Significance and rationale of studies of health-related quality of life in anaphylactic disorders

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Purpose of review

Until recently, quality-of-life measures were only used in allergic diseases with ongoing symptoms, such as asthma and rhinoconjunctivitis. Anaphylaxis is a chronic disease without ongoing physical symptoms, but the problems concerning quality of life are related to the continuous vigilance required to prevent accidental exposure. This raises specific issues concerning the validation of quality-of-life instruments.

Recent findings

The preferred independent measure for validation generally is an objective measurement of the severity of disease (e.g. spirometry in asthma). In patients suffering from anaphylaxis, the perceived expectation of what will happen following exposure can be used as the key independent measure. Recently, a specific instrument measuring this expectation (the 'Expectation of outcome' questionnaire) has been developed, and successfully used in insect-venom anaphylaxis.

Summary

Also, in diseases without ongoing symptoms like anaphylaxis, quality of life can be measured and the disease-specific instrument validated. It is to be expected that many new instruments will be developed in the coming years to address important issues in anaphylaxis. They may provide a better understanding of the major problems of certain patient subgroups and may give direction to the kind of information that should be addressed and what kind of interventions could be important and whether they are useful or not.

Keywords

anaphylaxis, expectation of outcome, food allergy, insect venom allergy, quality of life

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Abbreviations

EoO Expectation of Outcome measure
HRQL health-related quality of life

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Introduction

Quality of life has become an important outcome in many diseases, especially chronic diseases, as it measures the impact of a chronic disease from the patient's perspective. Also, in allergic diseases, its use as an end-point in clinical trials [1,2] as well as the use in routine clinical practice are well recognized [3].

Until recently, quality-of-life measures were only used in allergic diseases with ongoing symptoms, such as asthma and rhinoconjunctivitis. This is in contrast to patients suffering from anaphylaxis, in which most patients only infrequently experience symptoms on accidental exposure to the offending allergen. The absence of ongoing symptoms, however, does not mean that these patients do not encounter problems related to their health status. Doctors treating anaphylactic patients recognize that these patients will do their utmost best to prevent exposure to the offending allergen in order to prevent an anaphylactic reaction. The problems concerning their quality of life are therefore related to the continuous vigilance required to prevent accidental exposure [4,5]. This paradox of having a chronic disease such as anaphylaxis without ongoing physical symptoms raises specific considerations in measuring the quality of life of these patients. In this article, we will focus on the specific issues measuring quality of life in this special group of patients.

What is quality of life?

Quality of life has various meanings, which encompass factors such as financial security, freedom, spiritual contentment, quality of environment, health and the way in which these factors interrelate [6]. The term has been used mainly in medical studies by recognizing that the personal burden of illness cannot be described fully by measures of disease status, such as tumor load or forced expiratory volume. Psychological factors, such as apprehension, functional impairments and difficulties in fulfilling personal and family responsibilities, have to be encompassed. Therefore, the area of quality of life as applied to medicine is more specifically known as 'health-related quality of life'. The main purpose is to study the various effects that illnesses and treatments have on daily life and life satisfaction, including the evaluation of the (net) benefit of interventions.

No consensus on the definition of quality of life as it is affected by health [health-related quality of life

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(HRQL)] exists. Definitions range from those with a holistic emphasis on the social, emotional and physical well-being of patients after treatment [7] to those that describe the impact of a person's health on his or her ability to lead a fulfilling life [8].

The term 'quality of life' was used for the first time by Pigou in 1920. In 1948, the World Health Organization defined health as 'a state of complete physical, mental and social well being and not merely the absence of disease or infirmity' [9].

There then followed a period of debate about the question of how to measure quality of life. It was not before the 70s that the first instruments were developed and tested. In 1977, the term 'quality of life' was added as a keyword in the Medical Subject Headings of the US National Library of Medicine MEDLINE computer Search System [10].

