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Impact of multidisciplinary care in amyotrophic lateral sclerosis hospitalizations in the public health system of Brazil

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There is evidence that multidisciplinary care improves quality of life and there is a growing appreciation of public policies in Brazil that favor home care with a multidisciplinary team in chronic diseases. This study aimed to determine the epidemiological profile of amyotrophic lateral sclerosis in the Federal District and the impact of tertiary reference center creation on patient care. A descriptive, cross-sectional study analyzing secondary data regarding mortality and hospitalizations for amyotrophic lateral sclerosis patients over 10 years and clinical and epidemiological profiles of patients evaluated at the Center of Reference for Neuromuscular Disease over three years was used. An incidence rate of 1.3/100,000 person-years over 20 years and an age at onset of 49.3 ± 15.1 years (Hospital Information System) and 57.2 ± 12.3 years (at the Center admission) was observed. The risk of death was greater in patients older than 75 years (RR = 4.05, p = 0.0018) and in bulbar-onset patients (RR = 2.53, p = 0.0027). Multidisciplinary care reduced 75% of hospitalization frequency and length of stay (p = 0.03) and 80 to 90% of the reimbursement value of hospitalization (p = 0.05). The adoption of multidisciplinary care has improved the efficiency of patient care for amyotrophic lateral sclerosis in the Brazilian public health system.

Key words: Amyotrophic lateral sclerosis, multidisciplinary care, public health.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) has an average worldwide incidence of 2.08/ 100,000 person-years (Chiò et al., 2013) and is a disease of unknown etiology that leads to motor disability, speech disorders, dysphagia and respiratory failure. The median survival time ranges from 24 to 48 months (Turner et al., 2013; Forbes et al., 2004). In the last twenty years, numerous clinical trials with drugs and cell therapies have been conducted, but only Riluzole has shown efficacy in slowing the progression of symptoms (Hardiman et al., 2011). Since

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1989, there is a large body evidence that shows multidisciplinary care improves quality of life, but there is still doubt as to if it increases survival time (Andersen et al., 2012, Miller et al., 1999). In European countries, this is well established; however, there is lack of evidence on the impact of the multidisciplinary treatment of ALS in Latin America, especially in relation to the public health system of Brazil. There is currently a growing appreciation of public policies in Brazil that favor home care with a multidisciplinary team in non-specific chronic diseases (Leopoldina et al., 2015). The objective of this study was to determine the incidence of ALS, the epidemiological and clinical profiles of patients and their survival at three years of follow-up, analyzing the efficiency of a tertiary Reference Center for Neuromuscular Diseases (CRDN) in the Public Health System (SUS) in the Federal District, Brazil.

METHODOLOGY

In September, 2011, the CRDN was created; a multidisciplinary unit composed of Medical Neurologists, Pulmonologists, Physical Therapists, Occupational therapists, Psychologists, Nutritionists and Speech Therapists. The goals included: guiding patients and their families; reducing complications of immobility, dysphagia and respiratory failure; implementing the home ventilation program; and giving support to professionals of the home care program (PID). In April, 2013, the Secretariat of Health of Federal District (SES-DF) approved a dehospitalization protocol and started hiring home care, restricting the length of hospitalization of chronic patients in the ICU. A cross-sectional, descriptive study was performed, using three data sources:

1. Mortality data were obtained using the TabWin application from the mortality information system (MIS) of the Federal District, Brazil, between January, 2005 and December, 2014, to estimate the incidence of disease. We used the 2010 Census (IBGE, 2014) for calculating incidence.
2. Admissions data were obtained using the TabWin application from the reduced hospitalar information system (HIS) of the Federal District, between January, 2005 and December, 2014, related to hospital admissions in the SUS.
3. Records from the CRDN at the Secretariat of Health of the Federal District (SES-DF) were analized through the TrakCare software application, with data obtained between September, 2011 and December, 2014. Probable and defined ALS with diagnosis performed by neurologists using El Escorial criteria (Ludolph et al., 2015) after exclusion of other diseases were included. All patients used Riluzole and underwent electromyography.

