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Treatments and Prescriptions in Advanced Dementia Patients Residing in Long-Term Care Institutions and at Home

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Introduction

Dementia is an incurable condition resulting in a progressive but patchy decay characterized by dementia related events such as recurrence of infections and eating problems, as well as by acute conditions typical of frailty and/ or the worsening of chronic comorbidities. Its duration is reported to range from three to over nine years.[1,2] Although not everyone will reach the advanced stage, many patients experience a highly severe and persistent disability.[3] Health professionals may not always acknowledge advanced dementia as a terminal disease,[4] and this may result in patients being exposed to aggressive treatments. The prescription regimen should be reconsidered not only to avoid overtreatment and side effects of drugs, but also to improve comfort and symptom control. In far advanced stages, some medications previously prescribed for comorbidities could likely be discontinued to reduce burden, adverse effects, and costs.[5,6]

A model for defining the concept of prescriptions' appropriateness in advanced dementia was proposed by Holmes and colleagues[6] taking into account factors such as patients' life expectancy and goals of care. Many patients with advanced dementia are cared for until death in nursing homes (NHs),[7] and studies have shown that drug regimens may be far from optimal.[4,8,9] However, others die at home, cared for by home care service (HC).[7] Information on the treatments and prescriptions for patients with advanced-stage dementia cared for at home are scarce.[8,9] We expected differences, because drug regimes may be critically reconsidered and revised upon admission to institutional long-term care by physicians on staff of NHs. The aim of this paper is to assess and compare treatments and prescriptions of patients with advanced dementia cared for in NHs and in HC and assess their appropriateness from a palliative care perspective.

Methods

A multicenter prospective observational cohort study was conducted from June 2007 to May 2009 to describe treatments, discomfort, and end-of-life critical decisions taken for patients with advanced-stage dementia (the EOLO-PSODEC study: End-Of-Life Observatory: Prospective Study on Dementia patients Care). Due to the regional regulations, the organizational model of care (NH versus HC) in Italy implies important differences in services provided to patients with dementia. The study was carried out in two regions. First was the Lombardy region, with assistance for patients with advanced dementia mainly based on NH admission[10] (in 2010 there were in Lombardy 631 NHs for approximately 9.5 million residents, size from 19 to 700 beds, overall 54,000 beds). Second was the contiguous Emilia-Romagna region, providing district primary HC services.[11]

In Lombardy, the NHs have their own staff of physicians, their residents are elderly people with major disabilities (especially dementia) and post-acute patients who need long term rehabilitation. In Emilia Romagna, assistance is provided by multidisciplinary teams consisting of the patient's general practitioner and visiting nurses. It may also include psycho-geriatricians and PC consultants, social workers, and volunteers. Patients are admitted to HC services only if they have a specific problem that requires nursing care, such as an indwelling catheter, a feeding tube, or a pressure sore, and to NH only when and if the family caregiver is not able to deal with HC. Due to the larger provision of HC, the number and size of NHs is smaller than in Lombardy (64 for a population > 4.2 million residents; maximum size, 60 beds). We recruited all 14 NHs with > 300 beds, with a randomized sample (overall 8%) of

smaller NHs of the Lombardy region stratified into eight strata based on the number of beds, and all five districts (two city based and three country based) of the Reggio-Emilia and Modena provinces of the Emilia-Romagna region.

Patients with a Functional Assessment Staging Tool (FAST)[12] score > 7 were enrolled. To collect data that included at least one follow-up, only patients with an expected survival < 2 weeks according to their primary doctor's clinical judgment were enrolled. Data were collected by trained nurses of those same NHs or districts. Where the number of eligible patients exceeded the staff capacity to collect all data, a smaller randomized sample of patients was chosen.

The FAST, a test tailored to Alzheimer's Disease, consists of seven major stages. Stage 7 indicates the most advanced dementia, and is divided into six progressive sub stages: 7a, speech limited to one to five words; 7b, loss of all intelligible vocabulary; 7c, no walking; 7d, unable to sit independently; 7e, unable to smile; 7f, unable to hold head up. In this paper, data on FAST ≥7c patients are presented (410/496 patients with far advanced dementia, 82.7%), because this represents an advanced condition for which palliative care is clearly appropriate.

