



More concerns and stronger beliefs about the necessity of medication in patients with acromegaly are associated with negative illness perceptions and impairment in quality of life[☆]



Cornelie D. Andela^a, Nienke R. Biermasz^a, Adrian A. Kaptein^b, Alberto M. Pereira^a, Jitske Tiemensma^{a,c,*}

^a Department of Medicine, Division of Endocrinology and Center for Endocrine Tumors Leiden (CETL), Leiden University Medical Center, Leiden, The Netherlands

^b Department of Medical Psychology, Leiden University Medical Center, Leiden, The Netherlands

^c Psychological Science, University of California, Merced, CA, United States

ARTICLE INFO

Article history:

Received 27 March 2015

Received in revised form 10 June 2015

Accepted 24 June 2015

Available online 2 July 2015

Keywords:

Acromegaly
Growth hormone
Illness perceptions
Medication beliefs
Somatostatin analogs
Quality of life

ABSTRACT

Objective: Patients with acromegaly can be treated with surgery, radiotherapy and/or medical treatment. In general, patients' beliefs about medication are associated with illness perceptions, a contributory factor of Quality of Life (QoL). At present, there are no quantitative studies on medication beliefs in patients with acromegaly. Here, we aimed to examine possible associations between medication beliefs, illness perceptions, and QoL. Furthermore we aimed to explore whether illness perceptions of patients with remission of acromegaly receiving medical treatment differ from patients without medical treatment.

Design: Cross-sectional evaluation of 73 patients with remission of acromegaly (n = 28 patients with medication, n = 45 without medication). The Beliefs about Medicines Questionnaire (BMQ), Illness Perception Questionnaire-Revised (IPQ-R), EuroQoL-5D, and AcroQoL were used for the assessment.

Results: Stronger beliefs about the necessity of medical treatment and stronger concerns about the adverse effects were associated with attributing more symptoms to acromegaly, perceiving more negative consequences, and having a stronger belief in a cyclical timeline (BMQ, all P < 0.05). Stronger beliefs about the necessity of medical treatment were associated with a worse disease-specific QoL (BMQ, P < 0.01). Patients with medical treatment perceived a more chronic timeline of their disease, compared to patients without medical treatment (IPQ-R, P = 0.002).

Conclusion: Negative medication beliefs were related to more negative illness perceptions and worse disease-specific QoL. Patients receiving medical treatment for acromegaly tend to perceive a more chronic timeline of their disease, compared to patients with remission without medical treatment. These psychological factors need to be taken into account when treating patients and developing a psychosocial education program aiming to improve QoL.

© 2015 Elsevier Ltd. All rights reserved.

1. Introduction

Acromegaly is characterized by exposure to elevated growth hormone (GH) levels, most frequently due to a GH-producing pituitary adenoma. Patients are usually treated with transsphenoidal surgery and sometimes by additional radiotherapy. When this treatment is not (completely) successful, or when surgery and/or radiotherapy is not preferred, patients can be medically treated with somatostatin analogs (SA) (e.g. Octreotide, Lanreotide) and/or a GH receptor antagonist

(e.g. Pegvisomant). Patients with acromegaly report impairments in Quality of Life (QoL) [1,2], which may persist even after long-term remission [3,4]. These persistent impairments have been (partly) attributed to comorbidities, such as osteoarthritis [5], musculoskeletal pain [6–8], and psychopathology [9]. Besides physical factors, Tiemensma et al. elucidated psychological factors (i.e. negative illness perceptions) which were related to QoL impairments in patients after long-term remission of acromegaly [10].

Recently Gurel et al. carried out structured interviews that explored patients' perceived impact of acromegaly. These interviews revealed that patients did not feel "cured" after treatment, particularly when patients realized they had to take medication for the rest of their life. The use of medication resulted in confusion between being a patient and being a person. Furthermore, patients had to make specific injection schedules to plan their medication around work, travel, and big events, in order to minimize the negative influence of side-effects on everyday

[☆] Précis: Patients with acromegaly report concerns and strong beliefs about the necessity of medication, which are related to more negative illness perceptions and impaired QoL.

* Corresponding author at: University of California, Merced, SSHA, Psychological Science, 5200 North Lake Road, Merced, CA 95343, United States.

E-mail address: jtiemensma@ucmerced.edu (J. Tiemensma).

life [11]. A previous focus group study carried out by our group elucidated medicine beliefs and illness perceptions in patients with acromegaly. Specifically, during these focus group conversations patients reported that they experienced the use of injections as awful [12] (for illustrative, unpublished quotes, see Table 1). These two qualitative studies point toward the potential existence of negative beliefs about medicines in patients medically treated for acromegaly. Furthermore, it illustrated the need for self-management skills in patients with acromegaly in order to minimize the negative influence on their daily life.

Beliefs about medicines can be quantitatively assessed by using the Beliefs about Medicines Questionnaire (BMQ) [13], which assesses beliefs about *necessity* and *concerns* of taking a specific medicine. Until now, there are no quantitative studies available about beliefs about medication for acromegaly (i.e. SA) and beliefs about medication in general in patients with acromegaly.

The important influence of beliefs about medicines on illness perceptions, coping strategies, and therefore QoL, is demonstrated in the Common-Sense Model of self-regulation (CSM) [14]. This model describes how individuals come to understand their illness and how they develop coping strategies. The model comprises three stages. During stage one, illness perceptions are identified and organized around five categories: identity, cause, timeline, consequences, and cure/control. These illness perceptions determine coping strategies (stage two). The third stage comprises the appraisal of these coping strategies. Recently, the extended CSM was formulated by including beliefs about medicines. Specifically, it was demonstrated that beliefs about medicines were associated with illness perceptions in patients with chronic diseases (e.g. asthma [15]), adrenal insufficiency [16]. In addition, beliefs about medicines have also been found to be predictive of self-management behavior, such as adherence to medication [15,17].

