Clinical Nutrition 28 (2009) 141–146

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://intl.elsevierhealth.com/journals/clnu

Original Article

Characteristics of Alzheimer's disease patients with a rapid weight loss during a six-year follow-up

Olivier Guérin [a,d,*], Sandrine Andrieu [b], Stéphane M. Schneider [c], Frédéric Cortes [a], Christelle Cantet [b], Sophie Gillette-Guyonnet [a], Bruno Vellas [a]

[a] INSERM U558, Department of Internal Medicine and Clinical Gerontology, CHU de Toulouse, Université Paul Sabatier, France
[b] INSERM U558, Department of Public Health, CHU de Toulouse, Université Paul Sabatier, France
[c] INSERM U907, Department of Gastroenterology and Clinical Nutrition, CHU de Nice, Université de Nice Sophia-Antipolis, France
[d] Department of Gerontology, CHU de Nice, Université de Nice Sophia-Antipolis, France

ARTICLE INFO

Article history:
Received 26 August 2008
Accepted 26 January 2009

Keywords:
Rapid weight loss
Nutritional assessment
BPSD
Alzheimer's disease
Undernutrition
Elderly

SUMMARY

Background & aims: Weight loss in Alzheimer's disease (AD) may be either progressive or rapid, with different consequences. The aim of this study was to characterize massive weight loss (≥5 kg over 6 months) during a 6.5-year follow-up.

Methods: 395 patients with AD (mean age 75.4 years) were included in a prospective single-centre cohort study (mean follow-up 2.5 years). A standardized gerontologic assessment was performed every six months, including nutritional, neuropsychological, functional, and caregiver burden evaluations, along with recording all intercurrent events before weight loss.

Results: Among the 127 cases of weight loss (in 110 subjects, 27.8% of the population), we identified 60 cases of intercurrent illnesses and 88 cases of behavioral and psychological symptoms of dementia (BPSD) during the six months before weight loss. Three factors were independently associated with rapid weight loss: higher initial weight (HR = 1.06, 95% CI [1.02, 1.08]), higher Prognosis Inflammatory and Nutritional Index (HR = 2.16, 95% CI [1.26, 3.72]) and a higher Cohen-Mansfield agitation inventory score, reflecting BPSD (HR = 1.05, 95% CI [1.01, 1.10]). Cholinesterase inhibitors appeared as protective (HR = 0.33, 95% CI [0.15, 0.73]). Rapid weight loss was predictive of death at 6 months (HR = 3.01, 95% CI [1.73, 5.22]).

Conclusion: BPSD play an important role in rapid weight loss and should be managed effectively. Biological assessment of malnutrition may be warranted.

1. Introduction

In patients with Alzheimer's disease (AD), weight loss contributes to the alteration of general health, to the frequency and severity of complications, especially infectious, and to a faster loss of independence. It occurs in about 40% of AD cases, including very early stages, before diagnosis is even possible.[1]

We have previously reported two different modes of weight loss in AD after a one-year follow-up[2]: a gradual weight loss (4% or more, known as an independent factor of morbidity and mortality in the elderly[3]), present in one third of the cohort, whose major risk factor was disease severity (assessed by the Reisberg score). Another mode of weight loss, observed in 10% of patients, was rapid (≥5 kg in the first six months); risk factors for this rapid weight loss were an intercurrent event such as an acute disease, hospitalization or a change of living arrangements.

Characterizing weight loss in AD patients may be crucial: indeed, the progressive and irremediable weight loss featured in late-phase dementia is considered a contra-indication to nutritional support, whereas an acute weight loss may benefit from an aggressive nutritional support.[4] Also, an early intervention strategy could be implemented in the latter, in order to prevent or at least decrease the loss.[5]

The main purpose of this study was to characterize this population of AD patients showing a rapid weight loss (defined as the loss of at least 5 kg in 6 months) during a 6.5-year follow-up.

Abbreviations: AD, Alzheimer's disease; ADL, Activities of Daily Living; BMI, Body Mass Index; BPSD, behavioral and psychological symptoms of dementia; CRP, C-Reactive Protein; ELSA, Etude Longitudinale de Suivi de la Maladie d'Alzheimer; IADL, Instrumental Activities of Daily Living; MMSE, Mini Mental State Examination; MNA, Mini Nutritional Assessment; PINI, Prognostic Inflammatory and Nutritional Index.

* Correspondence to: Dr Olivier Guerin, Hôpital de Cimiez, CHU de Nice, 4 avenue Reine Victoria, 06000 Nice, France. Tel.: +33 4 92 03 61 68; fax: +33 4 92 03 40 32.
E-mail address: olivguerin@hotmail.com (O. Guérin).

0261-5614/$ – see front matter
doi:10.1016/j.clnu.2009.01.014

2. Materials and methods

2.1. Study design

This was a single-center, prospective cohort study in the hospitals of Toulouse, France, as part of the Etude Longitudinale de Suivi de la Maladie d'Alzheimer (ELSA study), which has followed ambulatory patients with dementia of Alzheimer type since 1994.

Follow-up comprised a 6-monthly evaluation in the daycare hospital and the collection of intercurrent events by telephone from the general practitioners and/or caregivers every three months during 6.5 years after enrollment.

