REVIEW ARTICLE

Ethical issues in end of life treatments for patients with dementia

M. Congedo[a], R. I. Causarano[b], F. Alberti[c], V. Bonito[d], L. Borghi[e], L. Colombi[f], C. A. Defanti[g], N. Marcello[h], C. Porteri[i], E. Pucci[j], D. Tarquini[k], M. Tettamanti[l], A. Tiezzi[m], P. Tiraboschi[n] and M. Gasparini[o] For the Bioethics and Palliative Care in Neurology Study Group of the Italian Society of Neurology

[a]ASS n. 4 Medio Friuli, Ambulatorio di Neurologia, Distretto di Udine; [b]Hospice Il Tulipano, Ospedale Niguarda Cá Granda, Milano; [c]U.O. Neurologia Ospedale di Sanremo (IM); [d]Neurologia, Ospedali Riuniti di Bergamo; [e]Università Campus Biomedico, Roma; [f]Dirigenza Infermieristica AREU della Lombardia, Milano; [g]Centro Alzheimer Ospedale Briolini, Gazzaniga (BG); [h]Neurologia, A.O. Santa Maria Nuova, Reggio Emilia; [i]Unità di Bioetica IRCCS Centro S. Giovanni di Dio, Brescia; [j]U.O. Neurologia ASUR Marche ZT9, Macerata; [k]Neurologia, PTP Nuovo Regina Margherita, Roma; [l]Istituto M. Negri, Milano; [m]Centro Alzheimer, U.O. Neurologia, Ospedale S. Donato, Arezzo; [n]Neurologia, Ospedale Niguarda Ca' Granda, Milano; and [o]Istituti Clinici di Perfezionamento, Ambulatorio di Neurologia, Milano, Italy

Dementia is a terminal disease, associated with great suffering and difficult decisions in the severe stage. The decision-making process is characterized by uncertainty because of lack of scientific evidence in treatments and by the need to reconcile conflicting points of view. In intercurrent diseases, aggressive interventions are used without consideration of its futility; in comparison with cancer, several consequences of physicians' attitude not to consider dementia as a terminal disease have been reported, especially concerning pain relief. Lack of evidence of artificial nutrition and hydration effectiveness makes advance care planning relevant.

Introduction

Several elements contribute to complicate the decision-making process in severe dementia. Involving patients in planning treatments is difficult as most of them are not informed of their diagnosis and prognosis [1], when they are still competent. The physicians' traditional role is to relieve suffering and sustain life, but also to promote quality of life and respect human dignity, when dealing with the new frontiers of modern medicine. Facing a patient with severe dementia, how can we evaluate quality of life, suffering and cures to relieve it? Which prognostic criteria for survival can be used? How long can our treatments actually prolong life?

Do severe patients with dementia access palliative care?

In the United States of America more than 90% of the nearly five million patients affected by dementia die in nursing homes [2]. A great part of relatives and health professionals believe that palliative care is an effective answer to terminal stage needs [3]. The social costs for

Correspondence: Maria Congedo, via di Romagna, 40 34134 Trieste, Italy (tel.: +39040367032; fax: +390432553786; e-mail: mariolinacongedo@libero.it).

hospice care are lower than conventional therapies [4,5]. In 1996, it was reported that only 1.5% of patients with dementia could access US Medicare Hospice Programs [6], whilst a great number were admitted to hospitals and invasively treated, although life expectancy was short [7,8]. From 1998 to 2005, a gradual change in trend was reported with the admissions increase for patients with dementia in Medicare hospices (from 12 829 in 1998 to 60 488 in 2008) [9].

Contrary to metastatic patients with cancer, they are not considered terminal by family and health professionals and probably cannot take part in adequate programs for end of life care. Mitchell compared two groups of patients: one affected by dementia (1609) and another by cancer (883), both in the severe stage and residents in nursing homes in New York, USA. Six months after the admission, 92% of patients with cancer and 71% of patients with dementia died, but at recovery only 1.1% of the latter had a prognosis of < 6 months [10].

In the mid 1990s, Medicare and the US National Hospice Organization (NHO) elaborated the hospice care access guidelines for patients with terminal diseases other than cancer, to foresee a survival period of 6 months or less. Nevertheless in 2003, Shonwetter documented that patients responding to Medicare prognostic criteria and those not responding had a similar survival trend [11]. Factors predicting shorter

survival were as follows: advanced age, anorexia, and functional status limitations as defined by the Karnofsky Performance Scale [12].

Integrating the Medicare guidelines with the Minimum Data Set [13], the NHO included comorbidity, intake of <25% of the daily nutritional needs, hypersomnia, male gender, age over 83 years, amongst the factors predicting mortality. Using these criteria and a cut-off of 7c for the FAST scale [14], Mitchell tested a system based upon 12 variables; actually the rating system application excludes, from palliative care access, patients not satisfying the criteria but dying within 6 months [15].

