Clinical Neurophysiology 125 (2014) 1255–1260

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

Loss of motor unit size and quadriceps strength over 10 years in post-polio syndrome

A. Bickerstaffe [a,*], J.P. van Dijk [b,c], A. Beelen [a], M.J. Zwarts [c], F. Nollet [a]

[a] Department of Rehabilitation, Academic Medical Center (AMC), Postbus 22660, 1100 DD Amsterdam, The Netherlands
[b] Radboud University Nijmegen Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Department of Neurology/Clinical Neurophysiology, Postbus 910, 6500 HB Nijmegen, The Netherlands
[c] Epilepsy Centre Kempenhaeghe, Postbus 61, 5590 AB Heeze, The Netherlands

ARTICLE INFO

Article history:
Accepted 2 November 2013
Available online 12 November 2013

Keywords:
Post-polio syndrome
Motor unit size
Quadriceps strength
High-density surface EMG
Prospective cohort study

HIGHLIGHTS

- Patients with post-polio syndrome (PPS) lost both strength and motor unit (MU) size over 10 years, and the rate of decline in strength was related to the rate of decline in both MU size and number of active MUs.
- Patients with PPS lost relatively less strength than healthy controls, possibly indicating reduced sarcopenia of the remaining muscle mass of the patients.
- Size diminution of enlarged MUs combined with a reduced number of active MUs contributes to the gradual strength decline in PPS.

ABSTRACT

Objective: To investigate whether strength decline in post-polio syndrome (PPS) results from excessive distal axonal degeneration of enlarged motor units.
Methods: We assessed changes over 10 years in isometric quadriceps strength, mean motor unit action potential (MUAP) size, root mean squared (RMS) amplitude, and level of interference (LOI) in 47 patients with PPS and 12 healthy controls, using high density surface EMG. At baseline, all patients had symptomatic quadriceps dysfunction, evidenced by transmission defects on single-fibre EMG.
Results: MU size and strength declined significantly by 20% and 15%, respectively in patients with PPS. Those with the largest initial MU sizes exhibited the greatest losses of mean MU size (27%) and proportional decreases in quadriceps strength (23%). Initial strength, change in LOI and change in RMS amplitude together explained 35% of the variability in strength changes in patients. MU size of controls did not change, although they lost 29% strength.
Conclusions: MU size and strength declined concomitantly in a homogeneous cohort of patients with PPS and quadriceps dysfunction.
Significance: This long term follow-up study provides evidence that size diminution of enlarged MUs combined with a reduced number of active MUs contributes to the gradual strength decline in PPS.

1. Introduction

Post-poliomyelitis syndrome (PPS) is a neurological condition that occurs 25–40 years after acute polio and affects a large proportion of the estimated 20 million polio survivors worldwide (March of Dimes Foundation, 2000). In PPS, muscle strength declines at a rate of 1–2.5% annually (Stolwijk-Swuste et al., 2005, 2010; Daube et al., 2009). Based on studies that demonstrated isolated atrophy of muscle fibres rather than the loss of whole motor units (MUs), the loss of strength is thought to result from

Abbreviations: PPS, post-polio syndrome; MU, motor unit; EMG, electromyography; HDsEMG, high density surface electromyography measurements; MVC, maximal voluntary contraction; MUAP, motor unit action potential; RMS amplitude, root mean squared amplitude; LOI, level of interference; IQR, interquartile range.

* Corresponding author. Tel.: +31 20 5666915.
E-mail addresses: a.bickerstaffe@amc.uva.nl (A. Bickerstaffe), dijkh@kempenhaeghe.nl (J.P. van Dijk), j.a.beelen@amc.nl (A. Beelen), ZwartsM@kempenhaeghe.nl (M.J. Zwarts), f.nollet@amc.nl (F. Nollet).

1388-2457/$36.00
http://dx.doi.org/10.1016/j.clinph.2013.11.003

excessive distal axonal degeneration of pathologically enlarged MUs (MU size diminution) (Wiechers and Hubbell, 1981; Cashman et al., 1987; Dalakas, 1995). Despite wide acceptance of this theory, recent electromyography (EMG) studies have reported the opposite: group increases or no change in average MU size over time along with loss of whole MUs (Maselli et al., 1992; Ivanyi et al., 1994; Grimby et al., 1998; Sandberg and Stalberg, 2004; Daube et al., 2009). The absence of evidence for loss of MU size in PPS so far, besides sporadic findings of MU size and strength diminution in people with very large initial units (Ivanyi et al., 1994; Grimby et al., 1998), warrants further research into the role of axonal loss in the pathophysiology of strength decline in PPS (Nollet, 2010).

In 2000, based on high-density surface EMG (HD-sEMG) measurements, we observed low strength and greatly enlarged MUs in the vastus lateralis muscles of 66 patients with PPS that had proven quadriceps dysfunction, compared to 13 healthy controls (Horemans, 2003; Drost et al., 2004). The present study investigated this homogenous cohort 10 years later and compared changes in MU size and muscle strength with those in healthy controls. We hypothesised that both MU size and muscle strength would decrease over time; that the rate of decline of these two variables would be related in patients with PPS, with the greatest declines occurring in those with severely enlarged MUs at baseline; and occur at a higher rate than in healthy controls.

