

Neuropsychiatric symptoms as a predictor of caregiver burden in Alzheimer's disease

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Aims: Patients with Alzheimer's disease need assistance and supervision of their daily activities. They survive for protracted periods of time, placing an extensive burden of care on the caregiver prior to the patient's death. The present study addressed the predictive value of behavior-related burden on Alzheimer's disease caregivers.

Participants: 82 patients with probable Alzheimer's (73.7 ± 8.1 years), and their primary caregivers (59.6 ± 14.8 years, 81.5% women), were assessed.

Methods: Cognitive impairment, neuropsychiatric symptoms, and dementia severity were assessed with Mini Mental State Examination (MMSE), Neuropsychiatric Inventory (NPI), and Clinical Dementia Rating (CDR), respectively. Caregivers were given Zarit's Burden Interview and Carer Activity Inventory.

Results: Neuropsychiatric symptoms like delusions, hallucinations, restlessness, anxiety, euphoria, disinhibition, unusual motor behavior, sleep disturbances, and appetite alterations were the best caregiver burden predictors (NPI $r=0.482$, $p<0.001$). No correlation with cognition, disease stage, or negative neuropsychiatric symptoms (depression and apathy) was found.

Conclusion: Increased caregiver burden was related to increased levels of patient behavioral disturbance. Of these symptoms, hallucinations, unusual (motor) behavior, and abnormal behavior at nighttime were the most significant. No correlation with neuropsychiatric symptoms such as apathy and depression was found. This may have relevance to appropriate interventions for caregivers.

Keywords: caregivers, caregiver burden, Alzheimer's, behavior, neuropsychiatric

Introduction

The prevalence of dementia in developed countries ranges from 1.4% in 65- to 69-year-old subjects to 38.6% in individuals aged 90–94 years (Jorm 1990). The gradual progressive impairment and behavioral symptoms that may emerge in the course of Alzheimer's disease produce a requirement for care and supervision of daily activities. This usually falls upon relatives acting as informal caregivers, causing them great burden and stress. The term caregiver burden refers to the consequences derived from caring for demented patients. These consequences may be psychological, physical, and economic (Garre-Olmo et al 2002). Caregiver burden is not only present in Alzheimer's disease. This syndrome has also been noted in other illnesses like stroke, Parkinson's disease (Thommessen et al 2002), and vascular dementia (Annerstedt et al 2000).

Behavioral disturbances are a common feature in dementia and cause significant caregiver burden (Mangone et al 1993; Absher and Cummings 1994). The symptoms that more frequently caused caregiver burden are aggression, wandering, and delusions (Nagaratnam et al 1998). This demand on the caregiver has been associated with

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adverse psychological reactions and has been identified as a risk factor for caregiver mortality (Zarit et al 1980; Schulz and Beach 1999). These results have even been confirmed in studies performed with caregivers from different cultural backgrounds (Pang et al 2002). Other studies have tried to describe the differences in the impact of the symptoms according to the sex of the caregivers (Shanks-McElroy et al 2001).

The present study aimed to assess the predictors of burden in caregivers of Alzheimer's patients in Argentina.

Methods

The studied patients came from the Memory Clinic of the Zubizarreta Hospital and the CEMIC University Institute at Buenos Aires City. The assessment was part of a "Dementia Training Program" sponsored by the City of Buenos Aires Health Secretariat. From September 1 2001 to March 1 2002, a sample of 82 consecutively referred noninstitutionalized patients with probable Alzheimer's disease according to National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and related Disorders Association (NINCDS-ADRDA) criteria (McKhann et al 1984) and their primary informal caregivers (defined as the persons responsible for the day-to-day decisions and providing care) were studied. Patients who had paid caregivers were not included in this study.

Patient variables

All patients had to go through extensive neurological, neuropsychological, neuropsychiatric, laboratory, and neuroimaging assessments to fulfil all dementia criteria according to DSM-IV (APA 1994) and probable Alzheimer's as per NINCDS-ADRDA (McKhann et al 1984).

Cognitive functioning level was assessed by means of the Mini Mental State Examination (MMSE) (Folstein et al 1975), a Buenos Aires version (Spanish translation and norms) (Allegri et al 1999; Butman et al 2001); severity range was determined through Clinical Dementia Rating (CDR) (Hughes et al 1982). For the neuropsychiatric assessment a local Spanish version of the Neuropsychiatric Inventory (NPI) (Cummings et al 1994) was used, which takes into account the following subitems: delusions, hallucinations, restlessness-aggressiveness, depression, anxiety, euphoria-denial, apathy, disinhibition, irritability, unusual (motor) behavior, unusual behavior (at nighttime), and changes in appetite and food intake. Dementia duration and family income were also considered.