Table 1
Illustrative quotes on medication beliefs and illness perceptions in acromegaly.

| | |
|-------------------------------------|--|
| Medicine beliefs: concerns | <i>I take very intense medications, which is difficult.</i> <i>I noticed, toward the end of my injections, that my sleep problems increased. My body would start functioning differently when my injection would wear off.</i> <i>I find information about side effects very important. I thought those side effects were very severe.</i> |
| Illness perception: identity | <i>I believe I am just tired earlier and experience stress faster. You are more sensitive to stress, which has an impact on your physical well-being, I think.</i> <i>Your central nervous system must be damaged here and there because of the illness, it is almost inevitable.</i> |
| Illness perception: consequences | <i>It had a huge impact. You are working, you have a house, you have a good job, and all of a sudden you are ill.</i> <i>In the meantime, you basically lost your entire life. It is very two-sided of course. On the one hand, you are happy to know where your symptoms came from after getting the diagnosis. Subsequently, you undergo surgery, which goes well, and afterwards you are happy you are still alive, you can finally do all the fun things you haven't done in years, because I was always working and very busy.</i> <i>Afterwards, you still have a body that doesn't want to even though you want it to. That is difficult sometimes.</i> |
| Illness perception: timeline | <i>You feel like you may have been cured because the values normalized so the surgery was successful, but the damage that preceded this is permanent so you obviously have damage somewhere.</i> <i>Permanent damage, that troubles me the most.</i> <i>You may not actually be sick, but you do have a disease as a result.</i> <i>And you keep that with you for the rest of your life, so to what extent are you cured?</i> |

Unpublished quotes from a recent focus group study of our department. The main results are described in [12]. During the focus groups patients with acromegaly reported concerns about their medication, and perceptions about the identity of their disease, the consequences and the timeline.

In the present study, we aimed to assess the contribution of beliefs about medicines to illness perceptions and QoL in acromegaly. We examined possible associations between beliefs about medication, illness perceptions, and QoL in patients with remission of acromegaly. Considering the extended CSM we hypothesized that beliefs about medication are associated with illness perceptions and QoL. Furthermore, we evaluated whether there are differences in illness perceptions and QoL between patients with remission of acromegaly receiving medical treatment and patients without medical treatment. Considering the potential negative effect patients may perceive when taking medication for acromegaly [11,12], we hypothesized that patients medically treated for acromegaly have more negative illness perceptions and more impairments in QoL compared to patients in remission without medical treatment.

2. Patients and methods

2.1. Design

Patients with acromegaly were invited to fill out questionnaires on medication beliefs, illness perceptions, and QoL. Patients were asked to complete the questionnaires at home and return them in a prepaid envelope. Inclusion criteria were adult patients (age > 18 yr) and remission defined by strict biochemical criteria (see below for details) for at least 1 year. Institutional Medical Ethics Committee approved the protocol.

2.2. Patients

A clinical chart review of 156 patients with acromegaly was performed. All patients were in biochemical remission for at least 1 year at the time of the present study. We invited these patients to fill out the questionnaires. Seventy-three patients (47%) refused to participate for several reasons (e.g. too busy, old age, debilitating disease). Eighty-three (53%) patients returned the questionnaires and filled out at least one questionnaire. Seventy-seven of these patients (49%) completed both the *Beliefs about Medicines Questionnaire*, as well as the *Illness Perception Questionnaire*. Patients with acromegaly who used medication other than somatostatin analogs (SA), i.e. dopamine agonists (n = 2), or Pegvisomant (n = 2) were excluded from the analysis because of the low power for separate analyses. Therefore, a final number of 73 patients (47%) were included in the present study. Sixty-five of these patients (42%) also filled out QoL questionnaires. For an overview of this process, see Fig. 1.

The diagnosis of acromegaly had been established by clinical signs and symptoms, and by biochemical tests, including insufficient suppression of GH during the glucose tolerance test and increased IGH-I levels for age. Normal serum IGF-I levels for age and serum GH levels below 1.9 µg/liter defined biochemical control of acromegaly for all patients and, in patients without SA treatment, also by suppression of GH levels (<0.38 µg/L) during glucose tolerance test [18]. Remission was reconfirmed at yearly intervals. Pituitary function was monitored and pituitary hormone replacement was prescribed dependent on the results of the yearly evaluation of pituitary functions. In case of corticotrope insufficiency, documented by insulin tolerance test (ITT) or CRH test, hydrocortisone was prescribed (20 mg/d divided into 2–3 dosages). Evaluation of GH deficiency was performed by ITT or GHRH-arginine test, only in patients under the age of 70 years and only after at least 2 years of remission. Somatotrope insufficiency was treated with rhGH replacement, aiming at IGF-I concentrations in the normal range for age. In addition, free T4 and testosterone levels (in male patients) were assessed. If results were below the lower limit of the respective ranges, substitution with L-T4 and/or testosterone was prescribed. In the case of amenorrhea and low estradiol levels in premenopausal women, estrogen replacement was provided.

