Quality of life in haemophilia

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Summary. There is a growing interest in patient-reported outcomes as measures for evaluating the benefits of new and existing treatments. Health-related quality of life (HRQoL) is one of these patient-reported outcomes and represents the individual experience and perception of illness/health together with the psychosocial response to disease-related and treatment-related symptoms. Generic and disease-specific HRQoL questionnaires enable us to assess and quantify the multi-dimensional perception of well-being, namely the physical components and the psychological (emotional, mental, social and behavioural) components of patient’s well-being and functioning. These instruments should be standardized and validated and they should prove to be reliable, valid, specific and sensitive in a similar manner to instruments created for objective parameters. HRQoL assessment can help us to evaluate the benefits of new treatments from the perspective of patient’s values and expectations. It can also help to evaluate the quality of care provided, in order to be able to improve it at a local and national level. Moreover, HRQoL assessment can be routinely assessed to monitor improvement and progress or deterioration and decline from the global point of view of each single patient, integrating the otherwise limited angle of objective signs and instrumental or lab parameters.

Keywords: haemophilia, patient outcome measure, quality of life, well-being

It is characteristic of the military mentality that nonhuman factors (atom bombs, strategic bases, weapons of all sorts, the possession of raw materials, etc) are held essential, while the human being, his desires, and thoughts – in short, the psychological factors – are considered as unimportant and secondary...The individual is degraded...to ‘human materiell’

Albert Einstein, 1955[1]

Introduction

Why we should assess quality of life

Incredible progress has been made in medical sciences. We are not only able to categorize signs and symptoms into well-defined syndromes (to provide a name to a disease is always extremely reassuring to the clinicians), but we are now able to recognize the organ involved, and, more precisely, the suffering tissue, the implicated cells of that tissue, the concerned cellular organelles, the affected DNA genes, the molecular defect of that gene. With Andreas Vesalius or van Wescle, who wrote in 1543 De humani corporis fabrica (On the Workings of the Human Body) [2], the human body was no longer considered as a unit, but it was dissected into its single parts, bones, muscles and organs. Starting in 1953, with the precise description of the deoxyribonucleic acid [3] containing the genetic instructions for the development and functioning of all known living organisms including human beings, the congenitally diseased person has been regarded more and more as the carrier of a genetic imperfection. Thanks to the progress of medicine, new ways to treat these diseases have become available over time: starting with surgery in the Neolithic Age, we have become able to remove the damage in the involved organ (and today, we can transplant the organ if it cannot be repaired); subsequently, more and more effective medicines have contributed to the reparation of the suffering tissue or substitute the missing...
protein; in this day and age, we can ultimately attempt to transplant or to repair genes when they are affected, or to regenerate tissues and organs with stem cell therapy.

As a result of this exciting progress, what we have probably lost is the patient, an individual with his integrity, personality, feelings, problems, wishes and hopes. ‘Individual’ derives from Latin individus, indivisible, from in- + dividuus, divided; an individual can be dissected in pieces only when he has lost his life. A human being is different from any other living beings for his humaneness, which cannot be placed in any organ or tissue; nevertheless, it should not be sacrificed in name of Science.

For this reason, overall well-being, as subjectively perceived by the individual affected by a disease, must not be ignored or considered secondary to other organ-, tissue-, cell-, lab test-specific but limited parameters, precise but partial surrogates of health. Medicine is a science applied to individuals, like anatomy and physiology, but completely different from these.

When the management of haemophilia was a struggle against a premature death and a pain-endured crippled life, physicians’ efforts were concentrated on prolonging the patient’s lifespan and in fighting pain and disability and its causes. This battle has not yet been won, but enormous progress has been accomplished and more and more physicians and patients are now struggling to improve the quality of the life of people with haemophilia.

Consequently, the study of methods to evaluate and quantify quality of life (QoL), in order to be able to monitor the outcomes of new therapies, should not be regarded as a superfluous, intellectual exercise that has recently become fashionable, but it should be considered an essential part of medical management. The subjectivity of patients, their perception and personal judgement should be at least taken into the same account as objective signs and instrumental parameters. The same concepts of ‘health’ and ‘disease’ are paradigms not mutually shared by people and their doctors. In other words, patients’ assessment of their own well-being should have the same degree of importance as MRI scores or factor VIII levels.

What is quality of life?