Considering also European studies, other factors indicative of 6 months mortality are as follows: unstable clinical conditions, fecal incontinence, bedridden condition [15], severe cachexia and cognitive impairment [16,17], type of dementia, age, and gender [18–22].

Comparing dementia to cancer, several consequences have been reported:

• At the last evaluation before death, nursing home residents affected by dementia had expressed a directive for aggressive care limitation in a significantly lower proportion; both groups had advance directives in the same percentage before institutionalization [10] (Table 1).

Table 1 Advance directives [10]

%	Advance directives before institutionalization	DNR* before death (P < 0.001)	Directive to withhold tube feeding (P < 0.001)
Dementia pts	11.3	55.1	7.6
Cancer pts	11.8	86.1	12.9

*Do not resuscitate order.

• At the end of life, in patients with dementia, aggressive interventions were more often performed than in patients with cancer [10,16,23] (Table 2).

Table 2 Aggressive interventions [10]

%	ANH[a]	Blood samples	Physical restr[b]	Infusion ther[c]
Dementia pts	25.0	49.2	11.2	10.1
Cancer pts	5.2	32.3	6.3	7.1

[a]Artificial Nutrition and Hydration; [b]Physical restraints; [c]Infusion therapy.

• The nature of terminal symptoms was similar in the two conditions, even if frequency was different. [10,24–27] (Table 3).

Table 3 Terminal symptoms [10]

%	Pain	Dyspnea	Constipation	Pneumonia	Fever
Dementia pts	11.5	8.2	13.7	10.8	13.4
Cancer pts	56.6	27.6	32.7	3.6	6.8

• The indicators of nursing assistance poor quality – pressure sores, restraint use and antipsychotic medications – were more frequent in patients with severe dementia. One patient of four had had antipsychotic treatment immediately before death and 1 of 10 had been constrained. Even after the statistical adjustment for behavioural disorders, the probability of antipsychotic treatment was significantly higher amongst residents with advanced dementia [10].

• If these data are valid in European countries as well, the authors' hypothesis is that antipsychotic drugs had been administered to control agitation probably because of misdiagnosed pain. In case of hallucinations or delusional state their correct use is essential to improve quality of life and to provide patients with correct assistance [28].

How to face comorbidity in advanced dementia stages

Patients with dementia with acute intercurrent diseases [29,30] are often transferred in hospital for aggressive care without consideration of cognitive impairment worsening, behavioural symptoms, constipation, or pressure sores [31].

In autopsies, the main causes of death are pneumonia, cardio-vascular diseases, lung embolism, cachexia, and dehydration [32].

Antibiotics effectiveness in severe dementia is discussed: previous trials demonstrated they could not prolong life nor improve comfort. A discomfort increase was reported in 3–5 days from the onset of the infectious disease, in treated and untreated patients, without any substantial differences between groups in the terminal stage [33]. More recent references reported a palliative effectiveness of antibiotics before death [34]. In an observational study, 2 weeks after the diagnosis of pneumonia, patients with dementia treated with antibiotics had a lower mortality rate than the untreated (12% vs. 92%); the withholding of treatment followed the physicians' negative prognostic evaluation in the short term [35], confirming the prognosis importance in clinical choices. In palliative treatment analgesics, antipyretics, oxygen, morphine in terminal dyspnea are recommended [36]. Comorbidity is a cause of insufficient understanding of physical suffering: references about discomfort evaluation and treatments are uncommon [37,38]. The rating

scales used are: QUALID (QUALity of LIfe in late-stage Dementia scale) [39], EOLD (End Of Life in Dementia) [40], MSSE (Mini Suffering State Examination) [41], DS-DAT (Discomfort Scale-Dementia of Alzheimer-Type) [42]. In a trial about dying and palliation involving 71 patients with dementia, Aminoff reported a high suffering level in 63.4% of cases and a medium level in 29.6%; only 7% of cases presented a low suffering level [43]. End of life trials are methodologically poor because of the lack of randomization; in this context the physician's personal opinion becomes a self-fulfilling prophecy.

Are artificial nutrition and hydration appropriate treatments?

Weight loss is a common symptom in dementia and especially in Alzheimer's disease (AD). Cognitive impairment makes cooking or handling cutlery complicated; oral apraxia makes autonomous feeding, chewing and swallowing difficult; cerebral degeneration causes smell and taste disturbances; behavioural symptoms, affective disorders and possible comorbidity can cause weight loss. This can be reported, even with adequate food intake, as a result of ineffective assimilation or catabolic illness [44].

Mesial temporal cortex atrophy is related to low body weight in patients with AD [45]. Body mass index reduction in elderly could be associated to higher risk of developing AD in the same degenerative process [46].