Currently, there is still much debate in the literature about the definition of 'quality of life' and operationalization of this concept. Many agree on the concept of quality of life as 'well-being', which is determined by objective and subjective factors, across a number of life domains, such as the physical, psychological and social domains of health [11].

Why measure quality of life?

Physical measures provide information to clinicians, but often correlate poorly with functional capacity and well-being of patients. Thus, not everyone with a severe disease has a poor quality of life, and not all individuals who are disease-free have a good quality of life. It is a commonly observed phenomenon that two patients with the same objective clinical measures often have dramatically different responses to their disease [12]. This means that the relation between symptoms and quality of life is not direct, nor simple. Other factors such as individual perceptions, beliefs and feelings (resulting in expectations) are of importance. Therefore, the person's own appraisal of his or her health and well-being is the key factor in quality-of-life studies. Health-related quality of life focuses on the patient's perspective of his or her disease and measures the impairments which are a consequence of that disease and which patients consider to be important. In anaphylaxis, as in other disease entities, HRQL measurements may provide insight into the specific problems of this specific patient group. In addition, these measures may provide a better understanding of the major/specific problems of certain patient subgroups. This may give direction to the kind of information that should be addressed, what kind of interventions could be important and which specific research activities should be undertaken. It can also help to evaluate whether certain interventions are useful or not. In patients with anaphylaxis, therefore, HRQL measures are a major outcome in clinical management evaluations and intervention studies.

The impact of anaphylaxis on quality of life

An important aim of anaphylaxis treatment is centered on preventing future morbidity or even death. Symptoms vary from systemic cutaneous symptoms through gastrointestinal problems and respiratory distress to hypotension. The impact of a severe anaphylactic reaction is so great that many patients experience this reaction as a feeling of nearly dying.

In order to prevent exposure to the offending allergen, patients generally have to undertake extensive measures. Continuous vigilance is required for allergen avoidance [13]. Food-allergic patients have to be alert when shopping or eating out – a problem which is compounded by the fact that information about food allergens may be hidden or misleading [14]. Insect-venom-allergic patients have to be alert during all outside activities, as insect behaviour is unpredictable [5]. Patients also avoid situations which are potentially harmful. This means that in many patients, anaphylactic episodes often lead to a (drastically) altered style of living in order to prevent exposure to the offending allergen, and that (families of) anaphylactic patients may suffer social exclusion and stress.

The discrepancy between continuous vigilance in order to prevent symptoms, without actually experiencing symptoms, is particularly suitable for quality-of-life studies.

How can we measure quality of life?

The instrument used to measure quality of life is a questionnaire. In general, two kinds of HRQL instruments are distinguished: generic instruments and disease-specific instruments. Generic instruments are developed to measure the most important aspects influencing general well-being. They can be used to compare quality of life in different populations and different diseases [12]. The major disadvantage of generic instruments is that they do not measure the specific problems of a disease and therefore are only able to measure large changes in health status [12]. Disease-specific quality-of-life instruments focus on the areas of functioning that are relevant to that particular condition or specific population. As a result, they are more responsive to small but potentially important changes [15]. They do not, however, allow comparison between different diseases.

In anaphylaxis, HRQL issues are specifically related to the condition. This means that for measuring HRQL, disease-specific instruments are likely to be best. These instruments subsequently can be used to study differences between people who have a better HRQL and

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those who have a worse HRQL (the instrument must have adequate *discriminative* properties). They are especially of importance in studying treatment effects from the patient's perspective: the instrument must have adequate *evaluative* properties to measure how much the HRQL has changed after an intervention.

Measurement properties

Physicians cannot interpret quality-of-life measures until the measurement properties of these instruments are established. Major requirements for the HRQL instruments are *reproducibility* and *validity*.

Reproducibility relates to the way in which the instrument is able to quantitate the signal-to-noise ratio present in the data [12]. Reproducibility in discriminative instruments therefore translates into reliability, which means that the results in stable patients have to be more or less the same after repeated administration. Reproducibility for evaluative instruments translates into responsiveness, which means that they must be able to detect changes within patients during a period of time.