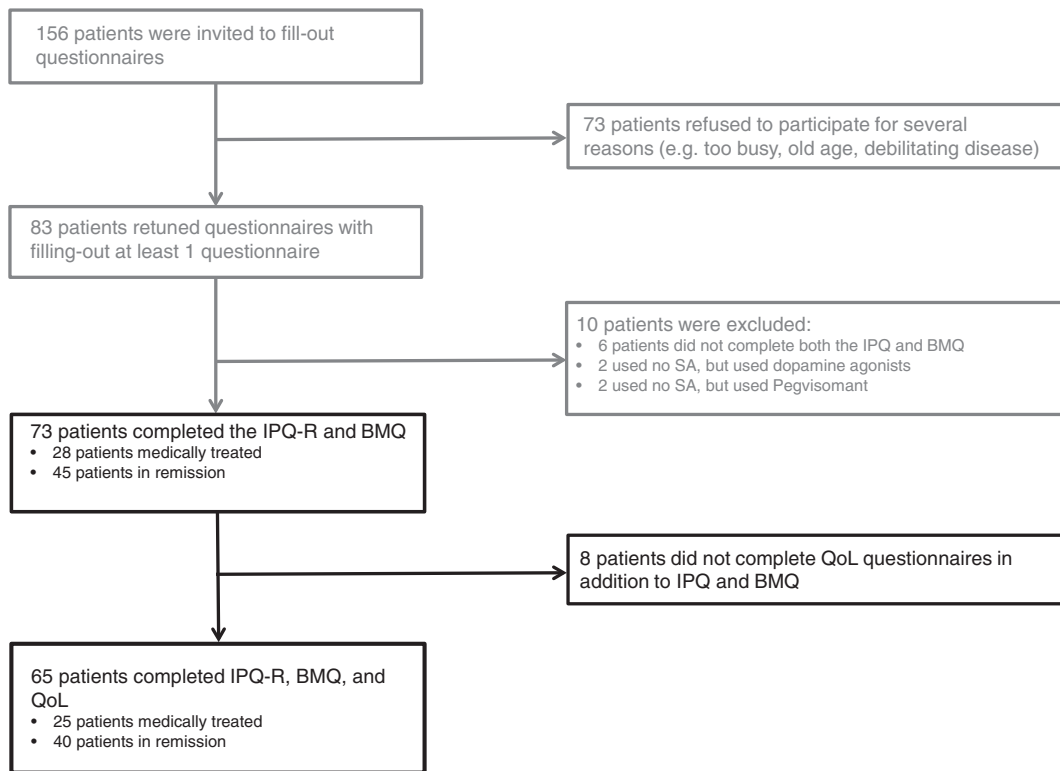


Fig. 1. Flow-chart of included patients.

2.3. Questionnaires

2.3.1. Beliefs about Medicines Questionnaire (BMQ)

The BMQ aims to assess cognitive and emotional representations of medication and comprises two sections (i.e. BMQ-Specific and BMQ-General), each divided into two subscales. The BMQ-Specific comprises two subscales assessing representations of medication prescribed for personal use (i.e. SA): the *Specific-Necessity* subscale, which is focusing on the perceived necessity of taking medications to remain healthy, and the *Specific-Concerns* subscale, focusing on concerns about the adverse effects of taking medications. The BMQ-General comprises two four-item subscales assessing beliefs about medicines in general: the *General-Overuse* subscale assesses beliefs that medicines are over-prescribed, and the *General-Harm* subscale assesses beliefs about medicines as harmful, addictive or poisonous. All items were rated on a five-point Likert-scale ranging from 1 strongly agree to 5 strongly disagree. The Specific-Necessity subscale ranged from 5 to 25 (midpoint = 15), the Specific-Concerns subscale ranged from 6–30 (midpoint = 18), and both General subscales ranged from 4 to 20. Higher scores indicate stronger beliefs. Among general medical patients, the Cronbach's alpha ranged from 0.51 to 0.86 [13].

2.3.2. Illness Perception Questionnaire – Revised (IPQ-R)

The Illness Perception Questionnaire – Revised (IPQ-R) was used to assess cognitive and emotional representations of illness. The questionnaire was developed to assess the components of the illness representation of Leventhal's Common Sense Model and is frequently used to study illness perceptions in chronic conditions [19–23]. The IPQ-R is divided into three sections. The first part consists of the illness identity dimension, with a list of fourteen general commonly occurring symptoms. Patients are asked to rate whether or not they experienced the symptoms, and if 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.

The second part of the questionnaire, assessing 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: timeline acute/chronic (beliefs about the chronic nature of the condition), timeline cyclical (beliefs regarding the cyclical nature of the condition i.e., perceived variability in symptoms), consequences (negative consequences of the disease), personal control (perceived personal controllability of the disease), treatment control (perceived treatment controllability of the disease), emotional representations (the emotional responses generated by the illness), and illness coherence (personal understanding of the disease). A higher score indicates a stronger belief in that particular dimension. The third and final part of the questionnaire is about the causal attributions. This section consists of 18 statements concerning possible causes that patients consider that contributed to their disease, scored on a 5-point Likert scale (strongly disagree to strongly agree).

As recommended by the developers of the questionnaire, a principal component analysis with varimax rotation was performed on the causal items to cluster variables with shared variance [24]. This analysis produced two factors: 1) psychological attributions (i.e. stress/worries, family problems/worries, emotional state, mental attitude, own behavior, overwork, aging, personality, altered immunity, poor medical care), and 2) risk factors (smoking, alcohol use, accident/injury, bacteria/virus, diet/eating habits, pollution in environment). The principal component analysis is described in detail by Tiemensma et al. 2010 [10].

2.3.3. EuroQoL-5D (EQ-5D)

The EQ-5D assesses the current health status reflected in five health dimensions; mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Scores are expressed on a 1–3 scale per dimension,

with higher scores indicating worse QoL. The questionnaire also includes a visual analog scale (VAS) which comprises a standard vertical 20 cm scale (similar to a thermometer) for recording an individual's rating for their current health-related well-being [25]. The VAS score ranges from 0 to 100, with higher scores indicating a better health status.

2.3.4. AcroQoL

The AcroQoL is a disease-specific QoL questionnaire assessing acromegaly related QoL. The AcroQoL consists of 22 items on a five-point Likert scale, measuring frequency of occurrence (ranging from always to never) and agreement (ranging from completely agree to completely disagree). The 22 items are subdivided into three subscales: physical scale (8 items), psychological–appearance scale (7 items), and psychological–personal relations scale (7 items). The total score ranges from 0–100, with lower scores indicating a more impaired QoL [26,27].

2.4. Statistical analysis

Data were analyzed using PASW Statistics version 20 (SPSS Inc., Chicago, IL). All data are presented as means \pm standard deviations, unless mentioned otherwise. To check the normality of data, the Kolmogorov–Smirnov test was used in addition to histograms and boxplots.

