Journal of the Neurological Sciences 352 (2015) 53–57

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

A longitudinal study of the Friedreich Ataxia Impact Scale

Geneieve Tai [a], Eppie M. Yiu [a,c,d], Louise A. Corben [a,b], Martin B. Delatycki [a,b,c,e,*]

[a] Bruce Lefroy Centre for Genetic Health Research, Murdoch Childrens Research Institute, Parkville, Victoria 3052, Australia
[b] School of Psychological Science, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, Victoria 3168, Australia
[c] Department of Paediatrics, University of Melbourne, Parkville, Victoria 3052, Australia
[d] Department of Neurology, Royal Children's Hospital, Parkville, Victoria 3052, Australia
[e] Department of Clinical Genetics, Austin Health, Heidelberg, Victoria 3084, Australia

ARTICLE INFO

Article history:
Received 18 November 2014
Received in revised form 16 February 2015
Accepted 13 March 2015
Available online 21 March 2015

Keywords:
Friedreich ataxia
Health status
Rating scales
Friedreich Ataxia Impact Scale

ABSTRACT

Background: Quality of life in Friedreich ataxia (FRDA) has been explored using various generic health status measurement tools, most commonly the Short Form Health Survey Version 2 (SF-36v2). The tool did not address many specific issues related to disease impact in people with FRDA. The Friedreich Ataxia Impact Scale (FAIS) was developed to examine clinically relevant areas in FRDA. The aims of the current study were to assess the relationship between the FAIS and clinical characteristics of FRDA, as well as to determine the responsiveness of the FAIS to change over one and two years.
Methods: One hundred and four individuals with FRDA, homozygous for the GAA expansion in intron 1 of *FXN*, completed the FAIS at baseline. Seventy individuals completed the FAIS again 12 months later and 49 completed the FAIS at 24 months. Clinical parameters and neurologic scales (Friedreich Ataxia Rating Scale (FARS)) were also recorded.
Results: The total FARS score, onset age and disease duration correlated significantly with FAIS subscales measuring symptoms and physical functioning. The physical and mental summary measures of the SF-36 V2 also correlated well with the FAIS subscales. Speech was the only subscale that demonstrated significant change over one and two years.
Conclusions: The FAIS provides valuable insight into the perspective of individuals with FRDA on their health status, and is an important measure of morbidity. It has, however, limited responsiveness to change and its use in intervention studies is questionable.

1. Introduction

Friedreich ataxia (FRDA) is an autosomal recessive neurodegenerative disorder that affects approximately 1 in 29,000 individuals [1]. It is characterised by progressive ataxia, scoliosis and cardiomyopathy [2]. The age of onset is typically within the first two decades of life, and individuals are wheelchair-bound approximately ten to fifteen years after disease onset [3].

The progression of FRDA can be assessed using neurological rating scales including the Friedreich Ataxia Rating Scale (FARS), the International Cooperative Ataxia Rating Scale (ICARS) and the Scale for the Assessment and Rating of Ataxia (SARA) [4–7]. These measurement tools provide objective information on the clinical status of individuals with FRDA but are limited as they do not encompass the perspectives of affected individuals with regards to the impact of disease on their health and well-being [5].

Patient reported outcomes (PROs) are valuable because they capture aspects of the disease that clinician administered measures are unable to. Additionally, the US Food and Drug Administration has decreed PROs be included in all therapeutic trials [8].

PROs can be classified as either generic or disease specific. Generic PROs can be used in specific clinical conditions or the general population. The most widely used PRO is the Medical Outcomes Study 36-item Short Form Health Survey (SF-36) [9–11]. Version 2 of the SF-36 was developed to reduce the floor and ceiling effects observed in the first version [12]. The main disadvantage of generic tools is that they do not take into account concerns that are specific to the condition of interest, and potentially provide an inaccurate reflection of an individual's perspective of their health status [11]. Disease-specific PROs, on the other hand, are designed to address issues unique to the condition being studied [11].

The health impact of FRDA has previously been studied using various generic health status measurement tools, including both versions of the SF-36 [13–15], as well as the self-reported Barthel Index (BI), the Generic Health Questionnaire (GHQ-12), EuroQoL (EQ-5D) [13], the PedsQL 4.0 Generic Core Module and the Multidimensional Fatigue Scale [16]. Limitations of these generic health measurement tools

* Corresponding author at: Bruce Lefroy Centre for Genetic Health Research, Murdoch Childrens Research Institute, Flemington Rd, Parkville, Victoria 3052, Australia. Tel.: +61 3 9496 4355; fax: +61 3 8341 6390.
E-mail address: martin.delatycki@ghsv.org.au (M.B. Delatycki).

http://dx.doi.org/10.1016/j.jns.2015.03.024
0022-510X/

include significant ceiling and floor effects [13,14], particularly in both versions of the SF-36, and poor responsiveness to change [13] which may indicate decreased sensitivity of the tool in identifying significant areas of health affected by FRDA.

The limitations of using generic PROs to measure health impact in FRDA supported the development of a FRDA-specific tool. As a result, the Friedreich Ataxia Impact Scale (FAIS) was developed. The FAIS aims to assess the health impact of FRDA on affected individuals [17] and is currently the only published FRDA-specific PRO. The FAIS comprises 126 items grouped into eight independent subscales, measuring three areas identified as being clinically important to individuals with FRDA: 1) symptoms, 2) physical functioning, and 3) psychological and social impact. Symptoms encompass speech and body movement. Physical functioning includes upper limb function, lower limb function and complex tasks. Psychological and social impact comprises mood, self-perception and isolation [17].