If related to an intercurrent state, dysphagia can be temporary, whereas in severe dementia, it can be a symptom of disease evolution with a negative prognostic value. In the first case, artificial nutrition and hydration (ANH) can be temporary and effective; in the second case, duration is undefined and aims are various:

- aspiration pneumonia prevention
- malnutrition prevention
- pressure sores relief or prevention
- other infections risk reduction
- best functional state and comfort
- prolonging survival

In the Finucane review [47], none of the trials considered prove that these aims could be achievable by tube feeding. Reported adverse effects are tube occlusion (2–34, 7%), leaking (13–20%), local infection (4, 3–16%), need of naso-gastric tube (NGT) replacement in two-thirds of the cases, and aspiration pneumonia (0–66%). The latter is related to the airways passage of oral secretions that cannot be avoided by tube feeding. Weight loss in severe dementia can remain unchanged even if appropriate nutrients are provided. Moreover, we do not find data demonstrating survival prolonging by tube feeding. Intra-operative and peri-operative risks are reported (0–2% and 6–24% respectively), as well as a mortality rate at 1 month of 2–27% and at 1 year of 50% with a median survival of 7.5 months. This wide range of adverse effects is related to methodological difficulties in studying these subjects. A possible consequence of tube feeding is the need of restraints followed by agitation leading to sedation [48].

In a trial [49], NGT was identified amongst mortality risk factors for patients rated 7 to FAST scale (risk ratio 3.5; $P = 0.003$); actually difficulty with eating is a marker of advanced dementia, which is a fatal disorder [48,50].

In favour of oral feeding, we must consider that without the pleasure of eating, patients' quality of life declines [51]; on the other hand, metabolic changes in dementia could favour homeostasis and survival with small intake of nutrients [52].

Does foregoing ANH produce discomfort for patients? It was measured using DS-DAT after the decision to withhold and regularly before death in a population of 178 patients, with a prevalence of dementia. A discomfort reduction was reported in people who died in 2 weeks, an initial reduction, followed by a gradual increase was reported in patients with a longer survival rate, less than the baseline [53]. In another observational study on 166 dementia patients with intake problems, artificial hydration was introduced only in 10 patients and it was associated with higher discomfort before death by DS-DAT [34].

It is difficult to obtain advance directives in patients with dementia about dysphagia; the choice is commonly made by the family, caregiver, or surrogate decision maker [54], possibly based on the previous patient will. The uncertainty about survival could justify ANH, if not excluded in advance directives [55].

ANH choice could be based on different considerations such as the reduction of time and costs required for feeding patients with percutaneous endoscopic gastrostomy (PEG), even if oral feeding is possible. Costs analysis [56] takes into consideration tube-feeding positioning, ANH products and time for manual feeding assistance, versus starting up a pump device (72.8 ± 16.5 min vs. 25.2 ± 12.9 min).

In the elderly at risk of malnutrition, oral supplementation is effective for weight regain as well as mortality rate reduction. Effectiveness was documented in subjects classified as affected by undernutrition, 75 years old or more, treated with 400 kcal of daily oral supplementation for 35 days or more [57].

Food refusal could be the manifestation of a patient's will, if not caused by dysphagia or paranoid delusional state. In the end of life stage, avoiding inappropriate nutrition and hydration lowers the risk of lung edema, ascites and respiratory distress, that are frequent in

patients parenterally hydrated [34,58], allowing the natural physiology of dying.

The Study Group diffused a questionnaire about feeding choices for severe patients with AD in the nursing homes known to members (about 30); 17 physicians and eight nurses answered. They were responsible for 1033 patients, 65 with NGT, and 53 with PEG. The variability amongst centers was wide: NGT from 13% to 0% and PEG from 17% to 0%. To be noted:

• patient's will is rarely known
• weight loss is not the main reason for tube feeding
• withdrawing ANH is admitted by half of physicians involved
• agitation, cough, pressure sores, malnutrition, and infections are reported in patients with ANH as in orally fed patients [59]

The questionnaire was sent to nursing homes that were asked to participate in a trial about feeding in severe dementia.

No randomized controlled trials comparing ANH to oral feeding are reported; observational or retrospective trials are not in favour of ANH [60]. A general indication for dementia is not motivated and it is preferable the single case evaluation without *a priori* ANH exclusion or routine practice [61].

In the absence of high methodological quality clinical trials [62], without clear evidence for survival and quality of life, the bioethical debate is conditioned by ideological positions.

Conclusions

From medical literature and our experience, we know that patients with dementia are at risk of acute suffering. Severe dementia treatment is uncertain for prognosis difficulties and lack of evidence for treatments, ANH, aggressive care, quality of life and survival. Advance care planning is infrequent because of unusual diagnosis disclosure to patients. In present uncertainty, it is preferable to favour case evaluation and individual preferences. The health care proxies' understanding of poor prognosis reduces burdensome interventions of undemonstrated benefit [50]. For the Study Group, the palliative approach is the most appropriate especially for pain relief and other symptom control. Palliative care skills should be common for health professionals at home and in the nursing home.

It is the duty of physicians to let the relatives express doubts and fears, to inform them about the objectives and limits of any intervention aimed at comfort and survival, to reduce family conflicts by evaluation of a patient's previous values and preferences.

Either as a team or individually, clinical evidence and scientific uncertainty can be expressed and, beyond requests for information, ethical questions can emerge from the family or surrogate decision maker.

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