The primary analysis comprised the relationship between medication beliefs, illness perceptions and QoL. Pearson correlation coefficients were calculated when data were normally distributed and Spearman's rho was calculated when data were not normally distributed. The secondary analysis comprised the evaluation of potential differences in illness perceptions between patients with medical treatment for acromegaly and patients without medical treatment. Independent sample *t*-tests were used when data were normally distributed and Mann–Whitney U tests were used when data were not normally distributed. Because of the exploratory nature of the primary and secondary analysis, adjustment of the level of significance for multiple testing was not performed, and the level of significance was set at $P \leq 0.05$.

3. Results

3.1. Patient characteristics (Table 2)

Seventy-three patients participated in the present study (40 males, 55%). The mean duration of follow-up was 16.1 ± 10 years. Eighty-five percent of the patients were treated with transsphenoidal surgery, and 23% of the patients were additionally treated with radiotherapy. Forty-five patients were not using medication for acromegaly. Of these patients, 44 patients (98%) were treated with transsphenoidal surgery and one patient was biochemically cured after pituitary apoplexy. Twenty-eight patients were receiving medical treatment for acromegaly. Of these medically treated patients, 18 patients (25%) used only SA, six patients (8%) used SA and Pegvisomant, three patients (4%) used SA and dopamine agonists, and one patient used SA, Pegvisomant, and dopamine agonists. Patients using only Pegvisomant ($n = 2$) or dopamine agonist ($n = 2$) had been excluded from the analysis. All medically treated patients were well-controlled as measured by GH (in SA patients only) and IGF-1 concentrations (in all 28 patients) that were below $2.5 \mu\text{g/L}$ and within the normal reference range, respectively (biochemical remission).

Of the SA treated, 79% reported the need for using SA (scores above the midpoint of the specific necessity subscale), whereas 50% of these patients reported concerns about the use of SA (scores above the midpoint of the specific concerns subscale).

3.2. Relationship between medicines beliefs and illness perceptions (Table 3, Fig. 2)

In the subgroup of patients using SA, *Specific-Necessity* SA (i.e. the necessity of taking SA to remain healthy) was positively associated with illness identity ($r = .406$, $P = .032$) and consequences ($r = .398$, $P = .040$). This indicates that stronger beliefs about the necessity of SA to stay healthy are related to attributing more symptoms to acromegaly and perceiving more negative consequences. *Specific-Concerns* SA (i.e. concerns about the adverse effects of taking SA) were positively associated with perceptions of a cyclic timeline ($r = .396$, $P = .037$),

Table 2
Patient characteristics.

| | All patients (N = 73) | Patients medically treated for acromegaly (n = 28) | Patients without medical treatment for acromegaly (n = 45) | P-value ^a |
|--|--------------------------|--|--|----------------------|
| Gender (male/female) | 40/33 | 13/15 | 27/18 | .257 ^c |
| Age (years) | 60.10 (11.6) | 59.96 (11.0) | 60.18 (12.1) | .860 ^b |
| Education (n) | | | | |
| Low | 29 (40%) | 9 (32%) | 20 (44%) | .403 ^c |
| Medium | 17 (23%) | 6 (22%) | 11 (25%) | |
| High | 27 (37%) | 13 (46%) | 14 (31%) | |
| Transsphenoidal surgery, n (%) | 62 (85%) | 18 (64%) | 44 (98%) | .000 ^c |
| Additional radiotherapy, n (%) | 17 (23%) | 5 (18%) | 12 (27%) | .387 ^c |
| Somatostatin analogs only | 18 (25%) | 18 (64%) | NA | NA |
| Somatostatin analogs & Pegvisomant | 6 (8%) | 6 (21%) | NA | NA |
| Somatostatin analogs & Dopamine agonists | 3 (4%) | 3 (11%) | NA | NA |
| Somatostatin analogs, Pegvisomant & dopamine agonists | 1 (1%) | 1 (4%) | NA | NA |
| Duration follow-up (years) | 16.07 (10.0) | 13.96 (10.8) | 17.38 (9.4) | .067 ^b |
| Hypopituitarism, n (%) | | | | |
| GH | 12 (16%) | 0 (0%) | 12 (27%) | .003 ^c |
| LH/FSH | 13 (18%) | 5 (18%) | 8 (18%) | .993 ^c |
| TSH | 19 (26%) | 6 (21%) | 13 (29%) | .480 ^c |
| ACTH | 19 (26%) | 5 (18%) | 14 (31%) | .210 ^c |
| ADH | 2 (3%) | 0 (0%) | 2 (4%) | .258 ^c |

^a Patients medically treated for acromegaly ($n = 28$) vs. patients without medical treatment for acromegaly ($n = 45$).

^b Mann–Whitney U test.

^c Chi-square test.

Table 3
Correlations between illness perception dimensions, EQ-5D dimensions, BMQ dimensions, and disease-specific quality of life.

| | Specific Necessity (SA) (n = 28) ^a | Specific Concerns (SA) (n = 28) ^a | General-Harm (n = 73) ^b | General-Overuse (n = 73) ^b |
|-----------------------------------|--|---|---------------------------------------|--|
| IPQ-R | | | | |
| Identity | .406* | .367 | .053 | -.040 |
| Timeline (chronic/acute) | .173 | -.278 | -.186 | -.202 |
| Timeline (cyclical) | .266 | .396* | -.020 | .066 |
| Consequences | .398* | .348 | .009 | -.040 |
| Emotional representations | .290 | .294 | .280* | .269* |
| Personal control† | .012 | -.076 | .141 | .139 |
| Treatment control | -.331 | -.298 | -.108 | -.109 |
| Illness coherence | -.069 | -.277 | .007 | -.002 |
| Psychological attributions | -.059 | .144 | .237* | .176 |
| Risk factors | -.050 | .253 | .240* | .157 |
| | Specific Necessity (SA) (n = 25) ^c | Specific Concerns (SA) (n = 25) ^c | General-Harm (n = 65) ^d | General-Overuse (n = 65) ^d |
| EQ-5D | | | | |
| Mobility | .265 | .034 | -.031 | .025 |
| Self-care | .206 | .155 | .117 | .132 |
| Activity | .275 | .099 | .017 | .060 |
| Pain | .140 | .262 | -.011 | -.018 |
| Anxiety | -.144 | .203 | -.073 | -.022 |
| VAS† | -.361 | -.281 | -.164 | -.112 |
| AcroQoL | | | | |
| Physical scale | -.383 | -.184 | .010 | -.002 |
| Psychological-appearance† | -.423* | .034 | .163 | .054 |
| Psychological-personal relations† | -.567** | -.311 | .029 | -.007 |
| Total score† | -.594** | -.006 | .078 | .025 |

Spearman's correlations; †Pearson's correlations. SA: somatostatin analogs.