All items on the FAIS initially offered five-point responses (*not at all bothered, a little bothered, moderately bothered, quite a bit bothered* and *extremely bothered*). However participants were unable to distinguish between the five options provided. Post hoc analyses were conducted and response options were firstly reduced from five to four (*not at all bothered, a little bothered, moderately bothered,* and *extremely bothered*). Further analysis resulted in the decrease of response options to three (*not at all bothered*, *moderately bothered*, and *extremely bothered*). The final tool resulted in six subscales with three response options (body movement, speech, upper limb functioning, complex tasks, self-perception, and isolation) and two subscales with four response options (lower limb functioning and mood) [17]. The FAIS was designed to be used together with current clinician-administered rating scales to capture the true health impact of FRDA [18,19]. It was constructed using Rasch methodology, and is psychometrically robust [17].

The aims of this study were to assess the relationship between the FAIS and clinical characteristics of FRDA, and to determine the responsiveness of the FAIS to change over one and two years. We hypothesized that the FAIS would correlate with disease characteristics of FRDA and summary scores of the SF-36 V2, and that the FAIS would be able to capture the impact of FRDA on health over time.

2. Materials and methods

2.1. Participants

Individuals aged 18 years and older and homozygous for a GAA expansion in intron 1 of *FXN* were recruited from the Friedreich Ataxia Clinic at Monash Medical Centre in Victoria, Australia. Participants were invited to participate at the time of their annual clinic appointment and received the FAIS via the post prior to their clinic appointment. This enabled participants to complete the FAIS in their own time without time pressures. Participants were encouraged to return completed forms at their clinic appointment. If participants were unable to complete the form due to physical limitations they were encouraged to seek assistance from a carer or family member to record their responses.

2.2. FAIS

The version of the FAIS used in this study was provided by Dr Jeremy Hobart to the authors in 2005. It differs slightly to the version that was ultimately published [17]. The version of FAIS used in the current study comprised 117 items, instead of 126 [17]. In addition, each item in the version used in this study consisted of five, rather than three or four responses. In order to provide a comparable scale to the published FAIS, responses were rescored and collapsed into either the three or four responses used in the original scale. Methods of collapsing the subscales were provided to us by Dr Hobart. The version of the FAIS used in this study is shown in Supplementary Table 1.

2.3. Data analysis

Overall FAIS subscale scores were generated by summing subscale item responses without weighting or standardization as per Likert's method of summated ratings [20]. The eight subscale scores were then transformed to have a range of 0 to 100, with a higher score indicating greater impact of FRDA on health and well-being. The subscales were scored independently to create eight separate scores. Further detail on how the scores were developed is described in Cano at el. (2009) [17].

Descriptive analyses were used to examine the baseline characteristics of the cohort. Normal distribution for the FAIS subscales was evaluated using the skewness and kurtosis test for normality and generating Q–Q plots. Given the data were not normally distributed, Spearman's rank correlation coefficients were utilized to correlate the FAIS subscales with disease parameters. Disease parameters included in the correlation analyses were age at disease onset, disease duration (age at review minus age at disease onset), GAA1 (smaller) and GAA2 (larger) intron 1 *FXN* repeat sizes and total Friedreich Ataxia Rating Scale (FARS) score [7]. The FAIS subscales were also correlated with the Physical Component Summary (PCS) and the Mental Component Summary (MCS) of Version 2 of the SF-36.

Responsiveness is the ability of a tool to detect clinically relevant change over a period of time [21]. This was examined in the FAIS by measuring the change in median subscale scores using Wilcoxon signed-rank test between baseline and 12 months, and between baseline and 24 months.

All statistical analyses were performed using Stata Statistical Software: Release 12 (StataCorp. 2011. College Station, TX: StataCorp LP).

2.4. Ethics committee approval

Approval for this study was obtained from the Southern Health Human Research Ethics Committee (HREC 02114A). All participants gave informed, written consent in accordance with the Declaration of Helsinki.

Table 1
Participant characteristics at baseline, Year 1 and Year 2.

	Baseline (n = 104)	Year 1 (n = 70)	Year 2 (n = 49)
Age at review (years)			
Mean (SD)	33.6 (12.1)	34.4 (11.4)	36.6 (12.4)
Range	18–70	19–59	20–62
Gender			
Male (%)	54 (51.9)	37 (52.9)	25 (51.0)
GAA1 repeat size			
Mean (SD)	632.9 (236.9)	642.4 (210.0)	642.1 (206.4)
Range	56–1099	182–1099	182–1050
GAA2 repeat size			
Mean (SD)	866.4 (210.7)	894.7 (200.3)	913.0 (198.0)
Range	182–1345	182–1345	182–1345
Age of onset (years)			
Mean (SD)	15.5 (7.5)	15.4 (6.5)	16.1 (6.5)
Range	3–40	3–30	3–30
Disease duration (years)			
Mean (SD)	18.0 (10.3)	18.8 (10.1)	20.2 (10.6)
Range	2–42.3	3–43.3	4–46.3
FARS score			
Mean (SD)	91.8 (30.4)	85.4 (24.6)	91.5 (24.3)
Range	19–151	28.2–132	30–127

Legend: SD—standard deviation, GAA1 smaller *FXN* GAA repeat size GAA2 larger *FXN* GAA repeat size FARS—Friedreich Ataxia Rating Scale.