

Mastication and oral motor function in McArdle disease: patient reported complaints

CV Kouwenberg¹, NC Voermans¹, R Quinlivan², L van den Engel-Hoek³

¹ Department of Neurology, Donders Institute for Brain, Cognition, and Behaviour, Radboud University Medical Centre, Nijmegen, the Netherlands

² MRC Centre for Neuromuscular Diseases and Department of Molecular Neuroscience, University College London Institute of Neurology and National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, UK

³ Department of Rehabilitation, Donders Centre for Neuroscience, Radboud University Medical Centre, Nijmegen, the Netherlands

Corresponding author:

Dr. N.C. Voermans
Neurologist
Radboud University Medical Centre
Department of Neurology
P.O. Box 9101
6500 HB Nijmegen
The Netherlands
Phone: 0031 243615187
Email address: Nicol.Voermans@radboudumc.nl

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Abstract

BACKGROUND: Exertional myalgia and cramps of the limb and trunk muscles are typical in McArdle disease, but mastication and oral motor limitations have not been systematically investigated before.

OBJECTIVE: Determine the reported prevalence and characteristics of limitations on oral motor activities, mastication, swallowing, and other oral motor activities in patients with McArdle disease.

METHODS: An observational study was carried out in 28 patients using a standardised questionnaire on mastication and oral motor function.

RESULTS: 57% of the participants reported difficulties with mastication. Muscle cramps during mastication occurred in 57% of the patients. Dysphagia including a feeling that food remains in the throat occurred in 32%. Adaptations during mastication were needed in 42% of the patients. Mastication difficulties, muscle cramps during mastication and mastication adjustments were inversely correlated with age ($r_2=-0.445$, $p<0.05$; $r_2=-0.509$, $p<0.01$; $r_2=-0.456$, $p<0.05$). Dysphagia, cramps during mastication and during other oral motor muscle activities, were correlated with disease severity ($r_2=0.476$, $p<0.01$; $r_2=0.463$, $p<0.01$; $r_2=0.461$, $p<0.01$; $r_2=0.432$, $p<0.05$).

CONCLUSIONS: In short, reported mastication difficulties are prevalent in people with McArdle disease, most frequently in younger people. Therefore, awareness of mastication and oral motor problems is required.

Keywords: McArdle disease, glycogen storage disease type V, mastication, oral motor function.

Introduction

McArdle disease (glycogen storage disease type V) is a rare autosomal recessive disorder of glycogen metabolism affecting exclusively striated muscle. Most affected individuals have no detectable muscle glycogen phosphorylase, as a consequence affected people cannot utilize stored muscle glycogen as an energy source. This leads to exercise-induced myalgia, muscle stiffness, fatigue and mild limb-girdle weakness in some patients over 40 years of age. When exercise is continued, painful muscle cramps occur, contracture and eventually rhabdomyolysis [1]. Another typical sign is the second wind phenomenon, which occurs due to a switch to extra-muscular fuel substrates required for aerobic metabolism with increased muscle blood flow [2, 3].

Since chewing and swallowing involves repetitive, sometimes powerful activity of the bulbar muscles, McArdle disease is expected to be associated with symptoms of oral motor activities. However, reports on oral motor dysfunction is limited to two case reports describing tenderness and myalgia of the masticatory muscles while chewing [4, 5]. We performed an observational study (1) to determine the prevalence and characteristics of patient-reported oral motor limitations (mastication, swallowing and other) in people with McArdle disease; (2) to determine the correlation between oral motor limitations and age and disease severity.

Materials and Methods

Participants

Participants were identified from the database of the Radboud university medical centre. We invited all 35 known patients with McArdle disease in our neuromuscular expertise centre on neuromuscular disorders. In this questionnaire-based study, 28 people with McArdle disease took part (10 males and 18 females), ranging ages between 18 and 83 years. The diagnosis of McArdle disease was confirmed by DNA analysis of *PYGM* in 25 of the participants and by muscle biopsy (demonstrating an absence

of muscle glycogen phosphorylase and accumulation of glycogen) and non-ischemic forearm test (ammonia rise without lactate rise) in two participants. In one person DNA analysis was not performed, because a sibling with the same symptoms showed compound heterozygous mutations in *PYGM* confirming McArdle disease. All participants were also registered in the EUROMAC registry [6].

Questionnaire

All participants received and returned a semi-quantitative questionnaire by mail or email. The questionnaire involved 11 questions concerning oral motor activities (mastication, swallowing and other) [7]. Disease severity was determined from the patients' medical records and was measured on a scale from 0 to 3, with 0: asymptomatic or virtually asymptomatic (mild exercise intolerance but no functional limitation in any daily life activity). 1: exercise intolerance during exercise, myalgia and limitation of acute and strenuous exercise and occasionally in daily life activities; no record of myoglobinuria, no muscle wasting or weakness. 2: same as 1 plus recurrent exertional myoglobinuria, moderate restriction in exercise and limitation in daily life activities. 3: same as 2 plus fixed muscle weakness with or without wasting and severe limitation on exercise and most daily activities [6]. This severity scale was validated for McArdle disease and other rare glycogenolytic disorders.

