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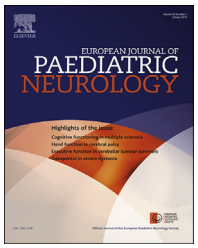

Original Article

Quality of life and cognitive functions in early onset multiple sclerosis

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ABSTRACT

Background: Multiple sclerosis (MS) is a demyelinating disease of the CNS occurring in young adults and even in children in 5% of cases. Lower quality of life (QoL) and cognitive impairment (CI) (40–54%) have been reported in early-onset MS (EO-MS) patients.
Objective: To assess QoL and cognitive function in EO-MS and their relationship, also considering demographic and clinical variables.
Methods: Paediatric Quality of life inventory Version 4.0 for patients aged 13–18 and 19–25 years, Beck Depression Inventory II (BDI II) and the Rao Brief Repeatable Battery were performed in EO-MS patients (onset age ≤25years). EDSS and MSSS were performed at same time. After testing for normal distribution, group comparisons were performed through the two-tailed Student's t test, one-way analysis of variance (ANOVA) and linear or logistic regression when appropriate. The Bonferroni correction for multiple testing was used when appropriate.
Results: 59 patients were included (mean age: 20 ± 3.6; Female sex 52.54%). 34 patients had a paediatric onset (<18 years) while 20 patients had a juvenile onset (18 < age < 25 years) of disease. 5 patients were excluded for missing data.

HR-QoL was higher in paediatric than juvenile MS patients ($p = 0.02$), and it was inversely related to EDSS ($p = 0.0005$) and Multiple Sclerosis Severity score (MSSS) ($p = 0.0001$).

Sixtyone % of patients showed a CI at BRB. No association was found between CI and any socio-demographic and clinical data.

HR-QoL total score was not related to CI status nor to any domain-specific cognitive function score, even considering BDI as possible bias.

CI was related to social, physical functioning score and EDSS ($p = 0.01$) at a logistic regression backward stepwise estimation.
Conclusion: HR-QoL resulted to be better in paediatric than juvenile MS onset patients and was inversely related to rapidity of disability accumulation, while cognitive impairment was

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influenced by physical disability and poor social involvement (school, education …). Social participation, affective relations and psychological flexibility could have a protective function on CI.

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1. Introduction

Multiple sclerosis (MS) is a chronic immune-mediated disease causing in inflammation, demyelination, and neurodegeneration of the Central Nervous System (CNS). Mean age at onset is 28 years old[1] but paediatric onset (before 18 years of age) is increasingly recognized, representing from 3% to 5% among adults with MS.[2–5]

Health-related quality of life (HRQoL) is a multi-domain concept that refers to the effect of an illness and its therapy upon a patient's physical, psychological and social wellbeing, as perceived by the patients themselves. In clinical research, HRQoL measures can capture the personal and social context of the patient's experience of the disease. QoL measures have increasingly been considered to evaluate disease progression, treatment and care in MS patients.[6,7] In addition, the US Food and Drug Administration (FDA) and the European Medicines Agency encourage the use of QoL assessment in patients with chronic illnesses,[8,9] and there are different detailed recommendations for QoL assessment.[10,11]

Despite the acknowledgement of the need to consider QoL issues, its assessment remains under-utilized in MS clinical practice, with particular regard to early onset MS.[12]

Recently paediatric MS patients reported lower HRQoL scores than healthy controls,[13] however little is still known about the correlations between cognitive impairment and QoL in early onset MS.

Cognitive impairment is well-documented in adult-onset cases of MS[14] and has been reported in 40–54% of the patients with early-onset MS.[15] Its role in affecting directly activities of daily living and overall quality of life, is still controversial in adult onset MS,[16] however its presence in the early phases of disease is considered as an unfavourable prognostic factor.[17]

Aim of our study is to assess HRQoL and cognitive functions in a cohort of EO-MS patients and to analyse their relationship, with additional regard to possible demographic and clinical influencing variables. We also evaluated the difference between QoL in paediatric and juvenile onset MS patients.

2. Patients and methods

This is a cross-sectional study carried out on MS patients referred to MS clinic for children and young people at Federico II University ("SMAG centre). Inclusion criteria were age older than 12 and early onset (before 26 y) of RRMS or CIS, diagnosed according to 2010 McDonald's criteria[18] at least 12 months previously (to avoid the influence of recent communication of diagnosis on psychological status). Patients were all living with their parents and were not married and had no children. At the moment of evaluation, all the cases were relapse-free and had not taken steroids for at least 30 days. Socio-demographic data (age, sex and education level) and clinical data (age at onset, disease duration, expanded disability status scale [EDSS], multiple sclerosis severity score [MSSS],[19] disease modifying therapy, DMT) were collected by trained neurologists (RL, AC). We classified patients into paediatric onset (<18 y) and juvenile onset (between 18 and 25 y).

HRQoL was self administered using the Paediatric Quality of life inventory (PedsQoL)Version 4.0. and than assessed by two psychologists (AN, VM).

This is a self-reported questionnaire in two versions, one for subjects aged from 13 to 18 years, the other for subjects aged between 19 and 25 years. The questionnaire consists of 23 items that constitute 4 sub-scales measuring: physical functioning (8 items), emotional functioning (5 items), social functioning (5 items) and scholastic/working functioning (5 items). Each item is accompanied by a 5-points Likert scale, where the subject has to indicate how often this situation occurred, with 0 meaning "never" and 4 meaning "almost always". The internal consistency of the instrument is very good (for alpha = . 90).

Scores are transformed on a scale from 0 to 100. Items are reversed scored and linearly transformed to a 0–100 scale as follows: 0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0, so that higher scores indicate better HRQoL. The Total Score is the sum of all the items over the number of items answered on all the Scales, while the Psychosocial Health Summary Score is the Sum of the items over the number of items answered in the Emotional, Social, and School Functioning Scales.[20]

Cognitive function was assessed using the Brief Repeatable Battery (BRB) of neuropsychological tests for multiple sclerosis, version A, by a trained neuropsychologist (TC).

The BRB includes: the Selective Reminding Test-Long Term Storage (SRT-LTS), Selective Reminding Test-Consistent Long Term Retrieval (SRT-CLTR) and Selective Reminding Test-Delayed/SRT-D) to assess verbal memory; the 10/36 Spatial Recall Test (10/36 SPART) and 10/36 Spatial Recall Test-Delayed (10/36 SPART-D) to assess visual memory; the Symbol Digit Modalities Test (SDMT) to assess information processing speed and executive functions; the Paced Auditory Serial Addition Test 2 and 3 s (PASAT 2–3) to assess attention, information processing speed, and working memory: the Word List Generation (WLG) to assess the semantic fluency.[21] We used the 5th percentile of normative data[21] as cut-off score for test failure. As normative BRB data are not available in paediatric MS patients and we did not include any healthy control (HC) group, we used normative data for adult MS patients.[21] Comparing normative data for adult with those of a paediatric control group,[15] when applicable, we found that the 5th percentile cut-off of each test for adults was more

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