Carer variables

A series of variables identified in the literature as being important for understanding caregivers' burden, health, and emotional well-being was evaluated by means of a semistructured questionnaire. Evaluated demographic-situational items included age, gender, marital status, relationship with the patient, duration of the patient's disease, hours per week spent with the patient (questionnaire by Gilleard et al 1984), and time spent in patient-related activities (eg, communication, feeding, dressing, transportation, supervision) (questionnaire by Davis et al 1997). The degree of burden experienced by caregivers was evaluated by means of Zarit's Burden Interview (Zarit et al 1985), consisting of 22 questions evaluated by means of a 5-point scale, ranging from nil=0 to overburdened=4.

Because depression influences negatively the caregiver's evaluation of the patient (Arguelles et al 2001), we defined the following exclusion criteria for the caregivers:

1. Presence of dementia, depression, or psychosis.
2. Contact with the patient for less than 10 hours per week.

Statistical analysis

Data were analyzed using the statistical package SPSS® 11.0.0 for Windows® (2001) (SPSS Inc, Chicago, IL, USA). Demographic variables in both populations (patients and caregivers) as well as MMSE, CDR, and NPI general results were expressed by medians and standard deviation. Neuropsychiatric symptoms evaluated by means of NPI were considered globally and partially for each of the areas under study, using the severity by disturbance presence frequency estimate. Influence of cognitive factors on caregiver burden (MMSE), duration stage (CDR), behavioral factors (NPI), time of disease duration, as well as economic level were analyzed by a linear regression model, applying burden level as a dependent variable. Correlations between global burden and different behavioral areas (NPI) were evaluated by means of Spearman's correlation coefficient.

Results

Eighty-two patients with probable Alzheimer's disease (NINCDS-ADRDA criteria) and their primary caregivers were assessed. There were 38 men and 44 women in the patient sample with a mean age of 73.7 years (range 50–90). The severity of dementia ranged from very mild to severe on all measures. The duration of illness was 38.7 ± 32.1 months. The mean age of the primary caregivers was 59.6 ± 14.8 years. Most were female (81.5%) and had

Table 1 Patient and caregiver demographic data

| | Patients with Alzheimer's | Primary caregivers |
|-------------------------------------|--|--------------------|
| Age (years) | 73.7 ± 8.1 ^a (range 50–90) | 59.6 ± 14.8 |
| Education (years) | 8.1 ± 3.9 | 9.3 ± 3.3 |
| Gender (m/f) | 38/44 | 15/67 |
| MMSE | 18.3 ± 7 | |
| CDR | 1.6 ± 0.8 (range 0.5–3) | |
| NPI | 24.0 ± 20.2 | |
| Duration of illness (months) | 38.7 ± 32.1 | |
| Income (family group) \$/month | 612 ± 729 | |
| Caregiver burden (Zarit et al 1985) | | 29.2 ± 18.0 |
| Relationship to patient | | |
| Spouse | | 54.6% |
| Children | | 36.0% |
| Son/daughter in law | | 0% |
| Other | | 9.4% |

^a Values expressed are median ± standard deviation (except for gender and caregiver relationship to patient).

finished primary school (mean 9.3 years of education). Most were either spouses (54.6%) or children (36%) of the patients. More demographic data for both groups are described in Table 1.

The proportion of caregivers who resided with the patients varied with the severity of the pathology (Table 2).

Caregiver burden ranged from minimal to severe (Zarit's scale = mean 29.2, range 4–72). The influence on caregiver burden of cognitive impairment (MMSE), disease stage (CDR), behavioral disturbances (NPI), evolution time, family income, and hours per week spent with patient was studied. Using Zarit's burden scale as the dependent variable, we found the NPI to be the best predictor of caregiver burden ($p < 0.001$) (Table 3).

To study which behavioral disturbances caused the burden, a correlation with the different areas of the NPI was performed. The elements of the NPI that correlated better were: hallucinations, anxiety, unusual (motor) behavior, and sleep disturbance ($p < 0.01$), and delusions,

Table 2 Number of caregivers residing with patients

| MMSE | Total patients | Living with caregiver | Institutionalized |
|-------|----------------|-----------------------|-------------------|
| > 20 | 21 | 12 | 0 |
| 11–20 | 24 | 16 | 4 |
| < 11 | 24 | 8 | 15 |

Abbreviations: MMSE, Mini Mental State Examination.