The diagnosis of AD was confirmed by initial evaluation through careful history taking (personal and family history), the assessment of psychometric tests to confirm cognitive impairment, as well as conventional tests to exclude other causes of dementia (standard biological tests, thyroid function, vitamin measurements, brain CT scan), and in some cases brain perfusion radio-isotope scan and apolipoprotein E genotyping, to screen for its type 4 allele, which represents a major biological risk factor for late onset AD.

All patients fulfilled the DSM-IIIr criteria for dementia (American Psychiatric Association 1987) and had probable AD according to the criteria of the National Institute of Neurological and Communicative Disorders and Strokes – Alzheimer's Disease and Related Disorders Association (NINCDS–ADRDA).[6]

The presence of a caregiver able to ensure the quality of follow-up was an inclusion criterion. Exclusion criteria were a diagnosis of AD established more than five years ago, an Activities of Daily Living (ADL) score <3, uncontrolled heart failure, severe or unstable angina, uncontrolled arterial hypertension, severe orthostatic hypotension, severe renal or liver failure, severe anemia, vascular disorders, systemic disease, clinically relevant hyper- or hypothyroidism, clinically relevant vitamin deficiency, concomitant malignancy, severe or total blindness or deafness. The study was approved by the local Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale (Toulouse).

2.2. Evaluation

The initial evaluation, as well as the 6-monthly assessments, was multidimensional and multidisciplinary. The patients underwent clinical, neuropsychological and biological investigations. The 6-monthly evaluation included:

- Cognitive evaluation, carried out by a neuropsychologist using Folstein's Mini Mental State Examination (MMSE)[7]; MMSE is a global cognitive assessment test that measures orientation to time and place, immediate recall and other executive functions.
- Functional status, evaluated after interviewing the family, using the ADL scale[8] and the Instrumental Activities of Daily Living (IADL) scale[9]; these scales allow for a correct assessment of a subject's autonomy.
- Mood, scored using Cornell's depression scale.[10]
- Behavior, with a focus on agitation, aggression, dis-inhibition and irritability, assessed by the Cohen-Mansfield agitation inventory[11]; these symptoms account for the psychosis factor of behavioral and psychological symptoms of dementia (BPSD); BPSD are frequent complications of AD that may occur during each stage of the disease, but are more frequent in advanced cases. The higher the global score on the Cohen-Mansfield scale is, the most severe the symptoms are.
- Nutritional evaluation, including weight, Body Mass Index (BMI), and biological variables (albumin, transthyretin, orosomucoid, C-reactive protein (CRP), Prognostic Inflammatory and Nutritional Index (PINI) [CRP $\times$ orosomucoid/albumin $\times$ transthyretin]). The latter reflects the prognostic value of the combination of undernutrition and inflammation.[12] Nutritional status was quantified with the Mini Nutritional Assessment (MNA).[13] A dietician also administered a dietary questionnaire to assess qualitative and quantitative food intake.
- The caregivers were interviewed for assessment of their material and psychological burden with the Zarit scale, which also allows predicting the caregiver's collapse.[14]
- Living arrangements were recorded: living alone at home, living at home with assistance, and living in an institution.

These evaluations taken together made it possible to classify the patients according to Reisberg's scale[15] that indicates the severity of the disease. Educational level was recorded at baseline (school, high school, Baccalaureate) College/University. Unfortunately, no information on oral/dental events was available to us.

Enrolment was completed in 2000 with 395 patients included.

Rapid weight loss was defined as the loss of at least 5 kg in 6 months.[2]

2.3. Analysis

All intercurrent events during the 6 months preceding the weight loss, whether medical or non-medical, were carefully recorded. Particularly, we recorded systematically every infectious episode (pneumonia, urinary tract infections, or other infections), neurologic accidents (stroke, epileptic fit, or others), cancer, acute heart failure, hydration disorder, swallowing disorder, trauma (with or without falls), recent surgery, behavioral disorder (delirium, anorexia, depression, agitation–irritability, delusion–hallucination, sleep disorders), institutionalization, caregiver's death or exhaustion, home aid increase, hospitalization, psychotropic prescription (neuroleptics, serotoninergic antidepressant drugs, benzodiazepines), and cholinesterase inhibitor prescription (start, stop, or modification). A descriptive presentation of these intercurrent events was performed.

With regard to the loss of 5 kg in 6 months, we performed a univariate and multivariate analysis of Cox's proportional hazards models from survey data taken on admission. All scales were used as continuous variables, except for MMSE, MNA and the Zarit score that were categorized.

The criterion for variable introduction into the multivariate model was $p < 0.2$ in the univariate study. If several strongly dependent variables satisfied this criterion, only one variable was selected to avoid the risk of multicolinearity. Variables were considered as significant for $p < 0.05$.

A descriptive analysis of the intercurrent events of all types (medical, social, environmental) that had occurred in the 6 months prior to the loss of 5 kg was performed.

Concerning the risk of death, the event "rapid weight loss" was examined as a time-dependent covariate in a Cox proportional hazards model with a bivariate analysis.

Statistical analysis of the data was carried out with the SAS statistical software (version 8.0.2; SAS Institute, Cary, NC).

3. Results

3.1. Population characteristics at inclusion

395 patients were included. These 395 subjects were followed-up for up to 6.5 years with a mean follow-up of 2.5 years. During follow-up, 65 subjects left the study at the request of their family and 86 died (Fig. 1). The characteristics of the population at inclusion in the ELSA study are mentioned in Table 1, and the flow chart of the cohort appears elsewhere.[2]