At baseline, in a given day, the following data were abstracted from clinical records: demographic data, date of admission and of diagnosis of dementia, type of dementia, main comorbidities, ongoing treatments (artificial nutrition and hydration, dialysis, rehabilitation, mechanical ventilation, oxygen, restraints), and current prescriptions—doses and indications were not collected. The drugs were classified following the Anatomical Therapeutic Chemical (ATC) classification system.[13] Pressure sores were documented only if ≥NPUAP stage II (NPUAP, National Pressure Ulcer Advisory Panel)[14] which involves partial thickness loss of dermis without slough or intact or open/ruptured serum- or serosanginous filled blister.

The appropriateness of each prescription was assessed according to the Holmes, et al.[15] classification proposal. The proposal considered the conceptual model of palliative medicine and classified prescriptions into four categories using a modified Delphi consensus panel: always, sometimes, rarely, or never appropriate, or ‘‘no consensus’’ when a consensus was not achieved (see Table 1).

Statistical analyses

Descriptive data are shown as absolute and/or relative frequencies for categorical data and as mean – SD or median and interquartile range (IQR) for continuous variables (age and years since diagnosis of dementia). The Shapiro-Wilk normality test was used to check the normality of the continuous variables. The chi-square test for categorical variables and the t-test—or Mann-Whitney test (in the case of non normally distributed data) with independent data for continuous variables were carried out to assess possible differences between NH and HC patients. Independent differences between the NH and HC group for drug prescriptions as the unit of analyses were assessed by fitting a multivariable model using logistic regression, where the probability of each drug prescription (yes versus no) represented the dependent variable and NH versus HC group, gender, and age were the independent variables. The model was adjusted for clustering of patients within NHs. For all tests the significance level was set at a = 0.05. All analyses were performed with Stata statistical software version 9.2 (Stata- Corp., College Station, TX).

Results

Thirty-four of 55 NHs participated and enrolled 245 patients (range 3–20 patients/NH); and 165 patients were enrolled in the 5 districts of the Emilia-Romagna region (range 14–62 patients/district), totaling 410 patients with FAST stage 7c or higher. The two populations are described in Table 2. In NHs, compared to HC, patients were younger, more frequently female, and more frequently had Alzheimer's Disease.

More patients had muscle-skeletal problems, ankylosis/contractures, and psychiatric problems, whereas in HC, pressure sores were more commonly reported. Only three NH patients (none in HC) had advance care directives. Nearly one out of ten (9.9%; see Table 2) patients were tube fed, with no difference between HC and NH. No patients received dialysis or mechanical ventilation. Restraints were used frequently in NHs and in HC. Urinary catheters were more commonly used at home.

Twelve patients (2.9%) —nine in NHs and three in HC— had no prescriptions; 12.4% had only one (34, 13.8% in NH and 17, 10.3% in HC); and 84.6% had more than one (202 in NH and 145 in HC). In general, patients received a median of four prescriptions (range 0–13; mean: 4.1). This figure did not differ between HC and NH($P = 0.78$). Table 3 shows the drugs according to the ATC classification. Antihypertensive drugs (47.1%) and anticoagulants/antiplatelets (41.7%) were the most frequently prescribed drugs,

and more frequently in HC than in NHs. Antihypertension drugs were prescribed together with antiplatelets to 86 patients (21.0%; not in tables).

Several other drug classes were prescribed frequently (to around one-third to one-quarter of patients), including laxatives, antiacids/gastroprotective drugs, antidepressants, antipsychotics, and anxyiolytics/hypnotics.

Laxatives, antipsychotics, and anxiolytics/hypnotics were more frequently prescribed in NH, and antihypertension drugs, anticoagulants/antiplatelets, and antidepressants in HC. Further, in HC, general nutrients and opioids were prescribed less frequently, and medication for benign prostate hypertrophy, antibiotics, cardiac stimulants, and steroids more frequently than in NHs. Of note, analgesics represented only 2.0% of all prescriptions: acetaminophen was prescribed to two patients in HC and eight in NHs; opioids were prescribed to six patients in HC and 12 in NHs, and NSAIDs (classified as ''other'' in Table 3) to two patients. Overall, 8.1% of patients were given at least one analgesic. According to the classification reported by Holmes and colleagues, patients residing in NH received ''always appropriate'' prescriptions more frequently than patients in HC (see Table 4).

Discussion

This study identified an excessive use of disease-oriented medication in HC patients with advanced dementia (far advanced, FAST ≥7c), higher than in the much more frequently studied NHs. Prescription patterns differed widely between NHs and HC in Italy, even after adjustment for gender and age, and prescriptions were more frequently ''always appropriate'' in NHs. For example, patients at home were more often prescribed antihypertensive drugs, anticoagulants, and cardiac stimulants (mainly cardiac glycosides and ethylephrine), suggesting a philosophy of cure mainly oriented to the treatment and prevention of comorbid diseases. This is evident also from prescription of drugs for benign prostatic hypertrophy. This may also indicate a general practitioner's reluctance to modify the therapies (generally) prescribed by specialists or long underway.