The value of quality-of-life questionnaires in medical research also rests upon their validity.

Validity examines whether the instrument is measuring what it is intended to measure (by psychologists known as face validity). Thus, validation of an instrument that is designed to measure HRQL involves demonstrating that only that part of quality of life affected by the illness in question is being measured and not other aspects more generally related to quality of life as a whole. This is achieved by comparing potential questions or domains of the instrument or the instrument as a whole to an independent measure of the disease. The preferred independent measure generally is the best known indicator of the disease (the so-called gold standard), which most often is an objective measurement of the extent or severity of disease. Common examples include FEV1 in asthma, symptom-medications scores in allergic rhinitis and SCORAD in atopic dermatitis. These measures will generally correlate with quality of life because they are thought to be important determinants of quality of life. In this regard, they are not independent variables in relation to HRQL, but the name 'independent measure' drives from the fact that it is independent from any measures of quality of life.

Questions or questionnaires are validated by ascertaining construct validity between the questions and the independent measure(s). As patients with more severe disease will be expected to have a greater impairment of their HRQL, valid questions should show greater impairment with more severe disease as determined by the independent measure. In contrast, quality-of-life items which are not driven by the disease will show no particular relationship to disease severity.

Expectation of outcome as an independent measure

In patients suffering from anaphylaxis, an independent measure based on the occurrence of physical symptoms is inappropriate because patients are usually symptom-free. The perceived expectation of what will happen following exposure can be used as the key independent measure (expectation of outcome). A specific instrument to measure this expectation has been developed for insect-venom-allergic patients [5]. The 'Expectation of Outcome' measure (EoO) asks patients about their expectations of what will happen if they are stung again: how great is the chance that they will react and, if they react, what is the chance of having a severe reaction? In food-allergic patients: what is the chance being accidentally exposed to the offending allergen? Or how effectively can the offending allergen(s) be avoided? Answers to these questions are expressed on a seven-point scale, with responses varying from 'a negligible chance' to a 'very great chance'.

The aforementioned method can be used to validate both discriminative as well as evaluative instruments. It can be used for the development of a questionnaire by correlating the whole questionnaire or separate domains with the EoO. We used the EoO to validate each item separately, in order to select the most important items [5]. By showing a good correlation of the HRQL scores of the instrument with the EoO, the EoO can also be used to assess the discriminative capacities of the instrument as to validate the instrument longitudinally. This means that, also, in a disease without ongoing symptoms, quality of life can be measured and the disease-specific instrument validated.

A criticism of the EoO has been that it is not an objective measure of anaphylaxis severity, as it is reliant on the patient's perception, with all the potential inaccuracies that this involves. While the EoO is less objective than FEV1 or SCORAD, patients' expectations are the driving force which should determine HRQL: a patient who believes that he or she may die following exposure to allergens would be expected to have a poor HRQL, even if this belief was ill-founded. A second criticism of the EoO is that it is not really independent of HRQL: expectation of a bad outcome should directly cause deterioration in HRQL. This assumption is not supported by a large body of evidence on risk perception, as will be discussed later.

Risk perception and quality of life: the experience determining the expectation

Qualities of life summarize the judgments that people make to describe their experiences of health and illness.

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This is what distinguishes them from measures of disability that ask about an ability to complete specific tasks. People assess their health-related quality of life by comparing their expectations with their experience. Quality of life can be considered as the gap between expectations and experience [16].

As expectations are learnt from experiences, they are highly specific. Different people have different expectations. A patient evaluates his or her quality of life within the horizons of possibilities that he or she sees for him or herself. These horizons are determined by factors such as social class, age, sex, ethnic group, disability and personal biography [16].

Demographic factors such as age may influence risk behaviour [17]. Cultural aspects such as paying attention to and understanding the problem may facilitate social interactions despite the disease. Socioeconomic factors important in food-allergic patients may include the availability of or the ability to buy alternative products. Psychological factors include general anxiety level and general coping strategies.