Table 3 Results of regression analysis using Zarit's (Zarit et al 1985) burden scale score as the dependent variable

| Independent primary variable | Regression B coefficient | p |
|------------------------------|--------------------------|---------|
| MMSE | -0.106 | 0.382 |
| CDR | 0.115 | 0.340 |
| NPI (total score) | 0.482 | < 0.001 |
| Income | -0.037 | 0.751 |
| Evolution (months) | 0.081 | 0.525 |

Abbreviations: CDR, Clinical Dementia Rating; MMSE, Mini Mental State Examination; NPI, Neuropsychiatric Inventory.

restlessness, disinhibition, and appetite alterations ($p < 0.05$) (Figure 1 and Table 4)

Family burden level showed significant correlation with positive neuropsychiatric symptoms such as hallucinations, unusual (motor) behavior, and abnormal behavior at nighttime. Correlation was also found, but to a lesser degree, with delusions, restlessness, anxiety, disinhibition, and alterations in eating habits. No correlation with negative neuropsychiatric symptoms such as apathy and depression was found. It should be noted that the symptoms having the highest correlation with caregiver burden were not the most frequent.

The only demographic caregiver variable correlating with burden was education. Age, gender, marital status, and family relationship were not significant. Thus, a lower educational level shows a higher burden index ($p < 0.01$) (Table 5).

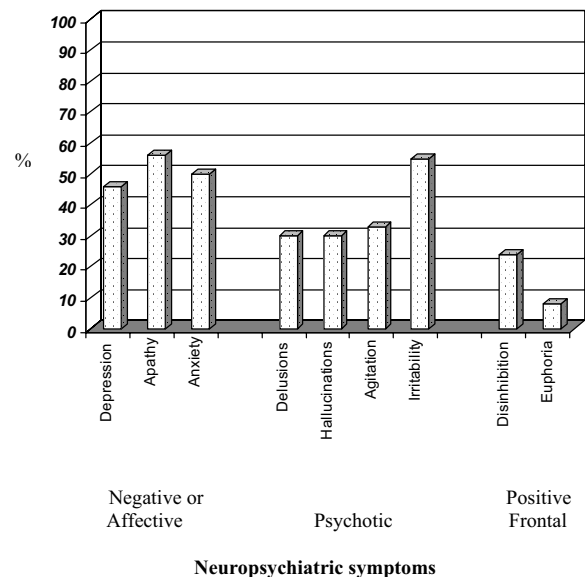


Figure 1 Patient's neuropsychiatric symptoms (percentage of subjects with symptoms).

Table 4 Correlation^a between caregiver burden (Zarit's Burden Interview [Zarit et al 1985]) and patient's neuropsychiatric symptoms (NPI)

| | Zarit's Burden Interview | |
|--------------------------|--------------------------|--------|
| | r | p |
| NPI total score | 0.482 | < 0.01 |
| Affective symptoms | | |
| Depression | 0.179 | ns |
| Apathy | 0.227 | ns |
| Anxiety | 0.570 | < 0.01 |
| Psychotic symptoms | | |
| Delusions | 0.289 | < 0.05 |
| Hallucinations | 0.398 | < 0.01 |
| Restlessness | 0.297 | < 0.05 |
| Irritability | 0.235 | ns |
| Frontal symptoms | | |
| Euphoria | 0.229 | ns |
| Disinhibition | 0.288 | < 0.05 |
| Other | | |
| Unusual (motor) behavior | 0.392 | < 0.01 |
| Sleep disturbances | 0.477 | < 0.01 |
| Appetite alterations | 0.30 | < 0.05 |

^a Correlation coefficient for nonparametric Spearman's test; ns, no significant values

Abbreviations: NPI, Neuropsychiatric Inventory.

Discussion

Alzheimer's disease patients need assistance and supervision of their daily activities. This frequently falls upon informal caregivers (family members), causing them significant burden and stress. A high prevalence of psychiatric disorders has been detected in caregivers, including a higher intake of psychotropic drugs compared with the general population (Clipp and George 1990). Despite the fact that studies have shown contradictory results (Irwin et al 1997), caregivers are also a target for several stress-related conditions affecting the immune system.

Caregiver burden as a term refers to the consequences of caring for demented patients, and such consequences can be psychological, physical, and economic (Garre-Olmo et al 2002). The term not only applies to caregivers of Alzheimer's disease patients, but also to caregivers of patients with other chronic or disabling conditions such as vascular dementia or Parkinson's disease (Thommessen et al 2002).