The following parameters were analyzed: Disease frequency, gender distribution, site of onset, age, diagnostic delay time, duration of disease, electromyography confirming the diagnosis, frequency and length of stay, reimbursements of hospital admission authorizations (AIH), use of the intensive care unit (ICU) in the SUS, and use of domiciliary mechanical ventilation.

The disease duration was defined as the time period between the first symptom and death or tracheostomy (in days). Efficiency measures were frequency, length of stay, reimbursement of AIH and ICU costs. Data were recorded in Excel 2010 and statistical analyses was performed using SAS 9.3 and SPSS 19.0 applications. Chi-square test was used for categorical variables and the two-tailed Student's t-test for quantitative variables, with a 0.05 significance level. Multivariate analyses of survival including all clinical variables was conducted. Initially, Cox regression univariate analysis with $p < 0.25$ was selected for inclusion in the multivariate Cox regression analysis. The final multivariate regression model was built by successive exclusion variable-to-variable from the initial multivariate model, using the likelihood ratio test to determine the importance of each variable excluded (Collett, 2003). The level of significance was 0.05. The survival functions for the patients were estimated using the Kaplan-Meier method and compared using the log-rank test.

This study protocol was approved by the Ethics Committee of the Research and Education Foundation in Health Sciences – (FEPECS/SES, number 820 117/2014 Protocol). The Ethics Committee waived the written consent form because the study consisted of analysis of patient records (many of them were deceased) and public domain databases.

RESULTS

To estimate the regional incidence of ALS in ten years, we used mortality data (MIS). Between 2005 and 2014, the MIS of the Federal District recorded 162 deaths above 20 years of age: 93 men and 69 women with mean ages of 61.5 ± 12.6 years and 65.1 ± 12.2 years, respectively, which was not significantly different ($p = 0.059$). So, the adjusted incidence of the disease above 20 years of age was estimated in 1.3/100,000 person-years and 2.6/100,000 person-years, adjusted above 45 years of age, considering the population of 2,570,160 inhabitants, according to the 2010 Census of the Brazilian Institute of Geography and Statistics – IBGE (IBGE, 2014). It was observed that 97 (59.9%) deaths occurred between 60 and 79 years of age (data not shown). In the same 10-year period, the HIS recorded 172 hospitalar admissions with the same diagnosis: 103 men and 69 women, with a mean age of 49.3 ± 15.1 years. In females, the average age was 45.6 ± 13.9 years, significantly lower than the average male age of 51.7 ± 15.4 years ($p = 0.01$).

Figure 1 compares the ALS incidence mortality-based with the hospitalar admissions and shows that the frequency of ALS hospitalization has fallen by 75% between 2012 and 2014, while the incidence based on mortality was sustained. Between 2005 and 2011, the average annual rate of hospitalizations was 21.6 ± 5.6 hospitalizations/year (range: 15 to 27). Between 2012 and 2014, this average dropped to 7 ± 1.7 admissions per year, with a range of 5 to 8 ($p = 0.03$). The average length for an in-hospitalar stay was 17.1 ± 3.2 days in the first period and 15.0 ± 2.5 days in the second, which was not significant ($p = 0.48$).

Table 1 shows the annual change in frequency, length of stay and reimbursement amounts to the AIH, and amounts transferred by the SUS for ICU spending. It was observed that the higher frequency of hospitalizations occurred in the years 2009, 2007 and 2005 and there was a sharp decline between the years 2012 and 2014. Although the average length of stay did not show significant variation, the total days of hospitalization

