QUALITY OF LIFE: HOW TO ASSESS IT IN CLINICAL TRIALS

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It has been estimated that as much as eighty percent of the U.S. health care expenses goes toward the care of patients with chronic diseases. The goal of therapy for these patients is not "cure", but improvement in function as a result of decreased symptoms or severity of illness, or limitation in the progression of their disease[1]. The question of interest today is whether or not medical treatments result in a life of better quality, thus enabling the patient to live a more comfortable, productive and satisfying life. Physicians must take into consideration when selecting their treatment modalities the quality of life as well as the prolongation of life.

Quality of life is a collective term that encompasses multiple components of a person's physical, social and mental status. Simply defined it is the person's ability to function normally within society as perceived by the individual persons[2].

The multiple components of quality of life are frequently divided into three basic categories: functional capacity, patient perceptions and symptoms and their consequences. Functional capacity can be further subdivided into[1]: sense of well-being and satisfaction with life, physical state, emotional state, intellectual functioning and ability to perform in social roles and the degree of satisfaction derived from those roles.

It should be emphasized that the quality of life is important as it is perceived by the individual patient; therefore, it is a subjective rather than an objective measure.

In 1947, the World Health Organization incorporated a definition of health in its constitution affirming that "health is not only the absence of infirmity and disease, but also a state of physical, mental and social well-being"[3], thus insinuating the concept of quality of life. The first scale of performance, developed over 40 years ago, is still widely used by clinicians and has been shown to correlate well with quality of life indices.

More recently there has been a trend to use quality of life measures as target outcomes for treatment in specific diseases, including various cancers, arthritis, hypertension, endstage renal disease and diabetes. Spitzer and colleagues in 1981[4] developed one of the few early scales designed specifically to measure quality of life. Since then a significant number of scales and indices have been developed. Many clinicians acknowledge the need for good outcome indicators that can be useful in structuring and transmitting clinical information.

Quality of life assessment

Questionnaires are frequently the basis for most quality of life instruments. It is strongly recommended that the questionnaire be compact enough to enable repeated use, yet comprehensive enough to adequately evaluate components of quality of life[5]. Many clinicians will be unfamiliar with the concept of "quality of life", and will likely reject any instrument which is not short, concise and easy for them to administer.

Development of an evaluation generally includes six stages[6]: item selection, reduction in number of items, questionnaire format, pretesting, reproducibility and responsiveness, and validity.

Reproducibility refers to the test's ability to reproduce the same results in similar test situations. The responsiveness or sensitivity of the test is its ability to detect clinically important changes that may recur as the result of a treatment. Validity is the test's ability to measure what it purports to measure.

There is no standard set of rules available to design a quality of life instrument. Often investigators find it necessary to construct disease-specific indices or indices that can be used in a single clinical trial. Proper selection of an already existing test instrument is determined by the disease under study, the design and hypothesis of the clinical trial, the psychometric requirements and the practical considerations such as time, cost and mode of administration[1]. Factors, including how easy the test is to administer and score, how reliable and valid are the measures, and how sensitive the measures are to change, should also be considered.

Quality of life measurements can be easily biased by the respondent or the analysis process. Responses to questionnaires may be influenced by the patient's knowledge and expectations of both the disease state

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and treatment[7]. Deaths and withdrawals from the study are often unreported in the study analysis and thus contribute a major source of bias in that the results will be based only on those patients who are able and willing to complete the study.

Despite these and other difficulties in measuring the concept of quality of life, investigators should accept the measurements as a means of determining the benefits and consequences of treatment in clinical trials. Quality of life variables may be particularly useful when marginal differences in survival between treatments are being compared, when a treatment is highly effective in decreasing mortality, but is toxic with resultant morbidity, when the therapy is life long, when the disease complication rate is low and when patients are asymptomatic or have mild symptoms[1].

Some of the more popular test measures used in research and development include: sickness impact profile[8]—a self—or interviewer administered test in which the patient reports dysfunction in behavior which they attribute to their illness; McMaster health index questionnaire[9]—an index which includes measuring of physical, social and emotional behavior; Nottingham health profile[10]—a two-part instrument which measures the extent to which the patient's health problems effect their everyday activities; Psychological general well-being schedule[11]—scores the effects of health status on psychological general well-being, uniquely including both positive and negative well-being measurements; General health rating index [12] ¾ a subjective index based on an excellent-good-fair-poor appraisal system; Quality of well-being scale[13]—an interview style assessment of physical activity, mobility, social activities, symptoms and health problems.

Hypertension therapy: implication in quality of life

In a clinical trial involving chronic therapy, the effectiveness of the intervention is greatly dependent on the patient's adherence to the therapy schedule. The treatment of a disorder may have profound effects on the quality of life, which can in turn affect patient adherence. Quality of life evaluations help the patient to record any attitude or lifestyle changes that can ultimately influence their compliance with a particular drug therapy. Side-effects due to medications have been known to interfere with long-term compliance of treatment. This is especially true with asymptomatic conditions such as mild to moderate hypertension. If physicians were to select drugs that do not worsen quality of life for the hypertensive patient, it is more likely that the intended long-term benefits of the therapy would occur as the result of improvement in compliance rates.