Statistical analysis

Descriptive statistics were used to determine the general characteristics of the participants, and the prevalence of the reported complaints concerning mastication, swallowing and other oral motor activities. The Spearman correlation coefficient was used to determine the relation between age and disease severity, and symptoms associated with mastication and dysphagia. Results with two-tailed p -values < 0.05 were considered significant. Statistical analyses were carried out using SPSS 22.0 for Windows (IBM Corp., Armonk, NY, USA).

Results

A total of 28 people with McArdle disease participated in this study, of which 29% ($n = 8$) had a disease severity score of 1; 57% had a disease severity score of 2; and 14% a score of 3 (Table 1). None were asymptomatic. Of the participants, 57% reported difficulties with mastication. Thirteen participants (46%) reported the need for adaptations during mastication that involved chopping the food or avoiding chewy meat. Three participants (11%) reported to eat very slowly, one of whom needed more than 30 minutes to complete his meal. Muscle cramps during mastication occurred in 57% of the participants, one of them reported 'very frequent' cramps (multiple times a day). Cramps in muscles of the jaw, tongue or lips during other oral motor activities were reported less often (46%, $n = 13$). These activities included blowing, laughing, talking, sucking or playing a wind instrument. Most cramps took place during blowing (11%) or laughing (11%). Two participants reported more cramps in the evening, and one had more cramps in the morning. Dysphagia in terms of the inability to swallow occurred 'rarely' (less than once daily) in only three of the participants (11%). Almost one third of the participants (32%, $n = 9$) reported that they sometimes experienced a feeling of food sticking in their throat.

Mastication problems ($r_2 = -0.445$, $p < 0.05$), cramps during mastication ($r_2 = -0.509$, $p < 0.01$), and mastication adjustments ($r_2 = -0.456$, $p < 0.05$) were significantly inversely correlated to age (Table 2). The correlation between age and other characteristics was not statistically significant. Three characteristics were significantly correlated with disease severity with $p < 0.01$, namely feeling of food sticking in the throat ($r_2 = 0.476$), cramps during mastication ($r_2 = 0.463$), and cramps of the jaws, tongue or lips during other oral motor activities ($r_2 = 0.461$). The correlation between disease severity, and cramps in muscles of the jaw, tongue or lips during other oral motor activities (blowing, laughing, talking, sucking or playing a wind instrument) was 0.432 , $p < 0.05$. The prevalence of mastication problems was correlated with mastication adjustment (yes/no) ($r_2 = 0.546$, $p = 0.003$).

Discussion

This questionnaire-based study in 28 people with McArdle disease showed that mastication limitations are frequently reported (57%). Mastication difficulties were reported more frequently in younger people, while in most other neuromuscular disorders limitations increase during age. Most likely, people with McArdle disease learn to cope with these limitations over time. This is in line with Martin et al. (2014) who showed that most affected people can have relatively normal lives, because they learn to adjust their daily activities [8]. In people over age 40 years, fixed skeletal muscle weakness, mostly proximal, was described to be more common, and occurred in about one fourth of the participants [8]. Weakness of masticatory muscles was not investigated; this would be focus of future research. However, we hypothesize that older patients adapt to the masticatory weakness if it occurs and experience no or only mild mastication limitations. We showed that indeed almost 50% of the participants adapted their solid food intake by cutting it into smaller pieces, by the consumption of softer foods or limited amount of solid foods. This compensation advice is in line with the general recommendations given to prevent limb and trunk muscle cramping in McArdle disease.

Fibre-type composition of the jaw and tongue muscles is very different from that of limb and trunk muscles, which have a combination of type I, IIa and IIx myosin heavy chains (MyHC). Jaw muscle fibres are more hybrid, with contractile properties providing fine gradation of movement and force. Glycogen accumulation in McArdle disease occurs in type II fibres, which are also found in the tongue and masseter muscles [9]. Korfage et al (2005) stated that the large variation in fibre types among individuals is influenced by the amount and pattern of activation [9]. Furthermore, a study by Krag et al (2016) showed that relationships between fibre type composition and glycogen metabolism are complicated [10]. We hypothesize that possible differences between fibre type composition of the masseter in McArdle disease and the unclear relationship between fibre type composition and glycogen metabolism might explain differences and wide range of complaints on mastication in our study group.