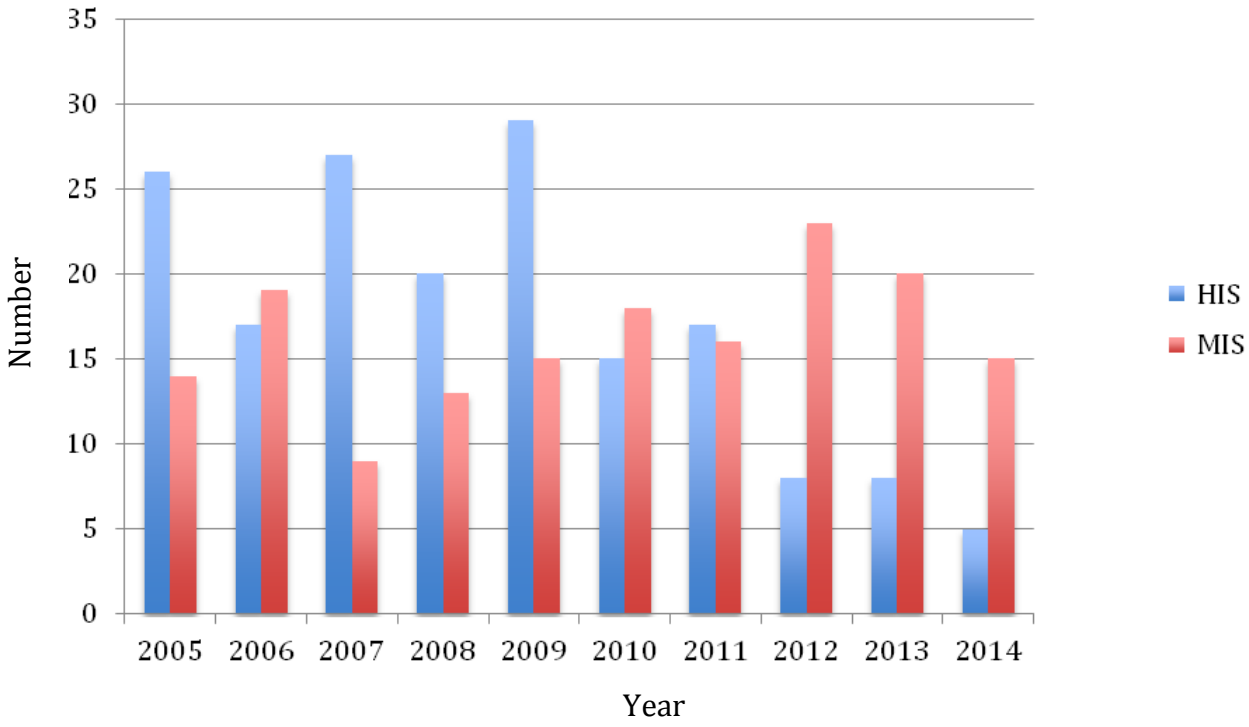

Figure 1. Correlation between mortality (MIS) and frequency of admissions (HIS) in Distrito Federal due to amyotrophic lateral sclerosis. Period: 2005 to 2014.

Table 1. Frequency, length of stay and reimbursement of hospitalization in Motor Neuron Disease in SUS of Distrito Federal, Brazil. Period: 2005 to 2014.

Year	N	length of stay (avg) days	SD	Length of stay (sum)	ICU (ammount R$)	ICU (avg R$)	AIH (avg R$)	AIH (total ammount R$)
2005	26	15.3	18.4	399	10,089	388	1,031	26,826
2006	17	17.8	23.6	303	0	0	602	10,250
2007	27	11.8	11.1	320	0	0	588	15,897
2008	20	15.4	12.8	309	0	0	628	12,571
2009	29	17.4	18.2	504	0	0	562	16,313
2010	15	20	23.2	300	14,361	957	1,645	24,681
2011	17	21.7	28	369	44,042	2,590	3,113	52,921
2012	8	16	10.9	128	0	0	646	5,173
2013	8	12,7	18,7	102	0	0	355	2,841
2014	5	17,8	10,6	89	0	0	447	2,236
Total	172	-	-	2,823	68,492	-	-	169,712

followed the 75% drop observed in frequency (p = 0.03). The total SUS spending on AIH reimbursement also suffered a sharp decline, reaching 80 to 90% of all median and initial totals (Table 1). In 2005, the average cost per patient was R$1,031, and the total sum was R$ 26,826. In 2014, a drop in AIH reimbursement was observed, with an average of R$447 (p = 0.26), and a total of R$2,236. If we compare the period until 2011, the mean total AIH reimbursement was 22,780 ± 14,599 and the mean cost of the second period (2012 to 2014) was 3,416 ± 1,550 (p = 0,05). With regard to gender, there was no significant difference between spending with AIH (p = 0.79) or with ICU use (p = 0.81).