^a Patients medically treated for acromegaly who filled out IPQ-R and BMQ.

^b Total sample of patients with and without medication for acromegaly who filled out IPQ-R and BMQ.

^c Patients medically treated for acromegaly who filled out AcroQoL and EQ-5D, as well as IPQ-R and BMQ.

^d Total sample of patients with and without medication for acromegaly who filled out AcroQoL and EQ-5D, as well as IPQ-R and BMQ.

* P < 0.05.

** P < 0.01.

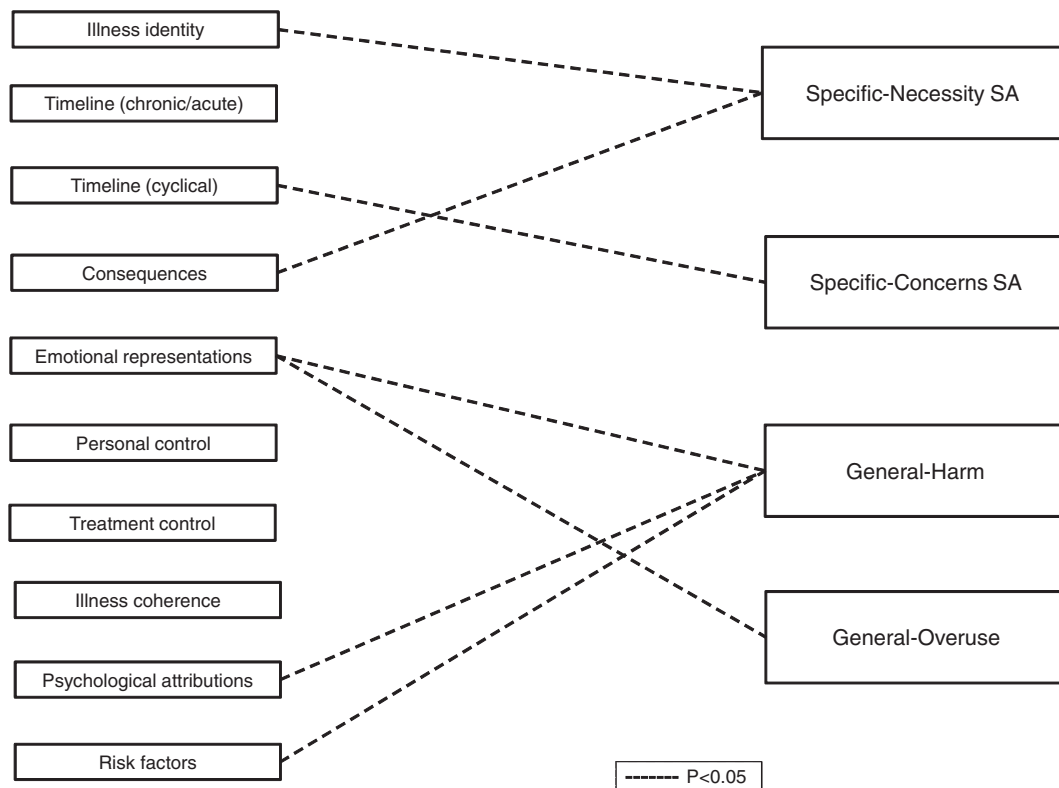


Fig. 2. Observed correlations between illness perceptions and medication beliefs. SA: somatostatin analogs. Absence of line indicates non-significant correlation.

indicating that stronger concerns about the adverse effects of SA are related to perceiving a more cyclic timeline of the disease i.e., more perceived variability in symptoms.

In the entire sample, the subscale *General-Harm* (i.e. beliefs about medicines in general being harmful, addictive or poisonous) was positively associated with emotional representations ($r = .280, P = .017$), psychological attributions ($r = .237, P = .048$), and risk factors ($r = .240, P = .045$). This indicates that stronger beliefs about harm of medication use in general are related to stronger emotional responses generated by the disease, having stronger beliefs about psychological causes of the disease, and perceiving risk factors to be the cause of the disease. The subscale *General-Overuse* (i.e. beliefs that medicines in general are over-prescribed) was also positively associated with emotional representations ($r = .269, P = .022$) indicating that stronger beliefs about the overuse of medication in general are related to having stronger emotional responses generated by the disease.

3.3. Relationship between medicine beliefs and QoL (Table 3)

Specific-Necessity SA (i.e. the necessity of taking SA to remain healthy) was negatively associated with AcroQoL subscales Psychological-appearance ($r = -.423, P = .035$) and Psychological-personal relations ($r = -.567, P = .009$), and the total score on the AcroQoL ($r = -.594, P = .007$). This indicates that stronger beliefs about the necessity of SA to stay healthy are related to a worse disease-specific QoL.

The other specific, as well as general subscales of the BMQ were not significantly associated with QoL.

3.4. Illness perceptions and QoL in patients undergoing medical treatment vs. patients in remission (Table 4)

Patients treated with SA reported to perceive the timeline of their disease more chronically compared to patients in remission (25.69 ± 4.07 versus $20.95 \pm 6.47, P = .002$).

There were no significant differences on the other illness perception subscales or QoL scores between patients with medical treatment and patients without medical treatment.