In our sample, 81.7% of the informal caregivers were women, while 54.6% were spouses and 36% were children of patients. Such percentages are similar to those reported in other studies (Cohen et al 1997). Although several studies have not related gender to caregiver burden, others indicate that this index could be even higher among female caregivers (Gallicchio et al 2002).

Table 5 Correlation^a between caregiver burden level (Zarit's Burden Interview [Zarit et al 1985]) and demographic carer data

| | Zarit's Burden Interview | |
|---------------------|--------------------------|--------|
| | r | p |
| Age | 0.016 | ns |
| Gender | 0.191 | ns |
| Education | -0.249 | < 0.01 |
| Marital status | 0.003 | ns |
| Family relationship | -0.062 | ns |

^a Correlation coefficient for nonparametric Spearman's test

In the present study, burden was not related to cognitive impairment (MMSE), or to disease stage (CDR). This lack of association is consistent with findings in the literature (Mangone et al 1993; Cohen et al 1997). Family group income level or duration of illness were also not related to burden.

Conversely, caregiver burden was positively related to behavioral disturbances in patients, as reported in other studies (Mangone et al 1993; Cohen et al 1997; Clyburn et al 2000), and negatively to caregiver's educational level. The influence of neuropsychiatric symptoms on burden becomes important if we consider that in different samples, the prevalence of these symptoms in Alzheimer's disease is over 50% (Lyketsos et al 2000). Within the spectrum of these symptoms, not all correlated similarly. Psychiatric symptoms that correlated positively ($p < 0.01$) with caregiver distress were hallucinations, abnormal behavior (eg, wandering), and sleep disturbances. Delusions, restlessness, anxiety, disinhibition, and appetite alterations also correlated with burden ($p < 0.05$). All of these symptoms are the so-called "positive symptoms". Most of the published papers showed similar findings for this group of symptoms, and some have even reported that such symptoms can trigger temporary or permanent institutionalization (Annerstedt et al 2000). Contrary to other papers that correlated patient's depression to caregiver burden (Teri 1997), no correlation with "negative" affective psychiatric symptoms such as depression or apathy was found in our sample.

In addition to the symptoms described above, another factor has been found to contribute to burden: the patient's awareness of his/her own deficit influences burden in the early stages of the disease (Selzter et al 1997). This was not studied in our assessment.

Caregiver quality of life and how it is affected in the course of caring for a dementia patient represents a central issue relevant to the environment of the patients. There may be a need for measures to reduce or control behavioral

disturbances, particularly positive psychiatric symptoms. This is significant not only for the quality of life of the caregiver and the patient but also for the influence these symptoms have on the caregiver's judgment of the patient's functional abilities (Arguelles et al 2001). In fact, caregiver burden is associated with an increased risk of nursing home placement for patients with dementia (Yaffe et al 2002).

Although this study was performed with patients having probable Alzheimer's disease, caregiver burden, as already mentioned, is not only found when this condition is present, but also among caregivers of vascular dementia patients. At mild stages of disease, the burden even seems to be higher in the caregivers of patients with vascular dementia (Vetter et al 1999).

Strategies, for example education and information, designed to ease caregiver distress have shown their effectiveness on the syndrome's features (Patterson et al 1999). When caregivers were informed of the disease's features and prognosis, their burden levels decreased compared with those who had not been informed (Hepburn et al 2001). The same happened following institutionalization of the patient. However, a year after institutionalization, a feeling of frustration still persisted in the caregivers (Elmstahl et al 1998).

Treatment of behavioral disorders helps to diminish caregiver burden (Shigenobu et al 2002). At present, there is clear evidence that pharmacological intervention with cholinesterase inhibitors reduces the prevalence and severity of psychiatric disturbances in Alzheimer's disease. Several studies have directly tested caregiver burden decrease after anticholinesterase treatment (Fillit et al 2000; Shikar et al 2000). Correct management of these disturbances, together with adequate educational intervention for caregivers, significantly reduces distress, improving quality of life for both caregiver and patient.

Finally, the time devoted to caring has been related to burden level. It could not be determined, however, if a longer time was caused by loss of efficiency due to the burden or by the fact that patients with psychiatric symptoms demanded more caring time.

Our study limitation has been the lack of caregiver psychological profile, and its relationship to burden and the decision to institutionalize the patient (Colerick and George 1986).

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