The period between September, 2011 and 2014 was evaluated in the CRDN and included 135 patients with probable or definite diagnosis of the disease. There were 78 (57.8%) men and 57 (42.2%) women, with male-female ratio of 1.4:1. The mean age was 57.2 ± 12.3 years, ranging from 25 to 86 years. The average age was 56.3 ± 12.3 years in males and 58.6 ± 12.3 years in females, with no difference between the sexes (p = 0.179).

Table 2. Patients profile at CRDN (Period: sep 2011 - dec 2014)*El Escorial Classification of ALS patients on admission . NIV: Non-invasive ventilation; IV: invasive ventilation; NV: no ventilation.

Parameter	Onset N (%)			
	Bulbar	Leg	Arm	Total
Possible*	8(24.2)	12(36.4)	12(39.4)	33(24.5)
Definite*	12(15.2)	28(35.4)	39(49.4)	79(58.5)
Probable*	1(7.1)	5(42.9)	7(50)	13(9.6)
Suspect*	5(50)	2(20)	3(30)	10(7.4)
NIV	3(14.3)	8(38.1)	10(47.6)	21(15.5)
IV	3(25)	1(8)	8(67)	12(8.9)
NV	20(19.6)	40(39.2)	42(41.2)	102(75.6)
Total	26(19.1)	48(35.3)	61(45.6)	135(100)

The distribution of patients on admission to the CRDN according to the El Escorial criteria is presented in Table 2. It was observed that 79 patients (58.5%) had a definite form of the disease and in 61 patients (45.6%) the site of onset was in the upper limb. Additionally, according to Table 2, 92 (68.1%) patients had diagnostic confirmation at admission (definite and probable forms), whereas in 43 (31.9%) of them, the diagnosis was confirmed during follow-up. The median time to diagnosis from the first symptoms was 22.7 months in men and 23.5 months in women. Table 2 also shows the frequency of home mechanical ventilation use. It was observed that a majority 102 (75.6%) of the patients did not use mechanical ventilation, while 21 (15.5%) patients used non-invasive ventilation and only 12 (8.9%) used invasive ventilation by tracheostomy. There was no statistically significant difference between the use of ventilation and the form of onset.

Electroneuromyography helped confirm the diagnosis in 119 patients (88.1%), but in cases initially classified as suspected disease, the exam failed in 5 patients (50%). In patients with bulbar-onset, the exam was negative in 4 patients (15.4%) and in those with upper limb-onset, it failed in 10 patients (16.9%). All patients received guidelines from the multidisciplinary team in at least two consultations, with a range of three to four months. Thirty-six patients (26.5%) received between 3 and 6 consultations.

Figure 2 shows the survival curve of patients according to age. In the log-rank test, a survival curve of an age group that differs from the others ($p = 0.0043$) was observed. With the Bonferroni adjustment, it was noted that the survival time for patients aged below 50 years was significantly higher than the survival time for patients over 75 years. For patients younger than 50 years old, approximately 83% were still alive one year after the start of follow-up, while only 22% of patients over 75 years of age were still alive.

Table 3 shows the clinical features associated with lower survival in the group over 75 years of age. When analyzing the unadjusted hazard ratio, the following variables were not statistically significant and were excluded: sex, pyramidal syndrome, dementia, smoking, alcohol consumption, use of pesticides, heavy metals, clinical and diagnosis of ALS (data not shown). The multivariate Cox regression model showed that only the age of onset and shape were significant risk factors for survival time. The risk of death among patients older than 75 years was approximately four times higher ($RR = 4.05$, $p = 0.0018$) than among patients younger than 50 years. However, the risk of death in patients in the age groups 51 to 60 and 61 to 75 years did not differ significantly compared to patients younger than 50 years. The risk of death for patients with the early bulbar form of ALS was approximately two and a half times ($RR = 2.53$, $p = 0.0027$) that of patients with the early spinal form of ALS.