4. Discussion

The present study demonstrates that medication beliefs in patients with acromegaly are related to illness perceptions and QoL. Stronger beliefs about the necessity of SA were associated with attributing more symptoms to acromegaly, perceiving more negative consequences, and lower disease-specific QoL. More concerns about the perceived side effects of SA were associated with perceiving more variability in symptoms. Furthermore, patients who are medically treated for acromegaly with adequate biochemical control of disease have stronger beliefs about the chronicity of the disease than patients in remission without medical treatment for acromegaly.

The found correlations, together with the previously described correlations between illness perceptions and QoL in patients with acromegaly by Tiemensma et al. [10], support the theory of the extended CSM. This extended model shows how medication beliefs are associated both with illness perceptions and QoL in patients with chronic diseases [15,16].

Concerns about medication and negative illness perceptions in patients with acromegaly have been previously elucidated in a recent qualitative focus group study by our research group [12] (see Table 1). The present study provided quantitative data about these medication beliefs and illness perceptions. The important role of medication, and therefore of medication beliefs, is also properly illustrated by a recent interview study of Gurel et al. in which patients reported they felt not “cured” after treatment, particularly when they realized the medication had to be taken lifelong. The use of medication resulted in confusion between being a patient and being a person [11]. The results of our study are in accord with the latter study, since we demonstrate that patients using medication reported stronger beliefs about the chronicity of the disease than patients not using medication. This negative illness perception about a more chronic time line of the disease may lead to more impairments in QoL, as demonstrated by Tiemensma et al. [10]. This would be in accordance with previous literature demonstrating that patients with controlled acromegaly treated with Lanreotide reported worse QoL, compared with controlled patients who did not have to take medication [28], and patients cured by a single surgical intervention reporting better QoL than patients cured with SA, radiotherapy, or treated for hypopituitarism [3]. However, in the present study we did not find differences in QoL between patients medically treated and patients without medical treatment, which is in accord with other studies [29,30], but which could also be due to limited power due to the relatively small sample size.

It might be that the association between medication beliefs and disease-specific QoL is mediated by the previously demonstrated relation between medication beliefs and self-management behavior (e.g. adherence to medication) [15], since adequate self-management skills are needed to optimize coping with the disease and its consequences, in order to minimize the negative influence on daily life (i.e. QoL). Future research in a larger group of medically treated patients with acromegaly is needed to further elucidate the role of medication beliefs in self-management behavior and QoL. Furthermore, it would be interesting to examine whether medication beliefs (and illness perceptions) can be modified by offering a psychosocial intervention, and whether changes toward more adaptive beliefs affect QoL. In addition, it should be acknowledged that illness perceptions and beliefs about

Table 4
Illness perceptions of patients with medication vs. patients in remission.

| | Patients medically treated (n = 28) | Patients in remission (n = 45) | P-value |
|-----------------------------------|-------------------------------------|--------------------------------|---------|
| IPQ-R | | | |
| Identity | 2.86 (2.22) | 2.31 (2.56) | .202 |
| Timeline (chronic/acute) | 25.69 (4.07) | 20.95 (6.47) | .002* |
| Timeline (cyclical) | 10.11 (4.14) | 10.23 (3.80) | .788 |
| Consequences | 16.89 (5.44) | 16.67 (5.11) | .898 |
| Emotional representations | 12.18 (3.20) | 12.71 (3.73) | .361 |
| Personal control† | 17.06 (4.14) | 17.44 (4.94) | .734 |
| Treatment control | 18.68 (3.03) | 17.69 (3.51) | .299 |
| Illness coherence | 17.86 (2.81) | 17.07 (2.69) | .137 |
| Psychological attributions | 16.18 (5.61) | 19.26 (7.19) | .076 |
| Risk factors | 9.22 (3.33) | 10.60 (3.74) | .161 |
| BMQ | | | |
| Specific necessity SA | 17.04 (3.54) | NA | NA |
| Specific concerns SA | 17.75 (2.61) | NA | NA |
| General-harm | 9.69 (2.67) | 9.71 (2.64) | .914 |
| General-overuse | 10.13 (2.69) | 10.77 (2.09) | .215 |
| EQ-5D ^a | | | |
| Mobility | 1.44 (0.51) | 1.33 (0.47) | .354 |
| Self-care | 1.08 (0.28) | 1.05 (0.22) | .627 |
| Activity | 1.56 (0.65) | 1.52 (0.60) | .885 |
| Pain | 1.80 (0.65) | 1.75 (0.59) | .787 |
| Anxiety | 1.28 (0.54) | 1.42 (0.64) | .342 |
| VAS† | 69.58 (14.68) | 69.77 (16.31) | .963 |
| AcroQoL ^a | | | |
| Physical | 64.32 (21.33) | 61.14 (20.56) | .551 |
| Psychological-appearance† | 62.14 (22.14) | 52.56 (18.84) | .069 |
| Psychological-personal relations† | 81.43 (11.45) | 77.38 (14.56) | .289 |
| Total score† | 71.83 (15.50) | 63.57 (14.09) | .052 |

Mann–Whitney U test; †independent sample *t*-test. Data presented as mean (standard deviation). SA: somatostatin analogs.

^a Patients medically treated for acromegaly (n = 25) and patients without medical treatment for acromegaly (n = 40).

* P < 0.01.

treatment are related to cultural background [31–33]. In the present study, ethnicity or cultural background was not assessed, and therefore analyses could not be adjusted for culture.