The treatment of mild hypertension has always been a controversial issue, with many authorities questioning the extent of benefits achieved from therapy. Most experts will recommend that even the asymptomatic patient with mild hypertension be placed on therapy in order to prevent the progression of the disease or its related disorders.

Use of antihypertensive drugs has been found to impair several aspects of quality of life including sexual function, mental alertness, psychological status and exercise tolerance. For these and other reasons, compliance with antihypertensive therapy is a major obstacle facing the physician at all levels of treatment. Up to 50% of patients fail to follow through with referral advice; more than 50% of those who begin treatment drop out within one year and only two-thirds of those who continue treatment consume enough medication to achieve adequate blood pressure reduction[14]. It becomes difficult to convince patients to continue in treatment of their mild hypertension when the effects of the treatment make them feel worse than they did before drug therapy. This becomes a serious drawback for mild hypertensive patients who will often not reap the benefits of treatment until years later.

Health related quality of life research has gained importance as a result of changes in the health care industry, with perhaps increased competition being the most significant factor. There are often several alternative therapies for a specific condition, all approved for efficacy and safety. Demonstrating that one therapy yields a better quality of life than its competition is a valid and effective method of differentiation [15].

Pressure on cost-containment has also contributed to research of quality of life as government restrictions attempt to reduce medical reimbursements. Health care providers hope to insure that patients receive the best drugs for their money with increased concern over the quality of life that these drugs provide.

There has been much recent attention focused on quality of life and antihypertensive therapies as a result of the captopril advertising campaign. The captopril study was an attempt to assess the physical, social and psychological components of quality of life as they relate to antihypertensive drugs. The study was conducted as a multicenter, randomized, double-blind clinical trial that compared the effects of three major antihypertensive drugs—captopril, methyldopa and propranolol—on the quality of life and control of blood pressure in mild to moderate hypertension[1]. At periodic intervals during the trial questionnaires were administered to assess quality of life. Five components were measured, including: sense of well-being and satisfaction with life; physical state; emotional state; intellectual functioning and ability to perform in social roles.

Well-being included factors of mood, energy level, life satisfaction and morale. Captopril was the only drug that demonstrated an improvement in general well-being. Twenty percent of those on methyldopa and 15% of those on propranolol reported worsening in their well-being status. Negative effects using capto-

pril were not found in any of the quality of life categories, whereas methyldopa and propranolol did. Nevertheless the study also demonstrated captopril's inferior effectiveness as a monotherapy in the treatment of hypertension[8].

The Working Group for Mild Hypertension in 1984 estimated the number of mild hypertensive (DBP > 90 and < 104 mmHg) in USA to be about 24 million, with over 10 million currently receiving antihypertensive medications at an estimated cost of $ 2.5 million[16]. More than 50% of these patients can achieve blood pressure control with a single agent and up to 90% are controlled with the addition of a second drug. Many critics of the health care system believe that the condition is often treated without regard to any adverse effects on a patient's quality of life. Therapy may affect quality of life by demands on the patient's daily routines and lifestyle, such as medication-taking, dietary alterations and time commitments for long-term follow-up visits[17]. Mental and physical side effects often make it necessary for the patient to reappraise the value of their therapy.

It has been reported that an adverse effect on quality of life occurs in almost two-thirds of the patients on antihypertensive drugs. In a 1982 study in Great Britain by Jachuck[18], quality of life after antihypertensive drug therapy was measured in 75 patients using questionnaires administered to the patients, their relatives and their physicians. Physicians identified a 100% improvement in patients based on blood pressure control and absence of clinical deterioration or patient complaint. Patient self-assessment showed 48% with improved feelings and 8% with actual worsening of feelings. Relatives indicated improvement in only one patient, while 25% showed mild adverse changes, 45% with moderate changes and 30% with severe worsening of the condition after anti-hypertensive therapy.

It should be acknowledged that the "labelling effect" or "sick roll behavior" that previously asymptomatic patients experience after diagnosis of hypertension may affect psychological well-being, but these findings are not significant enough to dismiss the effects on quality of life.

Final considerations

In summary, we feel that traditional medical concepts are much concerned with classifying and measuring symptoms, whereas quality of life concepts examine the ways and extent to which these symptoms affect a person's ability to function in daily life activities. Quality of life is concerned with self-reports of health and for that reason, has been faulted for being dependent on subjective information. Studies have shown that a person's perception of his/her health is the best predictor of the person's consumption of health care[19]. Subjective perceptions provide information regarding patient concerns that are not accessible from laboratory tests or physical examination[8].

Quality of life research has the potential to affect government regulations, medical practice and consumer behavior. As a result of the captopril advertising campaign focusing on the drug's quality of life effects, sales rose 71% in the second quarter of 1986, indicating that both physicians and consumers have weighed a higher cost and slightly inferior efficacy against an enhanced quality of life and decided that feeling better while getting better may be more important than cost and effectiveness[8].

In conclusion the use of quality of life measures in clinical trials provides valuable information regarding patient concerns and perception of illness and medical care and may lead to the production of drugs that are more attractive to the public.

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