Disease-oriented prescriptions may be more frequently provided in HC than in NH, possibly because the drug regimen in NHs is generally revised upon admission by the physician in charge, who may treat more dementia patients and patients with multimorbidity in long-term care settings than a general practitioner providing care at home.

In our study involving over 400 patients with advanced dementia, the patients received a median of four prescriptions, both in NHs and in HC. The median number of prescriptions is lower than observed for NH patients[16] and in a small U.S. nursing home study (6.5).[17] This may also be due to non opioid analgesics ranking second after cardiovascular drugs in that study, whereas analgesics were rare in our study. Furthermore, a recent study reports a decrease in the number of prescriptions with the increase of dementia severity.[18] Prescription of ''never appropriate'' drugs overall was lower than in the Tjia and colleagues study[17] (2.1% versus 5%).

Despite pain being common among dementia patients (21% to 83%)[19,20] and the high prevalence in our population of painful comorbidities such as ankylosis/contractures (69.0% in NH and 41.8% in HC), the use of pain relieving medications, such as opioids and acetaminophen, was notably rare in both settings (8.1% overall). The inadequate treatment of pain and symptoms in end-of-life patients has been reported in Italy;[21] in other countries, pain treatments are underprescribed in dementia patients.[18]

The prevalence of tube feeding (9.1%) is consistent with what has been reported mainly in U.S. studies (4% to 39%).[2,22] However it is lower than expected after the long media quarrel on the ''Eluana Englaro Case,'' and after the explicit stand of the Italian government and the Vatican[23,24] on defining artificial nutrition/ hydration an ''always mandatory proper care'' and not a medical treatment. Restraints were used ubiquitously in our study compared to other reports (from 15% to 66%)[25] and in the vast majority of NH patients. Data on the indications of antibiotics were not collected, but perhaps their higher prescription in HC is due to the higher prevalence of urinary catheters (nearly five times higher than in NH).

The use of antipsychotics (29.8% in NH), despite the evidence that they are not indicated in patients with advanced dementia, [26] was almost identical to the figures reported by Tjia and colleagues for the U.S.CASCADE nursing home study in the last 90 days of life (27.9%).[22] Holmes and colleagues consider antipsychotics and antidepressants as ''sometimes appropriate.''[15] Anti-psychotics may, however, produce severe adverse effects,[26] and it may be argued that their use should be limited even when resistance to care is present.[27]

The criteria on appropriateness of some prescriptions may deserve reconsideration in view of the very poor condition of the patients with FAST7c-f (far advanced dementia) in our study. However, the reconsideration of drug treatments and the discontinuation of medications in patients with far-advanced dementia at the end of life have not been thoroughly discussed. So far, most

recommendations derive from clinical trials where elderly and dementia patients are not included,[28] whereas the palliative care guidelines mostly refer to cancer patients. Furthermore, appropriate prescribing in advanced dementia at the end of life is challenging, because appropriateness according to a palliative care approach may be influenced by the perception of the patient's prognosis, but the ability of health care professionals to predict death even in better studied populations is limited.[29] Nevertheless, prescriptions should be reviewed in view of a goal of improving quality of life.

Our study was limited by prescriptions having been assessed in a cross-sectional survey, on a single day. Data on the duration of treatments were not collected, and it was not possible to distinguish the therapies long underway from those just started. Further, the aim of prescriptions was not registered, therefore the appropriateness of antibiotics could not be assessed.

Conclusions

Implementation of regular revision of drugs is recommended not only in nursing homes, but also in patients with dementia residing at home, taking into account the patient's condition as well as life expectancy and goals of care. An awareness of dementia as a terminal disease may help physicians and families consider comfort care as the main goal and use drugs consistent with this goal. Further studies on attitudes towards medication in HC versus NHs and on how to assess drug appropriateness in different settings are warranted, in particular in dementia patients near the end of life in variable stages.

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Author Disclosure Statement

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Appendix

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Table 1. Holmes et al. Classification[19] with ATC Code

Always appropriate

Antiemetics (A04A); Laxatives A06; Antidiarrheals (A07); Lidoderm (N01BB05); Narcotics (N02A); Non-narcotic analgesics (N02B); Antiepileptics (N03); Anxiolytics (N05B); Inhaled bronchodilators (R03A); Expectorants (R05); Lubricating eye drops; Pressure ulcer products.