In a previous study by our research group in patients with adrenal insufficiency treated with hydrocortisone, we demonstrated strong and consistent correlations between beliefs about hydrocortisone and illness perceptions [16]. The correlations found in the present study are similar to those in patients with adrenal insufficiency and demonstrated the same direction of correlations (i.e. stronger necessity beliefs and more concerns are related with more negative illness perceptions). However, in the present sample of patients medically treated for acromegaly, fewer correlations were found and correlations were less strong. This could possibly be explained by limited power due to a relatively small sample size. On the other hand, it could also be that the impact of medication in acromegaly is less strong compared to hydrocortisone treatment. Comparing the mean medicine beliefs about SA in the present sample with medicine beliefs in patients treated with hydrocortisone (i.e. necessity beliefs ranging from 18.4 to 20.9, and concerns ranging from 18.1 to 18.9 respectively) [16], it can be noted that medicine beliefs about SA are less strong. As suggested by the authors of the BMQ, differences between groups could be explained by differences in diagnosis, type of treatment, and perceived side effects [34]. Therefore, we postulate that these distinctions could indeed be related not only to the different diagnoses, but also to the differences in types of treatment (i.e. suppressant medication vs. replacement therapy, injections vs. pills). Furthermore, there could be differences in perceived side effects (e.g. forgetting hydrocortisone intake could be life threatening, while forgetting SA is not).

The results of this study can be used by the treating physician during their consultations, but also by medical psychologists during psychological treatment. Awareness of clinicians about the potential existence of negative medication beliefs and/or illness perceptions would be helpful in order to assess those beliefs. Furthermore, an adequate assessment of these beliefs is needed to determine the potential strategy to adapt these beliefs in order to improve self-management behavior, and therefore QoL. When needed, physicians could cooperate with medical psychologists and refer patients for psychological treatment, since a medical psychologist can assist patients to adapt inadequate cognitions in order to develop effective self-management strategies. This strategy is in accordance with the multi-phase approach described in a previous paper by our research group [16]. This multi-phase approach consists of three phases: 1) provide patients with a clear rationale for their medication, 2) assess and address patients' concerns regarding their medication use (when necessary in cooperation with a medical psychologist), and 3) support patients in the optimal and persistent use of their medication by assessing the potential barriers regarding their medication use. We believe that such a multi-phase approach that includes collaboration with a medical psychologist, enables improving medication beliefs, more positive illness perceptions, better self-management strategies, and thereby improving QoL.

In conclusion, specific beliefs about the necessity of somatostatin analogs and concerns about its adverse effects are strongly associated with more negative illness perceptions and worse disease-specific QoL. Furthermore, patients with remission of acromegaly who are medically treated perceive a more chronic timeline of their disease than patients in remission without medical treatment. The findings of the present study could be incorporated in routine clinical care of patients with acromegaly, enabling optimized clinical care, and are instrumental in the development of a self-management intervention aiming to improve QoL.

Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

Disclosure statement

The authors have nothing to disclose.

Conflict of interest

The authors have no conflict of interest to report.

Acknowledgments

We thank all patients for their contribution to this study.

References

- [1] M.D. Johnson, C.J. Woodburn, M.L. Vance, Quality of life in patients with a pituitary adenoma. *Pituitary* 6 (2003) 81–87.
- [2] R. Trepp, R. Everts, C. Stettler, S. Fischli, S. Allemann, S.M. Webb, E.R. Christ, Assessment of quality of life in patients with uncontrolled vs. controlled acromegaly using the Acromegaly Quality of Life Questionnaire (AcroQoL). *Clin. Endocrinol. (Oxf)* 63 (2005) 103–110.
- [3] N.R. Biermasz, S.W. van Thiel, A.M. Pereira, H.C. Hoftijzer, A.M. van Hemert, J.W. Smit, J.A. Romijn, F. Roelfsema, Decreased quality of life in patients with acromegaly despite long-term cure of growth hormone excess. *J. Clin. Endocrinol. Metab.* 89 (2004) 5369–5376.
- [4] C.D. Andela, M. Scharloo, A.M. Pereira, A.A. Kaptein, N.R. Biermasz, Quality of life (QoL) impairments in patients with a pituitary adenoma: a systematic review of QoL studies. *Pituitary* (2015) (Epub ahead of print).
- [5] M.J. Wassenaar, N.R. Biermasz, M. Kloppenburg, A.A. van der Klaauw, J. Tiemensma, J.W. Smit, A.M. Pereira, F. Roelfsema, H.M. Kroon, J.A. Romijn, Clinical osteoarthritis predicts physical and psychological QoL in acromegaly patients. *Growth Hormon. IGF Res.* 20 (2010) 226–233.
- [6] N.R. Biermasz, A.M. Pereira, J.W. Smit, J.A. Romijn, F. Roelfsema, Morbidity after long-term remission for acromegaly: persisting joint-related complaints cause reduced quality of life. *J. Clin. Endocrinol. Metab.* 90 (2005) 2731–2739.
- [7] A. Miller, H. Doll, J. David, J. Wass, Impact of musculoskeletal disease on quality of life in long-standing acromegaly. *Eur. J. Endocrinol.* 158 (2008) 587–593.
- [8] T. Psaras, M. Milian, V. Hattermann, B.E. Will, M. Tatagiba, J. Honegger, Predictive factors for neurocognitive function and Quality of Life after surgical treatment for Cushing's disease and acromegaly. *J. Endocrinol. Invest.* 34 (2011) e168–e177.
- [9] V.J. Geraedts, C. Dimopoulou, M. Auer, J. Schopohl, G.K. Stalla, C. Sievers, Health outcomes in acromegaly: depression and anxiety are promising targets for improving reduced quality of life. *Front. Endocrinol. (Lausanne)* 5 (2014) 229.
- [10] J. Tiemensma, A.A. Kaptein, A.M. Pereira, J.W. Smit, J.A. Romijn, N.R. Biermasz, Affected illness perceptions and the association with impaired quality of life in patients with long-term remission of acromegaly. *J. Clin. Endocrinol. Metab.* 96 (2011) 3550–3558.
- [11] M.H. Gurel, P.R. Bruening, C. Rhodes, K.G. Lomax, Patient perspectives on the impact of acromegaly: results from individual and group interviews. *Patient Prefer Adherence* 8 (2014) 53–62.
- [12] C.D. Andela, N.D. Niemeijer, M. Scharloo, J. Tiemensma, S. Kanagasabapathy, A.M. Pereira, N.G. Kamminga, A.A. Kaptein, N.R. Biermasz, Towards a better quality of life (QoL) for patients with pituitary diseases: results from a focus group study exploring QoL. *Pituitary* 18 (2014) 86–100.
- [13] R. Horne, J. Weinman, M. Hankins, The Beliefs about Medicines Questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol. Health* 14 (1999) 1–24.
- [14] H. Leventhal, D. Meyer, D. Nerenz, The common sense representation of illness danger. in: S. Rachman (Ed.), *Contributions to Medical Psychology*, 2nd ed. Pergamon, New York 1980, pp. 7–30.
- [15] 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).
- [16] J. Tiemensma, C.D. Andela, A.M. Pereira, J.A. Romijn, N.R. Biermasz, A.A. Kaptein, Patients with adrenal insufficiency hate their medication: concerns and stronger beliefs about the necessity of hydrocortisone intake are associated with more negative illness perceptions. *J. Clin. Endocrinol. Metab.* 99 (2014) 3668–3676.
- [17] K. Krauskopf, A.D. Federman, M.S. Kale, K.M. Sigel, M. Martynenko, R. O'Connor, M.S. Wolf, H. Leventhal, J.P. Wisnivesky, Chronic obstructive pulmonary disease illness and medication beliefs are associated with medication adherence. *COPD* 2014. (Epub ahead of print).
- [18] N.R. Biermasz, F.W. Dekker, A.M. Pereira, S.W. van Thiel, P.J. Schutte, D.H. van, J.A. Romijn, F. Roelfsema, Determinants of survival in treated acromegaly in a single center: predictive value of serial insulin-like growth factor I measurements. *J. Clin. Endocrinol. Metab.* 89 (2004) 2789–2796.
- [19] C. Fowler, L.S. Baas, Illness representations in patients with chronic kidney disease on maintenance hemodialysis. *Nephrol. Nurs. J.* 33 (2006) 173–186.
- [20] M. Fischer, M. Scharloo, J. Abbink, H.A. van 't, Rudolphus A. van RD, J. Weinman, K. Rabe, A.A. Kaptein, The dynamics of illness perceptions: testing assumptions of Leventhal's common-sense model in a pulmonary rehabilitation setting. *Br. J. Health Psychol.* 15 (2010) 887–903.