2. Methods

2.1. Participants

Sixty-six adults with PPS that had completed HD-sEMG measurements in a randomised controlled trial of pyridostygmine between 1999 and 2001, were invited to participate in the present study in 2010 (Horemans (2003)). Thirteen healthy controls that had undergone HD-sEMG measurements during the same period were also approached for retesting (Drost et al., 2004). The criteria for the diagnosis PPS were an onset of progressive and persistent new weakness and/or abnormal muscle fatigability in polio survivors, after a period of stable neurological functioning, and the absence of other medical conditions that could explain the symptoms (March of Dimes Foundation, 2000). In this study, all individuals with PPS specifically had symptoms of PPS in either one or both quadriceps muscles at baseline. The patients also showed evidence of neuromuscular transmission defects on a single-fibre EMG, indicative of ongoing denervation and reinnervation, and they had no important comorbidities. Detailed inclusion and exclusion criteria are described elsewhere (Horemans, 2003). No new inclusion criteria were applied in the present follow-up. The only new exclusion criterion was the presence of any newly developed disease that affected voluntary control of the quadriceps muscle under investigation. All participants provided written informed consent, and the study was approved by the institutions' Medical Ethics Committee.

2.2. Study design

In this prospective cohort study, all participants underwent strength and HDsEMG measurements at baseline (2000) and follow-up (2010). Baseline data was obtained during the pyridostigmine trial before starting medication (Horemans, 2003). Measurements were performed on the strongest symptomatic quadriceps muscle of each participant at baseline, and the same leg was tested at follow-up. In healthy controls, the strongest leg was chosen unless unilateral joint or muscle problems were present.

2.3. Measurements

The measurement protocol was as described previously (Drost et al., 2004). Briefly, a rectangular electrode grid composed of 130 gold-coated electrodes (electrode diameter: 1.5 mm; inter-electrode distance: 5 mm), was placed over the vastus lateralis muscle, such that 10 columns with 13 electrodes each were positioned parallel to the muscle fibres. A reference electrode was placed on the patella. Monopolar signals were recorded, amplified, bandpass-filtered, and analogue-to-digital-converted with a multichannel amplifier system; the BioSemi Mark-6 was used in 2000 (bandwidth 3–400 Hz, sampling rate of 2000 Hz); in 2010, a similar system was used: the passive version of the BioSemi ActiveTwo (bandwidth DC-400 Hz, sampling rate of 2048 Hz).

Peak knee extension force was defined as the highest of three isometric maximal voluntary contractions (MVCs). MVCs were performed on a hard-surfaced, fixed chair dynamometer with the knee and hip flexed at 90°. The lower leg was strapped to a lever arm containing force transducers and visual feedback was provided by displaying the attained force on a screen.

Force and HDsEMG recordings were synchronised using a common time code. HDsEMG data was high-pass filtered (10 Hz, fourth-order Butterworth filter) and stored for offline analysis. Single motor unit action potentials (MUAPs) were extracted from bipolar EMG recordings of five, 30-s contractions between 5% and 20% MVC with a new, semi-automated software programme (Gligorijevic et al., 2013) based on the principles used in manual analyses (Blok et al., 2001; Zwarts and Stegeman, 2003; Kleine et al., 2007). Results obtained with automated detection were highly correlated to results from manual decomposition of similar real data (Gligorijevic et al., 2013). To exclude variability in analysis techniques, all baseline data were re-analysed according to a standard protocol by the first author with this programme. After removing duplicate MUAPs, the area under the curve of each remaining MUAP was determined over a period of 50-ms of the monopolar signal, from the electrode nearest the endplate zone (Fig. 1). MUAP sizes were calculated after MUAP extraction had been completed for all participants at both time points; this eliminated the possibility of investigator bias. The average area under the curve of all detected single MUAPs (the mean MUAP size) was calculated for each patient. The accuracy of MU size determination based on MUAPs extracted from HD-sEMGs has been verified extensively (Roeleveld et al., 1997; Blok et al., 2001; Zwarts and Stegeman, 2003).

In addition, the raw HDsEMG signal at 60% MVC was analysed to identify complementary MU characteristics related to strength production and maintenance. All variables were determined from signals in the electrode column with the highest mean signal amplitude, over a 2-s segment of the HDsEMG-signal, taken during the first 10-s of a stable 60% MVC.

MU size calculations at 5–20% MVC are biased towards type I MUs; consequently, we investigated root mean squared (RMS) amplitudes under high force conditions for an additional indication of the average MU size, measured when all MU types were active. Also, the level of interference (LOI) provided information about the number of active MUs. The LOI was defined as the percentage of the total recording time that consisted of segments of electrophysiological activity, i.e. bipolar turns that exceeded the noise threshold (Drost et al., 2004). Data from 60% MVC was chosen over 100% MVC, because many patients with PPS were unable to sustain a stable maximal contraction.

2.4. Statistical analysis

Statistical analysis was performed with the SPSS statistical software package (version 19.0.0.1). The primary outcome measures