DISCUSSION

Estimating disease incidence is important for determining the size of public health services. Prospective epidemiological studies based on case records associated with the use of secondary databases, such as mortality, using capture-recapture techniques are the ideal approach (Bresch et al., 2014; Chiò et al., 2013). However, the record of incident cases requires the existence of reference centers with the formation of a registration basis. In the absence of such, mortality data was used, which produced an incidence rate of the disease at 1.3/100,000 person-years over 20 years of age and 2.6/100,000 person-years over 45 years of age, which were similar to other studies (Chiò et al., 2013). The use of adjusted rates by age is necessary because the incidence of ALS is more common over 45 years of age and because approximately 38% of the inhabitants of the Federal District are under 20 years of age (IBGE, 2014). Mean age at hospitalization (49.3 ± 15.1 years), at death by disease (61.5 ± 12.6) and at admission to the Reference Center (57.2 ± 12.3 years) were significantly lower than the average age of onset of the disease observed in European countries, which is between 61 and 66.2 years (Chiò et al., 2009). These findings are corroborated by other studies in Latin American

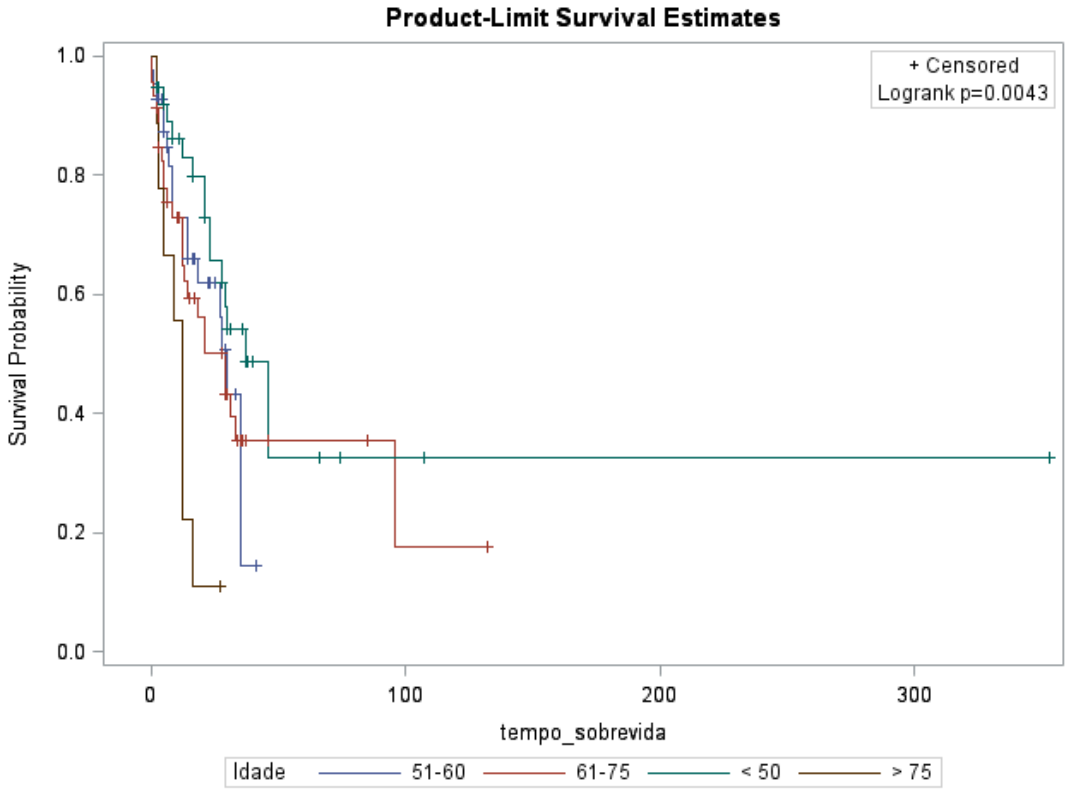

Figure 2. Survival Kaplan Meier Analysis of 135 ALS patients evaluated in CRDN according to age of onset. Period: September, 2011 to December, 2014.