Sometimes appropriate

Histamine-2-receptor blockers (A02BA); Proton pump inhibitors (A02BC); Insulin (A10A); Oral hypoglycemics (A10B); Electrolytes (A12); Nitroglycerin (C01DA); Diuretics (C03); Beta-blockers (C07); Calcium channel blockers (C08); Angiotensinconverting
enzyme (C09); Angiotensin receptor blockers (C09); Antifungal creams (D01); Corticosteroids (H02); Thyroid hormones (H03A); Antithyroid medications (H03B); Antibacterials (J01); Antivirals (J05); Capsaicin (N01BX04); Antidepressants (N06A); Allopurinol (M04AA01); Colchicine (M04AC01); Antipsychotics (N05A); Tricyclic antidepressants (N06AA); Antiparasitic agents (P0); Decongestants (R01); Inhaled corticosteroids (R03BA); Mucolytics (R05); Antihistamines (R06); Antiinflammatory eye drops (S01B); Antiglaucoma drops (S01E); Nutritional supplements (V06).

Rarely appropriate

Appetite stimulants (A15); Antispasmodics (A03A; A03B); Warfarin (B01AA03); Heparin and low molecular weight heparin (B01AB); Digoxin (C01AA); Antiarrhythmics (C01B); Clonidine (C02AC01); Hydralazine (C02DB02); Antiandrogens (G03H); Alpha blockers (G04CA01; G04CA03); Bladder relaxants (G04BD); Tamsulosin (G04CA02); Mineral corticoids (H02AA); Biphosphonates (M05BA).

Never appropriate

Antiplatelets, excluding Aspirin (B01AC excl B01AC06); Lipid lowering medications (C10); Sex hormones (G03H); Cytotoxic chemotherapy (L01); Hormone antagonists (L02B); Antiestrogens (L02BA; L02BB); Immunomodulators (L03); Nemantine (N06DX01); Acetylcholinesterase inhibitors (N07AA); Leucotriene receptor antagonists (R03DC).

No consensus

Meclizine (A04AB04); Vitamins (A11); Mineral supplements (A12); Aspirin (B01AC06); Iron (B03A); Red blood cell stimulating factors (B03XA); Bladder stimulants (G04BD); Finasteride (G04CB01); Calcitonin (H05BA); Muscle relaxants (M03); Sedatives and hypnotics (N05C); Central nervous system stimulants (N06B; N06D).

ATC, Anatomical Therapeutic Chemical classification system.

Table 2. Population Baseline Characteristics: Patients FAST ≥ 7c[c]

	All (n = 410)	Nursing homes residents(n = 245)	Home care service (n = 165)	p-value
Gender (%)				
Male	19.7	13.1	29.7	< 0.0001
Age				
Median (IQR)	86.0 (81.92)	85.0 (80–91)	88.0 (83–93)	0.0003[a]
Years since diagnosis of dementia				
Median (IQR)	7.0 (4–6)	7.0 (4–9)[b]	6.0 (4–9)[c]	0.747[a]
Type of dementia (%)				
Alzheimer's Disease	33.1	40.8	21.8	< 0.0001
Vascular Dementia	30.0	29.4	30.9	0.742
Mixed Dementia	25.6	21.2	32.1	0.013
Frontotemporal dem.	0.7	0.8	0.6	0.807
Lewy bodies dementia	0.5	0.4	0.6	0.776
Other	1.9	2.0	1.8	0.875
Not defined	8.0	5.3	12.1	0.013
Main concomitant conditions (%)				
Muscle skeletal	48.3	62.9	26.7	< 0.0001
Ankylosis/contractures	58.0	69.0	41.8	< 0.0001
Heart	48.3	46.5	50.9	0.384
Neurological	45.6	47.4	43.0	0.389
Vascular stroke[d]	35.6	38.8	30.9	0.103
Urologic	25.1	26.9	22.4	0.301
Metabolic	23.9	25.3	21.8	0.417
Bed sores	25.6	20.0	34.2	0.001
Respiratory	15.8	17.6	13.3	0.252
Psychiatric	12.6	15.9	7.9	0.016
Cancer	7.5	9.4	4.9	0.088
Skin	9.0	7.8	10.9	0.274
Infections	1.7	2.0	1.2	0.567
Supportive nondrug treatments (%)				
PEG	6.3	5.7	8.5	0.275
SNG	3.6	4.9	1.8	0.103
EV/SC hydration	16.1	16.3	15.8	0.893
Physiotherapy	13.2	19.2	4.3	< 0.0001
Oxygen therapy	4.1	4.1	4.2	0.936
Urinary catheter	33.4	13.5	63.0	< 0.0001
Enterostomy	0.7	0.8	0.6	0.861
Central venous catheter	0.2	0.4	-	-
Restraints, any	82.6	92.7	67.9	< 0.0001
Bed rails	53.2	89.0	-	-
Abdominal	29.3	49.0	-	-
Other treatments[e]	1.9	2.5	1.2	0.411

IQR, interquartile range.
[a]Mann-Whitney test.
[b]n = 239.
[c]n = 145.
[d]Other treatments.
[e]Restraints, any; bed rails; abdominal.