- [21] D. Hirsch, M. Ginat, S. Levy, C. Benbassat, R. Weinstein, G. Tsvetov, J. Singer, I. Shraga-Slutzky, S. Grozinski-Glasberg, Y. Mansiterski, I. Shimon, R. Reicher-Atir, Illness perception in patients with differentiated epithelial cell thyroid cancer, *Thyroid* 19 (2009) 459–465.
- [22] B. Callaghan, E. Condie, M. Johnston, Using the common sense self-regulation model to determine psychological predictors of prosthetic use and activity limitations in lower limb amputees, *Prosthetics Orthot. Int.* 32 (2008) 324–336.
- [23] A. Searle, P. Norman, R. Thompson, K. Vedhara, A prospective examination of illness beliefs and coping in patients with type 2 diabetes, *Br. J. Health Psychol.* 12 (2007) 621–638.
- [24] R. Moss-Morris, J. Weinman, K. Petrie, R. Horne, L. Cameron, D. Buick, The Revised Illness Perception Questionnaire (IPQ-R), *Psychol. Health* 17 (2002) 1–16.
- [25] EuroQoL group, EuroQoL—a new facility for the measurement of health-related quality of life. The EuroQoL Group, *Health Policy* 16 (1990) 199–208.
- [26] S.M. Webb, L. Prieto, X. Badia, M. Albareda, M. Catala, S. Gaztambide, T. Lucas, C. Paramo, A. Pico, A. Lucas, I. Halperin, G. Obiols, R. Astorga, Acromegaly Quality of Life Questionnaire (ACROQOL): a new health-related quality of life questionnaire for patients with acromegaly: development and psychometric properties, *Clin. Endocrinol. (Oxf)* 57 (2002) 251–258.
- [27] X. Badia, S.M. Webb, L. Prieto, N. Lara, Acromegaly Quality of Life Questionnaire (AcroQoL), *Health Qual. Life Outcomes* 2 (2004) 13.
- [28] S.C. Hua, Y.H. Yan, T.C. Chang, Associations of remission status and lanreotide treatment with quality of life in patients with treated acromegaly, *Eur. J. Endocrinol.* 155 (2006) 831–837.
- [29] Z. Karaca, F. Tanriverdi, G. Elbuken, I. Cakir, H. Donmez, A. Selcuklu, A.C. Durak, H.S. Dokmetas, R. Colak, K. Unluhizarci, F. Kelestimur, Comparison of primary octreotide-lar and surgical treatment in newly diagnosed patients with acromegaly, *Clin. Endocrinol. (Oxf)* 75 (2011) 678–684.
- [30] K.Z. Rubeck, M. Madsen, C.M. Andreasen, S. Fisker, J. Frystyk, J.O. Jorgensen, Conventional and novel biomarkers of treatment outcome in patients with acromegaly: discordant results after somatostatin analog treatment compared with surgery, *Eur. J. Endocrinol.* 163 (2010) 717–726.
- [31] R. Horne, Treatment perceptions and self-regulation, in: L.D. Cameron, H. Leventhal (Eds.), *The Self-regulation of Health and Illness Behaviour*, Routledge, London 2003, pp. 138–150.
- [32] R. Moss-Morris, W. Wrapson, Representational beliefs about functional somatic syndromes, in: L.D. Cameron, H. Leventhal (Eds.), *The Self-regulation of Health and Illness Behaviour*, Routledge, London 2003, pp. 119–132.
- [33] S. Dein, Explanatory models of and attitudes towards cancer in different cultures, *Lancet Oncol.* 5 (2004) 119–124.
- [34] R. Horne, J. Weinman, Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication, *Psychol. Health* 17 (2002) 17–32.