The limitation of this study is that it only consists of a semi-quantitative questionnaire. The questionnaire was validated in other diseases [7]. Hence, it was not specifically designed for use in McArdle disease and did not contain any specific questions on second wind phenomenon. Nevertheless, occurrence of a second wind phenomenon in general was reported by 82% of the participants, and second wind occurring specifically during chewing is frequently encountered in the population in our clinic. This study is the first to investigate experienced mastication and oral motor limitations in people with McArdle disease. The results of the questionnaire were not counterchecked by directly visiting patients and discussing with them about their masticatory (and other) problems. Hence, the logical next step would be to do further research with experimental data and to take notice of masticatory problems in the consulting room.

In short, this questionnaire study shows a prevalence of reported mastication impairment of 57% in people with McArdle disease. This impairment occurs more frequently in a younger age group. Therefore, awareness of mastication and oral motor limitations is required to adequately advise people with McArdle disease about mastication and oral motor function: avoid peak load during mastication, eat smaller pieces, choose soft food, start slow and take more time to eat. Furthermore, they can be reassured that limitations are not expected to worsen with ageing since most people seem to learn to adequately compensate for this.

Acknowledgements

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Conflict of Interest

The authors have no conflict of interest to report.

Table 1: Participant characteristics and frequencies of complaints concerning mastication, swallowing and oral motor function

Participants characteristics	<i>N (%)</i>
Mean age (SE)	45 (\pm 3.3)
Sex	
Male	10 (35.7%)
Female	18 (64.3%)
Disease severity*	
0	0
1	8 (28.6%)
2	16 (57.1%)
3	4 (14.3%)
Mastication problems	
Never	12 (42.9%)
Rarely	13 (46.4%)
Sometimes	2 (7.1%)
Very often	1 (3.6%)
Always	0
Mastication adjustments	
Never	15 (53.6%)
Chopping the food	1 (3.6%)
No chewy mead	6 (21.4%)
Limitation of solid food	1 (3.6%)
Only soft or ground food	0
Other adjustments	3 (10.7%)
Combination of chopping and no chewy mead	1 (3.6%)
Combination of chopping and other adjustments	1 (3.6%)
Mealtime duration	
Normal	27 (96.3%)
More than 30 minutes	1 (3.6%)
Feeling of food sticking in throat	
Never	19 (67.9%)
Rarely	8 (28.6%)
Sometimes	1 (3.6%)
Very often	0
Always	0
Muscle cramps during mastication	
Never	12 (42.9%)
Rarely	12 (42.9%)
Sometimes	3 (10.7%)
Very often	1 (3.6%)
Always	0
Muscle cramps during other oral motor activities	
Never	15 (53.6%)
Rarely	11 (39.3%)
Sometimes	2 (7.1%)
Very often	0
Always	0
Activity during cramps	
Never	18 (64.3%)
Blowing	1 (3.6%)
Laughing	1 (3.6%)
Talking	1 (3.6%)
Sucking	1 (3.6%)
Playing wind instrument	2 (7.1%)
Multiple activities	4 (14.3%)
Influence of time on cramps	
Yes	25 (89.3%)
No	3 (10.7%)
Not able to swallow	
Never	25 (89.3%)

Rarely	3 (10.7%)
Sometimes	0
Very often	0
Always	0
Influence of time on swallowing	
No	26 (92.9%)
Yes	2 (7.1%)

**Disease severity, 0: asymptomatic or virtually asymptomatic (mild exercise intolerance but no functional limitation in any daily life activity). 1: exercise intolerance contractures, myalgia and limitation of acute and strenuous exercise and occasionally in daily life activities; No record of myoglobinuria, no muscle wasting or weakness. 2: same as 1 plus recurrent exertional myoglobinuria, moderate restriction in exercise and limitation in daily life activities. 3: same as 2 plus fixed muscle weakness with or without wasting and severe limitation on exercise and most daily activities.*

Table 2: Spearman correlation coefficients between age and mastication complaints, swallowing and oral motor activities, and between disease severity and mastication complaints, swallowing and oral motor activities

Mastication complaints, swallowing and oral motor activities	Spearman correlation coefficients, n=28	
	<u>Correlation with age</u>	<u>Correlation with disease severity</u>
Sex	-0.66	-0.17
Age	-	-0.16
Disease severity	-0.16	-
Mastication problems	-0.45*	0.35
Mastication adjustments	-0.46*	0.34
Mealtime duration	-0.30	0.05
Feeling of food sticking in throat	0.18	0.48 **
Muscle cramps during mastication	-0.51 **	0.46**
Muscle cramps during other oral motor activities	-0.29	0.46**
Activity during cramps	-0.32	0.43 *
Influence time on cramps	-0.01	-0.10
Not able to swallow	-0.17	0.26
Influence time on swallowing	-0.22	0.27

Significance: * $p < 0.05$; ** $p < 0.01$.

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