Table 3. Crude and adjusted Risk Ratio for survival in Amyotrophic Lateral Sclerosis, by clinical selected variables in patients under multidisciplinar care and Riluzole. Period: set 2011 - dez 2014 [a] Adjusted for age and site of onset.

Parameter	Risk ratio - RR (CI 95 %)			
	Crude (CI)	p-value	Adjusted[a] (CI)	p-value
Age (years)		0.0212		0.0135
≤ 50	1	-	1	-
51 - 60	1.54(0.78 – 3.02)	0.2129	1.21(0.60 – 2.44)	0.4854
61 – 75	1.60(0.86 – 2.96)	0.1383	1.54(0.81 – 2.91)	0.188
> 75	4.48(1.88 – 10.72)	0.0007	4.05(1.69 – 9.75)	0.0018
Onset	-	0.0052	-	0.0027
Spinal	1	-	1	-
Leg	1	-	1	-
Arm	1.08(0.62 – 1.87)	0.7935	1.25(0.69 – 2.27)	0.4615
Bulbar	2.43(1.36 – 4.33)	0.0052	2.53(1.38– 5.62)	0.0027
Diagnostic delay time (months)	-	0.0334	-	-
≤ 12	2.11(1.12 – 3.96)	0.0205	-	-
13 - 24	1.96(1.05 – 3.66)	0.034	-	-
> 24	1	-	-	-

populations (Valenzuela et al., 2015; Vázquez et al., 2008; Zaldivar et al., 2009).

The frequency of hospitalizations from disease has fallen by 75% between 2012 and 2014, after the creation of CRDN, despite the increased incidence-based mortality rate from the disease. There are studies showing improved quality of life (Andersen et al., 2012; Miller et al., 1999; Traynor et al., 2003) from over the past decade, but it is still uncertain whether there is increased survival (Aridegbe et al., 2013; de Rivera et al., 2011) of

ALS patients with the multidisciplinary care. This includes physical and occupational therapy to preserve patient autonomy, respiratory therapy for elimination of airway secretions and strengthening cough, nutritional support and speech therapy associated with assistive technologies (Andersen et al., 2012; Miller et al., 1999; Venkova-Hristova et al., 2012).

Regarding the length of stay, the global average length of stay was 16.4 ± 18.4 days, with no significant change during the study period. Hospitalizations should be avoided whenever possible because both higher frequency and longer durations predispose the patient to increased risk of infections and greater immobility, contributing to increased risk of respiratory complications (Miller et al., 1999). It was also observed that there were reduced financial expenses with hospitalizations as a decline in AIH reimbursements, which were reduced in their average sum, reaching approximately 10 to 20% of the initial average and total value, according to Table 2. Evaluating the AIH reimbursement may be useful and has been used as an indirect measure of cost in Brazilian public health system, although it does not take into account the total direct and indirect costs of a health system (Bertó and Beulke, 2012), only the monetary reimbursement made by SUS.