Table 3. Prescribed Drugs per Patient (%) FAST ≥7c

Drugs	ATC code	All (n = 410) %	Nursing home (n = 245) %	Home care (n = 165) %	p-value[a]
Antihypertension drugs	C02;C03;C07-9	47.1	36.3	63.0	< 0.0001
Anticoagulants (+ antiplatelets)	B01A	41.7	33.5	53.9	< 0.0001
Laxatives	A06	31.5	43.3	13.9	< 0.0001
Antiacids/Gastroprotective drugs	A02A/B	30.2	33.9	24.9	0.052
Antipsychotics	N05A	25.6	29.8	19.4	0.022
Antidepressants	N06A	25.6	20.8	32.7	0.003
Anxiolytics/Hypnotics	N05B/C	24.2	29.4	16.4	0.003
Anti-epileptics	N03	16.1	17.6	13.9	0.978
General nutrients (included vitamins & mineral supplements)	V06;A11;A12	12.9	17.6	6.1	< 0.0001
Vasodilators used in cardiac diseases	C01D	11.5	10.6	12.7	0.552
Benign prostatic hypertrophy[b]	G04	11.1	3.1	16.3	0.016[c]
Anti-Parkinson's	N04	10.7	10.2	11.5	0.410
Thyroid therapy	H03	8.5	7.8	9.7	0.519
Antibiotics (antibacterials and antimycotics)	J01;J02	8.1	3.3	15.2	0.004
Antidiabetics	A10	8.1	7.4	9.1	0.269
Anti-anemic preparations	B3	7.3	8.6	5.5	0.216
Cardiac stimulants	C01A/C	6.8	4.1	10.9	0.015
Respiratory system drugs	R	4.9	5.3	4.2	0.962
Dyphosphonates	M05BA	4.9	6.1	3.0	0.09
Steroids	H02AB	4.9	3.3	7.3	0.014
Functional bowel disorders	A03A/B/F	4.6	4.5	4.9	0.717
Acetaminophen	N02B	4.2	4.5	3.6	0.901
Opioids	N02A	3.9	4.9	2.4	0.025
Hyperuricemia drugs	M04	2.4	2.0	3.0	0.431
Skeletal muscle relaxants	M03	2.2	2.0	2.4	0.128
Hypercholesterolemia drugs	C10	1.5	1.2	1.8	0.191
Anti-arrhythmics class I-III	C01B	1.2	1.2	1.2	0.745
Sensory organs	S01	1.2	1.2	1.2	0.813
Anabolic agents for systemic use	A14	0.8	1.0	0.6	0.226
Anti-dementia drugs	N06DA;N06FA	0.7	0.4	1.2	0.074
Other products (liquids, EV solutions, and drugs prescribed < 4 patients, including NSAIDs)	-	1.2	1.6	0.6	0.034
Not classifiable	-	1.7	1.2	2.4	0.300

IV, intravenous; NSAID, non-steroidal anti-inflammetory drug.

[a]Adjusted for gender and age.

[b]49 male patients in HC and 32 in NH.

[c]Adjusted for age.

Table 4. Prescriptions Appropriateness According to the Holmes's Consensus Panel Classification

Appropriateness according to the Holems et al. consensus survey	All patients (n = 410*)		Nursing home residents (n = 245)		Patients followed by home care services (n=165)		
	N	%	N	%*	N	%[a]	p-value
Always	262	63.9	178	72.6	84	50.9	< 0.0001
Sometimes	327	79.9	190	77.7	137	83.0	0.1897
Rarely	78	19.0	43	17.5	35	21.2	0.3489
Never	9	2.2	7	2.8	2	1.2	0.274
No consensus	206	50.2	118	48.1	88	53.3	0.3017
Not included in classification	91	22.2	56	22.8	35	21.2	0.7020

[a]As most patients received more than one drug, the sum of percentages is higher than 100.