The essence of QoL, a synonym of well-being, was already being discussed in Aristotle’s time. In his Nicomachean Ethics [4], he announced the concept of eudaimonia or eudemonia (εὐδαιμονία), a Greek term consisting of the word ‘eu’ (‘good’ or ‘well-being’) and ‘daimōn’ (‘spirit’), a contented state of being happy and healthy and prosperous: eudaimonia should be our ultimate aspiration. Governments have tried to find objective indicators of QoL: the best known composite quality of life scale is the United Nations Development Programme’s Human Development Index [http://www.undp.org]. This index is a single value that puts together health, longevity, knowledge (literacy and school enrolment) and standards of living (GDP per capita) [5]. Alternatives to this purely economic approach include attempting to measure the non-economic aspects of the QoL [6], well-being as a hierarchy of needs [7], and even the ‘Gross National Happiness’ [8]. This interesting approach ‘links the economy with social and environmental variables to create a more comprehensive and accurate measurement tool’. In 1994, the World Health Organization has also provided a general definition of QoL [9], summarized as ‘the individual’s perception of his position in life in the context of culture and value system in which he lives, and in relation to his goals, expectations and concerns’.

In all of these definitions, from Aristotle to WHO, we can recognize two main subsets: QoL directly related to health (health-related quality of life, HRQoL) and QoL not related to health (non-health-related quality of life, NHRQoL); the latter consists of internal and external components, such as individual’s motivation, personality, coping strategies, social networking, financial status and also geographical and societal environments [10]. Both types of QoL have a great influence on the overall concept of quality of life and they reciprocally influence each other. Therefore, it is logical that even though in individuals in good health NHRQoL factors have a major influence, in individuals with chronic illnesses HRQoL factors have a much greater importance.

As a consequence of this reasoning, HRQoL can be defined as the ‘qualitative dimension of functioning’ [11] or the individual experience of illness with the psychosocial response to disease-related and treatment-related symptoms [12].

Discussion

Can HRQoL be assessed?

If HRQoL is based on the subjective perception of well-being, the major issue is whether or not it can be measured objectively. It looks a contradiction in terms. Subjectivity is very suspicious in the eyes of supporters of Medicine as an exact, hard science. Psychology itself is considered by these hard-boiled...
merely the absence of disease or infirmity
physical, mental and social well-being and not
compare our patients
not specific to a particular disease and we want to
if we want to have a general estimation of HRQoL,
ments should be specifically designed for the age of
adults and elderly people. For this reason, instru-
differ among small children, adolescents, young
it is commonsense that well-being concepts greatly
instruments is represented by the age of respondents:
proxies, normally family members or care-givers) to
perceived well-being or to ask observers (so called
asking patients to give an overall value to the
health should be considered
WHO clearly stated in 1946, in its constitution, that
cover the different aspects of health. In fact, the
the latter being essential to assess very small children
or mentally disabled people.
Another critical issue is the scope of the evaluation:
questions must be immediately comprehensible, unambiguous, covering
a single aspect of that specific domain we are
investigating, in plain language appropriate to the
age and the culture of the patient being interviewed. Therefore, these instruments must be psychometri-
cally, linguistically and cross-culturally validated
[19,20].

What HRQoL instruments are available?
Over the last 30 years, a number of generic instru-
tools and importance. For these physicians, ‘subjective’ is a synonym of ‘abstract’ and consequently not
measurable, not different from pain. By contrast, like
pain, it can be assessed and quantified by means of
self-administered questionnaires or interviews that
cover the different aspects of health. In fact, the
WHO clearly stated in 1946, in its constitution, that
health should be considered ‘a state of complete
physical, mental and social well-being and not
merely the absence of disease or infirmity’ [15].

Other methods to quantify HRQoL consist of
asking patients to give an overall value to the
perceived well-being or to ask observers (so called
proxies, normally family members or care-givers) to
rate HRQoL or to answer HRQoL questionnaires,
the latter being essential to assess very small children
or mentally disabled people.

An important issue concerning HRQoL assessment
instruments is represented by the age of respondents:
the latter being essential to assess very small children
or mentally disabled people.

