortisone, but 66% of these patients reported that they did have concerns about using HC.

Comparing patients with Cushing's syndrome, Addison's disease, and NFA on the several subscales of the BMQ-specific, patients with Cushing's syndrome reported significantly stronger beliefs regarding the necessity of taking HC to remain healthy, compared with patients with Addison's disease or NFA ($P = .039$ and $P < .001$, respectively). Patients with Addison's disease and patients with NFA did not significantly differ on the specific necessity subscale. Furthermore, there were no significant differences on the differential score and the gen-

eral subscales of the BMQ between patients with Cushing's syndrome, Addison's disease, or NFA.

Discussion

The present study in patients with AI demonstrates that illness perceptions are associated with medicine beliefs. Stronger beliefs about the necessity of hydrocortisone replacement to stay healthy and stronger or more concerns about the adverse effects of hydrocortisone were related to attributing more symptoms to AI, perceiving AI as being more cyclical (ie, patients perceived AI as being unpredictable with symptoms coming and going in cycles), perceiving more negative consequences of AI, and having stronger emotional representations (ie, patients reported feeling angry, worried, anxious, and afraid when thinking about AI). Stronger beliefs about the necessity of HC were associated with feelings of less personal control over AI. Furthermore, patients who mistrust their HC reported more negative perceptions about their AI because stronger concerns about the adverse effects of HC were associated with lower perceived treatment control (ie, patients perceived a lower degree to which AI can be controlled by HC) and lower illness coherence (ie, having a less

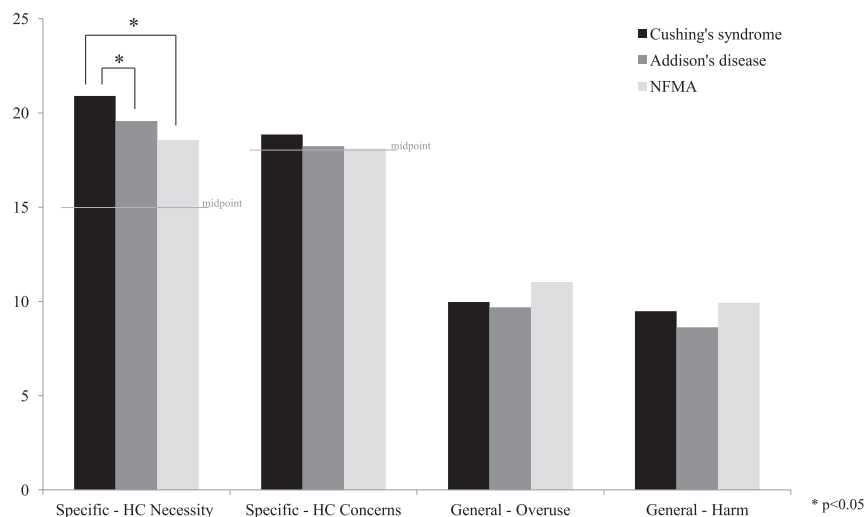


Figure 2. The scores on the subscales of the BMQ for the 3 different patient groups with AI. The midpoints were calculated for the first two subscales, as recommended by the creators of the questionnaire.

erally, patients with AI perceived AI as being unpredictable with symptoms coming and going in cycles), perceiving more negative consequences of AI, and having stronger emotional representations (ie, patients reported feeling angry, worried, anxious, and afraid when thinking about AI). Stronger beliefs about the necessity of HC were associated with feelings of less personal control over AI. Furthermore, patients who mistrust their HC reported more negative perceptions about their AI because stronger concerns about the adverse effects of HC were associated with lower perceived treatment control (ie, patients perceived a lower degree to which AI can be controlled by HC) and lower illness coherence (ie, having a less

clear understanding of AI). Perceiving AI as being more cyclical and having stronger emotional representations were related to stronger beliefs about the harm of general medication but not to beliefs that medicines in general are overprescribed. The results of the present study, together with results published earlier about focus group interviews with this patient population (14), revealed that patients with AI hate their medication. Patients who mistrust their HC also report more negative perceptions about their AI. This study supports the extended CSM, which has been instrumental in inspiring research that shows how illness perceptions are correlated with medication beliefs in patients with various chronic somatic disorders (eg, reference 4).

