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Initial development and validation of a mitochondrial disease quality of life scale

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Abstract

Mitochondrial diseases are a clinically diverse group of genetic disorders that often present to neurologists. Health related quality of life (HRQOL) is increasingly recognised as a fundamental patient based outcome measure in both clinical intervention and research. Generic outcome measures have been extensively validated to assess HRQOL across populations and different disease states. However, due to their inclusive construct, it is acknowledged that not all relevant aspects of a specific illness may be captured. Hence there is a need to develop disease specific HRQOL measures that centre on symptoms characteristic of a specific disease or condition and their impact. This study presents the initial conceptualisation, development and preliminary psychometric assessment (validity and reliability) of a mitochondrial disease specific HRQOL measure (Newcastle Mitochondrial Quality of life measure (NMQ)). NMQ is a valuable assessment tool and consists of 63 items within 16 unidimensional domains, each demonstrating good internal reliability (Cronbach's $\alpha \geqslant 0.83$) and construct validity.

Keywords: Quality of life; Mitochondrial disease; Questionnaire

1. Introduction

Mitochondrial disorders are a clinically multifarious group of genetic disorders that affect the central nervous system and skeletal muscles and other organs heavily dependent on aerobic metabolism. They are typically characterised by multi-system involvement. They have extensive phenotypic and disease burden variability and although a disease rating scale [1] exists which monitors the spectrum and rate of progression of disease, it does not assess the psychological and social impact of having a mitochondrial disorder.

Health related quality of life (HRQOL) is increasingly recognised as a fundamental patient-based outcome measure in both clinical intervention and research. Generic outcome measures have been extensively validated to assess HRQOL across populations and different disease states. However due to their inherent generic construct they may not fully capture all relevant aspects of a specific illness [2]. It is recognised that there is a need to develop disease-specific HRQOL measures that centre on the symptoms and impact characteristic of

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a specific disease or condition [3]. We present the initial conceptualisation, development and preliminary psychometric evaluation (validity and reliability) of a mitochondrial disease-specific HRQOL measure.

2. Methods

2.1. Subjects and source of items

Eligible participants were defined as adult patients (18 years and above) with a known biochemical or genetic diagnosis of mitochondrial disease. Subjects were excluded if they had cognitive impairment that prevented questionnaire comprehension or were unable to read English.

Domain and item content validity of the pilot questionnaire was assured by deriving item content through semi-structured key-informant interviews. Investigators conducted two focus groups to explore patients' perceptions of the physical, psychological and social impact of mitochondrial disease through open questions and the employment of the 'Gap Model' technique [4]. Themes which were perceived as influential on HRQOL in mitochondrial disease and arose during the interview processes or from review of other neurological and HRQOL instruments [5–8] were categorised into representative life domains as verified independently by three investigators.

2.2. Questionnaire design

Questionnaire design was determined by reference to questionnaire design guidelines and by advice from a survey methods consultant. A four week recall period and an adjective rating scale (never, occasionally, sometimes, often, always, not applicable) were selected as the most appropriate recall time-frame and response scale respectively. To test basic comprehension and acceptability, and prior formal piloting, a first draft questionnaire was piloted on randomly selected patients with mitochondrial disease. Relevant changes were made.

2.3. Item reduction and validation

Patients attending the Newcastle mitochondrial disease clinic were asked to complete the pilot questionnaire to (1) confirm that the items and domains selected from the interviews and review of other HRQOL instruments were representative; (2) to highlight any issues that may have been omitted; (3) to facilitate item reduction. Preliminary data were evaluated to assess endorsement rate, scale reliability and variability. With the use of five criteria, both item and domain contributions to the scale were evaluated. Domains were assessed by prespecified criteria [9]: (1) Items as a whole were evaluated using frequency of endorsement. Those with very high (>80%) or low (<20%) endorsement rates, of any one category, were removed as such items are unlikely to be sufficiently discriminatory. (2) Domain variability was assessed using factor analysis. An Eigen value cut off point of 0.95 was used, as it was a requirement that each domain would be unidimensional. Any items within a domain with a cumulative Eigen value >0.95 were eliminated. (3) To test the internal reliability of each item within a domain, item-total correlations were calculated; an item-total correlation of greater than 0.20 were accepted as indicative of adequate internal reliability; items with item-total correlation of $\leqslant$0.20 were eliminated. (4) Items were removed where the Cronbach's α for the constituent domain was greater if that item was removed than if the item was retained. (5) Domains with a Cronbach's α <0.70 or >0.95 were dropped. Once redundant items were removed face to face cognitive interviews were conducted to verify comprehension and ensure face validity.

2.4. Psychometric evaluation

The amended questionnaire (NMQ: Newcastle Mitochondrial-Quality of life measure) was piloted again to facilitate further content validity and psychometric evaluation. Subjects were asked to complete NMQ and a validated HRQOL measure (SF-36) [10]. Data were evaluated to assess endorsement rate and scale reliability (internal consistency reliability) and variability. Construct validity was assessed by comparing questionnaire responses to comparable elements of the SF-36. Multi-trait analysis was used to examine correlations within and across similar and dissimilar domains in each instrument; we anticipated that scales measuring similar constructs (for example, Role physical (SF-36) and mobility (NMQ)) would be more highly correlated with one another than those tapping dissimilar constructs. Known group validity was established using the Newcastle Mitochondrial Disease Adult Scale (NMDAS) [1], a validated measure of disease burden and a surrogate for phenotypic severity, with one-way analysis of variance performed. Subjects were divided into 3 groups according to their NMDAS scores (Group 1: 0–24 (mild); Group 2: 25–49 (moderate); Group 3: 50 and above (severe)) disease burden. This allowed the assessment of how well the questionnaire was able to distinguish changes in quality of life in relation to disease severity. It was expected that there would be a negative relationship between NMQ and NMDAS scores, that is, the greater the disease burden, the poorer the perceived quality of life, reflected in lower NMQ scores.

2.5. Scoring methods

The raw score (obtained by adding across all items in the domain) for each NMQ domain (Never: 5; rarely: 4, sometimes: 3, often: 2 and always: 1) was transformed to a 0–100 score, as in the calculation of subscale scores for the SF-36, by the following formula