Another critical issue is the scope of the evaluation:
if we want to have a general estimation of HRQoL,
not specific to a particular disease and we want to
compare our patients’ status with that of patients
with different diseases we must use a so-called
‘generic instrument’ [17]. If we aim to evaluate more
precisely the health and well-being of patients with a
specific disease, we should use a targeted or disease-
specific questionnaire [18]. It is evident that we
cannot use the same disease-specific instrument in
two different diseases (i.e. a haemophilia-specific
HRQoL questionnaire for patients with asthma and
vice versa). More and more frequently are patients
assessed with both generic and disease-specific
instruments in order to get the best from each type
of instrument.

In addition, since we are going to ask patients (or
their proxies) for information about their perception
of well-being and functioning, the questions must be
immediately comprehensible, unambiguous, covering
a single aspect of that specific domain we are
investigating, in plain language appropriate to the
age and the culture of the patient being interviewed. Therefore, these instruments must be psychometri-
cally, linguistically and cross-culturally validated
[19,20].

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Name</th>
<th>Reference</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>KINDL</td>
<td>Lebensqualitätsfragebogens für Kinder</td>
<td>Bullinger et al. [21]</td>
<td>Germany</td>
</tr>
<tr>
<td>CHQ</td>
<td>Child Health Questionnaire</td>
<td>Landgraf et al. [22]</td>
<td>USA</td>
</tr>
<tr>
<td>TACQOL</td>
<td>TNO AZL Child Quality Of Life</td>
<td>Theunissen, et al. [23]</td>
<td>Netherlands</td>
</tr>
<tr>
<td>Peds-QL</td>
<td>Pediatric Quality of life Inventory</td>
<td>Varni et al. [24]</td>
<td>USA</td>
</tr>
<tr>
<td>KIDSSCREEN</td>
<td>Health Related Quality of Life Questionnaire for Children and</td>
<td>Ravens-Sieberer et al. [25]</td>
<td>Europe</td>
</tr>
<tr>
<td></td>
<td>Young People and their Parents</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DCGM-37</td>
<td>DISABKIDS Chronic Generic Measure</td>
<td>Bullinger et al. [26]</td>
<td>International</td>
</tr>
</tbody>
</table>
interesting to note that there are different versions of HaemoQoL according to children’s age (4–7 years, 8–12 years and 13–16 years) in order to better capture all the aspects of their well-being in the different developmental phases. In addition, it has an index version (HaemoQoL Index) that allows for comparison among the different age groups. There are three versions of the French Qual-Hemo questionnaire: for children, for adolescents and for adults.

Among the haemophilia-specific HRQoL instruments, there are differences and similarities: Table 5 shows the areas covered by the different questionnaires. It is important to note that the Italian Haem-A-QoL has a core instrument with shared items with the paediatric Haemo-QoL that allows for comparison between HRQoL of adults and children. This questionnaire for adult patients with haemophilia has been linguistically validated in over 20 languages. A version of this questionnaire has been developed for elderly patients and will be presented at Hemophilia 2008 World Congress.

Because of these instruments’ multiplicity, diversity and the lack of gold standard, physicians are not encouraged to use them. The choice is not simple and must be on the basis of the aim of the evaluation, the age of patients, the design of the study, and the characteristics of the instruments available. Table 6 shows the study-related issues and Table 7, the instrument-related issues to take into account when choosing the particular instrument to use [48].

Conclusions

Can HRQoL assessment contribute to haemophilia care?

HRQoL assessment has become more and more popular: in fact, it offers the unique opportunity to have a validated measure of the patient’s perception.
of the overall effect of haemophilia care provided, an irreplaceable patient-rated outcome measure. It helps to weigh the benefits of old and new treatment strategies or new drugs, by asking the patient what benefit, what improvement of well-being, he has eventually obtained from that particular treatment. Knowing the patient’s opinion of his health not only research benefits but also quality of the overall structure of haemophilia care and how it is delivered, promoting initiatives to correct and improve it. In addition, HRQoL assessment can help in comparing the health care systems or haemophilia care resources among countries, in order to push governments, administrators, communities and any other stakeholders to match and harmonize their national health services to that of other countries.

Last, but not the least, HRQoL assessment can be applied in the routine assessment of patients with haemophilia, similar to the annual check-up of joint status or viral screening. It can help to verify whether or not the treatment provided to each single patient is the right one, able to maintain or to improve his QoL, which is his perception of well-being, his ‘eudaimonia’, his happiness.

Table 5. Common domains of haemophilia-specific quality of life (QoL) questionnaires for adult patients.