The present study also demonstrates that different beliefs about HC are present in patients with adrenal insufficiency, dependent on the cause of adrenal insufficiency. Patients with Cushing's syndrome, Addison's disease, or NFA differ significantly on beliefs about the necessity of HC use, with patients with Cushing's syndrome reporting the strongest beliefs regarding necessity of hydrocortisone intake and patients with NFA the weakest beliefs. As suggested by the developers of the BMQ, such differences between groups could be explained by the difference in diagnosis, type of treatment, and perceived adverse side effects of treatment (6). Considering the fact that all patients were treated with HC tablets, we postulate that this difference in necessity beliefs might be explained by differences in etiology of AI and/or by differences in perceived adverse side effects of treatment between the 3 patient groups. Patients in remission of Cushing's syndrome reported more negative illness perceptions compared with the other patient groups. However, because this was a cross-sectional study, we were not able to assess what caused this difference in illness perceptions and medicine beliefs. Future studies might want to explore this interesting finding further.

A possible limitation of the present study is the fact that we cannot exclude the possibility that the most distressed patients were more likely to participate, which might skew the results. However, this is an explorative study aiming to investigate the possible association between illness perceptions and medication beliefs about HC in patients with AI. We believe that the present results give a good first overview of how patients think and feel about their medication. Another possible limitation is the lack of data on cortisol levels (eg, morning levels prior to HC) and adherence to HC. Future studies should include those measures to further explore the potential association between those factors and medicine beliefs.

Our findings are in accordance with the extended CSM of Horne and Weinman (5) and previous studies in patients with chronic diseases demonstrating illness perceptions to

be associated with treatment beliefs (15, 16). Furthermore, in the extended CSM, medication beliefs are strongly correlated with self-reported adherence (ie, self-management), and this relationship was also demonstrated by previous studies in patients with chronic diseases (eg, type 2 diabetes, heart failure) (17–21). Considering the chronic nature of AI, patients with AI also need to develop and maintain self-management behavior. The results of the present study provide new insights into potential modifiable contributing factors to optimize self-management behavior in patients with adrenal insufficiency. Future research should further investigate the relationship between treatment beliefs, illness perceptions, and self-management behavior (eg, adherence) in patients with AI. Previously we demonstrated a significant association between illness perceptions and QoL in patients with pituitary diseases and suggested that addressing and adapting these illness perceptions in a psychosocial intervention could improve QoL (22, 23). In addition, a qualitative focus group study in patients with pituitary diseases was performed at our department. Patients reported concerns about medication, among which HC was included. It was postulated that negative medication beliefs might be a potential contributing factor of impairments in QoL (14). Furthermore, Petrie et al (24) demonstrated that modifying illness perceptions and treatment beliefs improves adherence to preventer medication in patients with asthma.

Considering the results of these studies, the theory of the adapted CSM, and our present findings, we speculate that adapting beliefs about medicines in addition to illness perceptions will positively affect self-management behavior and QoL. Furthermore, awareness of the observed beliefs about hydrocortisone use could be helpful in clinical practice for endocrinologist in their communication with and provision of information to patients. Specifically, we hope our findings will make endocrinologists more aware of the psychological impact and consequences of AI and its required treatment with HC. When endocrinologists are more aware of the potential struggles of patients, particularly with regard to medication beliefs and their perception about their illness, endocrinologists would be better able to assess those perceptions. Based on a recent literature review on adherence (25), we propose a multiphase approach to facilitate optimal medication and illness beliefs, which will lead the way to optimal medication adherence. First, endocrinologists should give patients a clear rationale for their HC. Based on the findings in the present study, we believe that patients understand the necessity of taking HC. Second, endocrinologists should assess and address patients' concerns regarding their HC use. Some of those concerns might be addressed by reassurance and/or providing more information. However, it

might be necessary to refer patients to a medical psychologist when the endocrinologist and/or the patient feels that that might be a better approach. A medical psychologist can assist patients to adapt inadequate cognitions to develop effective self-management strategies. Lastly, endocrinologists should support patients in the correct and persistent use of HC by assessing the barriers patients might perceive regarding their HC use. Ultimately, this multiphase approach and the possible cooperation with a medical psychologist in this approach will lead the way to better medication beliefs, more positive illness perceptions, better self-management strategies, and therefore improved QoL.

In summary, patients with AI demonstrated disease-specific differences in the beliefs about the necessity of HC intake. Specific beliefs about the necessity of HC and concerns about its adverse effects were strongly associated with more negative illness perceptions. The result obtained from this study can be used for the improvement of discussing patient views about HC use and for the adaptation of a self-management intervention aiming to improve QoL in patients treated with HC replacement.

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