The risk of death among patients older than 75 years was approximately four times higher (RR = 4.05, p = 0.0018) than among patients younger than 50 years. The risk of death for patients with the early bulbar form was approximately two and a half times (RR = 2.53, p = 0.0027) that of patients with early spinal form (Table 4). These findings are consistent with other studies (Aridegbe et al., 2013; Turner et al., 2010). The ALS practice parameter of the American Academy of Neurology (AAN) recommended that, at an early stage of the disease, patients be sent to a multidisciplinary specialized center to assess their individual needs and to focus on their quality of life (Miller et al., 1999). The time from diagnosis to referral for the CRDN was long (22.7 months in men and 23.5 months in women), surpassing the time described in European studies, where the average time to diagnosis was approximately 10 months (Chiò et al., 2009). There is great discussion about the adoption of the criteria El Escorial and Awaji in electroneuromyography for the diagnosis of ALS (Carvalho and Swash, 2009; Ludolph et al., 2015). In cases initially classified as suspect and bulbar-onset, the exam did not help the diagnosis in 50 and 15.4% of cases, respectively, despite incorporating the Awaji criteria. This is confirmed by other studies showing, primarily in the bulbar form, that the procedure has a sensitivity of 16 to 19.5% (Bresch et al., 2014; Okita et al., 2011). In patients without diagnostic confirmation, follow-up in a specialized center has the objective of assisting with further diagnostic confirmation, based on clinical evolution, without delaying the introduction of multidisciplinary care.

A study conducted in England in 2012 with Cox regression in 437 patients with ALS showed that follow-up in specialized reference centers in relation to general outpatient care is an independent positive predictive factor for improved survival (HR 1.93, 95% CI 1.37 to 2.72, p = 0.001) (Aridebge et al., 2012). Another study conducted in Madrid claims that the specialized centers increase survival even in the bulbar-onset form because the treatment is provided early. Other recent European studies corroborate these findings (Chiò et al., 2006, Miller et al., 2009, Pouget, 2013; de Rivera et al., 2011; Traynor et al., 2003). In Barcelona, the program for the treatment of ALS adds multidisciplinary teams to home care teams, considering the evolution of the disease, because of increased difficulties in walking to specialized centers (Guell et al., 2013). In recent years, there has been significant growth in the scope of home care teams in the Federal District, which enabled this joint action (Leopoldina et al., 2015).

Despite several clinical trials of drugs and cell therapy, ALS remains an incurable disease (Hardiman et al., 2011). Respiratory failure is the natural course of the disease and advocates for the use of Non-Invasive Ventilation (NIV) (Andersen et al., 2012; Miller et al., 1999). In July, 2008, the Ordinance of the Brazilian Ministry of Health (Brasil, 2008), recognizing the need for deinstitutionalization of patients, established the Program of Noninvasive Ventilator Assistance to Neuromuscular Disease Carriers, but did not create sources of funding for it.

Invasive ventilation by tracheostomy is always a second choice and must be requested by the patient, except for young patients with the early bulbar form of disease and inability to use NIV (Heritier et al., 2013). A study conducted in Italy (Volanti et al., 2011) with 44 patients with ALS showed that there are difficulties in the acceptance and adaptation of NIV equipment, which make its use difficult, but it can be overcome by intensive training in multidisciplinary centers.

It was observed that there was a low frequency of use of home mechanical ventilation in this study, with 15.5% of patients using NIV and 8.9% using invasive ventilation by tracheostomy. In 2009, an extensive study conducted with ALS CARE database involving 5,600 patients in North America between 1997 and 2004 found that only 21% of patients used NIV (Miller et al., 1999). More recent studies from multidisciplinary and well-established centers showed greater adherence to the use of NIV, reaching 64.28% in early bulbar forms and 35.71 to 79% in the early spinal forms (Heritier et al., 2013; de Rivera et al., 2011; Volanti et al., 2011).

Conclusion

The incidence rates of ALS in the Federal District population was 1.3/100,000 person-years, adjusted for

the population aged over 20 and 2.6/100,000 person-years for the population over 45. Treatment by a multidisciplinary team showed increased efficiency with reduced hospitalization rates, length of stay and AIH reimbursement. Thus, under the public health systems, the adoption of a comprehensive national public care policy for patients with ALS is suggested along with the creation of multidisciplinary reference centers combined with a deinstitutionalization policy of the Home Care Program (PID) and Non-Invasive Ventilation Program Homecare.

Conflict of interest

The authors declare no conflicts of interest and use of Sources of Funding Statement. There were no sponsors in study design, collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

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