<table>
<thead>
<tr>
<th>Areas</th>
<th>Medtap</th>
<th>Haem-A-QoL</th>
<th>Hemofilia-QoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td>Physical function</td>
<td>Physical health</td>
<td>Physical health</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>Sports and leisure</td>
<td>Joint damage</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>–</td>
<td>Pain</td>
</tr>
<tr>
<td>Functional</td>
<td>Role function</td>
<td>Work and school</td>
<td>Daily functioning</td>
</tr>
<tr>
<td>Social</td>
<td>Psychosocial-related</td>
<td>Family planning</td>
<td>Relationship/social activities</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>Partnership and sexuali ty</td>
<td>–</td>
</tr>
<tr>
<td>Emotional</td>
<td>Fear/worry</td>
<td>Feeling</td>
<td>Emotional functioning</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>View</td>
<td>–</td>
</tr>
<tr>
<td>Mental</td>
<td>–</td>
<td>Future</td>
<td>–</td>
</tr>
<tr>
<td>Treatment and disease</td>
<td>Treatment worry</td>
<td>Treatment</td>
<td>Treatment satisfaction</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>Dealing</td>
<td>Treatment difficulties</td>
</tr>
<tr>
<td>No. of domains</td>
<td>6</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>No. of items</td>
<td>46</td>
<td>46</td>
<td>36</td>
</tr>
</tbody>
</table>

Table 6. Study-related Issues for the choice of a questionnaire.

<table>
<thead>
<tr>
<th>Issue</th>
<th>Type</th>
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</thead>
<tbody>
<tr>
<td>Study design</td>
<td>Prospective/cross-sectional</td>
</tr>
<tr>
<td></td>
<td>Observational/interventional</td>
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<tr>
<td></td>
<td>National/international</td>
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<tr>
<td></td>
<td>Cross-illness comparison</td>
</tr>
<tr>
<td>Study population</td>
<td>Children/Adults/Both</td>
</tr>
<tr>
<td></td>
<td>Capable or not to answer a questionnaire</td>
</tr>
<tr>
<td>Study outcomes</td>
<td>Clinical (functioning)</td>
</tr>
<tr>
<td></td>
<td>Psychosocial (quality of life, coping, etc.)</td>
</tr>
<tr>
<td></td>
<td>Cost-related (cost-utility, cost-benefit, etc.)</td>
</tr>
<tr>
<td></td>
<td>Patient preference</td>
</tr>
<tr>
<td></td>
<td>Patient satisfaction</td>
</tr>
<tr>
<td>Time of administration</td>
<td>Baseline</td>
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<tr>
<td></td>
<td>Short-term follow-up</td>
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<tr>
<td></td>
<td>Long-term follow-up</td>
</tr>
</tbody>
</table>

Table 7. Instrument-related issues for the choice of a questionnaire.

<table>
<thead>
<tr>
<th>Issue</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who fills in the questionnaire</td>
<td>Children/adults/both</td>
</tr>
<tr>
<td>Type of questionnaire</td>
<td>Patient/proxy</td>
</tr>
<tr>
<td>Psychometric characteristics</td>
<td>Generic</td>
</tr>
<tr>
<td></td>
<td>Chronic generic</td>
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<tr>
<td></td>
<td>Disease-specific</td>
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<tr>
<td>Feasibility of the instrument</td>
<td>Reliability</td>
</tr>
<tr>
<td></td>
<td>Validity</td>
</tr>
<tr>
<td></td>
<td>Sensitivity</td>
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<tr>
<td>Validation of the instrument</td>
<td>Comprehensibility</td>
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<tr>
<td></td>
<td>Acceptance</td>
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<tr>
<td></td>
<td>Relevance</td>
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<tr>
<td></td>
<td>Completion time</td>
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<tr>
<td></td>
<td>Linguistic</td>
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<tr>
<td></td>
<td>Cross-cultural</td>
</tr>
<tr>
<td></td>
<td>Physical (autonomy, functioning, pain, sport and leisure)</td>
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<tr>
<td></td>
<td>Mental (emotional, stress, etc)</td>
</tr>
<tr>
<td></td>
<td>Coping strategies</td>
</tr>
<tr>
<td></td>
<td>Social (integration and functioning, relationships)</td>
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</tbody>
</table>
References