The magnitudes of impact may be dependent upon the time at which the measurement is made. Patients who experience an anaphylactic reaction after an insect sting at the end of the season for the first time will not experience the influence of exposure to insects on their daily lives until the next season. This means that the effect of continuous vigilance and its subsequent effects on quality of life cannot be measured in these patients until the next season.

The reference value of the expectation may change over time due to new experiences, such as patient education or treatment [16].

Challenges in measuring and promoting HRQL in anaphylaxis

Expectations are a type of belief: they are beliefs about what will happen in the future. More specifically, patients with anaphylaxis have expectations about how they will feel and how their bodies will respond, about how they will be treated and how effective their treatment will be.

A primary aim of treatment in chronic diseases is to enhance quality of life by reducing the impact of the disease. By which strategies can impact be reduced in patients with anaphylaxis?

Strategies to improve patient education

If the clinician provides instruction about therapy and what patients should expect in the future, then patients' expectations may change. This assumes that clinicians provide patients with instruction about new expectations – and that patients understand and remember what the clinician says.

Education is based on common sense. Which aspects should be addressed? Patients enter and leave the clinic with a set of beliefs. Sometimes, the clinician knows what those beliefs are and sometimes they remain undiscovered. It is important to check these beliefs and, if necessary, attempt to re-adjust them. For example, a patient may have the erroneous idea that a next sting will likely be fatal.

In a study by Goldberg and Confino-Cohen [18], it turned out that despite immunotherapy, patients retained debilitating expectations which had an impact on their quality of life and were associated with increased distress. Thus, in this patient group, the knowledge that a treatment is effective was not always enough to change deeply held beliefs.

This is in contrast to our study [21] where standardized patient information together with immunotherapy in insect venom allergic patients was able to improve HRQL.

Thus, adequate information may help patients to adjust their expectations. HRQL measurements may be helpful in evaluating whether patients understand and remember the information and measure whether they have adjusted their experiences. This could lead to improvement of educational strategies which are truly evidence-based.

Strategies to reduce exposure

With the exception of insect-venom allergy, curative treatment is not available for most allergens and strict avoidance of the allergen is the only way to prevent a reaction. Current strategies are good dietary advice and improved labelling [19]. Other initiatives to support consumers at risk include a recognized standard for manufacturers seeking to eliminate an allergen from their production, and the integration of food allergy into training for caterers and food-standards enforcement professionals [19]. HRQL measurements can be used to evaluate whether these strategies are able to improve quality of life in affected patients.

Strategies reducing consequences of exposure

In addition to improving avoidance strategies, patients at risk for anaphylaxis should be supplied with kits for the self-injection of epinephrine and should be told to keep the kit with them at all times. In addition, in order to improve adequate therapy in the case of an anaphylactic reaction, patients subject to anaphylaxis can wear a Medic Alert bracelet or necklace and should keep an

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identification card in their wallet or purse. These strategies may have both positive and negative impacts on the quality of life. The burden of treatment with an Epipen has been studied in insect-venom-allergic patients [20]. It turned out that although, for many patients, it is reassuring to carry an Epipen and makes them feel safe, many patients also indicated that it is inconvenient and troublesome [20]. Patients who were negative about the Epipen especially indicated that they would not dare to use the Epipen if necessary and were afraid of possible side effects. Importantly, the Epipen could be perceived differently by food-allergic patients. This underlines the need for direct measurement with validated instruments before conclusions may be drawn.

Conclusion

The management of patients with anaphylaxis is challenging because patients only infrequently experience symptoms which are, however, of great clinical significance. As symptoms are infrequent, patients may easily develop erroneous expectations and unfounded beliefs about their illness. A major goal of management of these patients is appropriate education, and measurements of HRQL offer an opportunity to structure this point of the management of these patients in such a way that positive effects on HRQL are achieved. These effects can be measured with instruments specifically designed for this purpose, as outlined above. It is to be expected that many new instruments will be developed in the coming years to address these issues in the disease forms of anaphylaxis.

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