



ANTIEPILEPTIC DRUGS: TREATMENT IN ELDERLY PATIENTS.

Callegari C. *, Bianchi L., Vender S.

*Dipartimento di Medicina Clinica e Sperimentale Università degli Studi dell'Insubria, Via O. Rossi 9, 21100 Varese (Italy) Azienda Ospedaliera di Circolo e Fondazione Macchi - 21100 Varese (Italy)

Abstract: Introduction: This study aims to examine qualitatively the use of AEDs in a population of elderly patients in nursing homes, including the prescription of specialist and monitoring.

Methods: This prevalence study was carried out in a state-founded nursing home providing assistance and rehabilitation for elderly people. The first objective of the study is to determine the prevalence of the use of antiepileptic drugs. The second objective is to study the monitoring the dosage modification from the time of admission of the patient until the end of the study. Results: In the period of time that we took into consideration 65 of 402 patient's monitored patients had at least one anti-epileptic therapy (prevalence of 32%). The antiepileptic drug most prescribed was gabapentin with a frequency of 63.6%. Discussion: The prevalence use of AEDs has been 32%. The second objective concerns the drugs monitoring and it has also been achieved and shows how gabapentin is the most prescribed drug (53.8% psychiatrist) and was introduced mainly for anxiety disorders, psychosis, neuropathic pain and mood disorders.

Keywords: antiepileptic drugs, elderly patients, gabapentin

Introduction

The increase of the population aged > 65 years in Italy is the current evidence, as well as the inclusion of the elderly in nursing homes [1]. Despite the high presence of psychiatric disorders among institutionalized elderly, only a

part of patients is evaluated by a specialist psychiatrist, only when they show agitation (34.8%), aggressive behavior (23.5%), depression (17.2%), delusions and hallucinations (14%) [2]. And we need to assess the safety of prescribing psychopharmacological therapies because there is a correlation between polypharmacy and side effects such as falls [3][4].

Antiepileptic drugs are the primary treatment for epilepsy [5]. The incidence of epilepsy is generally around 50 per hundred thousandths per year and increases in patients older than 60

For Correspondence:

camilla.callegari@uninsubria.it

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years [6]. The use of antiepileptic drugs instead has a prevalence that ranges from 10.5 to 11% [7]. The treatment of seizures in the elderly is sometimes aggravated by comorbidities and polypharmacy [8] for many antiepileptic drugs the problem of the age is placed in terms of tolerability that was partially resolved with the introduction of gabapentin and lamotrigine [9]. AEDs have become an integral part of the treatment of psychiatric and neurological disorders and symptoms different from seizure disorder.

Some epidemiological studies have shown a high prevalence of psychiatric disorders among the elderly residents in nursing homes: the majority presents clinically significant depressive symptoms [10]. The use of AEDs has been introduced to treat symptoms such as anxiety, depressive symptoms, impulse control and episodes of psychomotor agitation [11][12][13][14][15]. The latest synthesis of AEDs (gabapentin, pregabalin, vigabatrin, lamotrigine, oxcarbazepine, topiramate) seem to have these characteristics of greater tolerability in elderly, especially when compared with benzodiazepines, with whom they share some therapeutic indications towards psychiatric symptoms more common (anxiety, agitation and insomnia) and showing a far less side effects (increased mental confusion in the elderly, addiction, withdrawal, delirium, postural instability and consequent falls) [16][17].

In psychiatry antiepileptic drugs are recommended in the treatment of bipolar depression [18] and other mood disorders associated or not to anxiety disorders [19]. The availability of a new generation of drugs has expanded therapeutic options for the treatment of bipolar patients who are resistant or intolerant to traditional mood stabilizers, such as carbamazepine and valproic acid, which have proved useful in the short-term treatment of manic episodes, of mixed states and for the long-term prevention of relapse of bipolar disorder [18]; both reported a good tolerance (the most common adverse effect is weight gain). Several studies show that carbamazepine and oxcarbazepine appear effective equivalently lithium or some neuroleptics in the treatment of acute manic episodes [20] and in the prevention

of manic relapse. Lamotrigine effective targeted acute bipolar depression and maintenance therapy, with special reference to the prevention of depression [21] either as monotherapy or in combination.

This study aims to examine qualitatively the use of AEDs in elderly patients in nursing homes.

Materials and Methods

This prevalence study was carried out at the “*Residenza Sanitaria Assistenziale (RSA) Fondazione Fratelli Molina*” in Varese (Italy), a state-founded nursing home providing assistance and rehabilitation for elderly people. The nursing home is composed of four buildings, or units, and it has about 450 beds. The units are heterogeneous as regards their architectural design, care protocols and the number of beds. Since March 2000, a consultation-liason project has been in place between this institution and the Psychiatry Unit of Department of Clinical and Experimental Medicine, University of Insubria in Varese.

The first objective of the study is to determine the prevalence of the use of antiepileptic drugs, for this reason we undertook an observation period of 3 months (from 20/08/2013 to 20/11/2013) during which we have examined the prevalence of treatment with these drugs and the reason of the introduction of this therapy. The second objective is to study the methods of administration of antiepileptic drugs, recording the changes relating to the use of these drugs, from the suspension to the change of the drug, the simple dosage modification from the time of admission of the patient until the end of the study with a consultation and follow-up lasted a year (20/11/2013 – 20/11/2014).

Data collection took place through the consultation of medical records of all guests, excluding patients in a coma and those affected by Alzheimer’s disease, for a total of 402 patients. Of each patient were collected the following data:

- Socio-demographic data: date and place of birth, gender, marital status, education, occupation, date of admission in the structure.
- Clinical data: total number of medical diagnoses per patient, presence of

neurological disease (brain atrophy, vascular encephalopathy, stroke, degenerative nervous disease, brain tumors, cerebral haemorrhages), number of psychiatric diagnoses, number of psychiatric consultation received, assessment of the degree of cognitive impairment, epileptic seizures or epilepsy and type of epilepsy.

- Data relating to drug therapy: the total number of drugs administered to the patient at the time of the observation, the total number of psychiatric drugs in therapy at the time of detection (ATC N06A antidepressants: tricyclics, SSRIs, SNRIs, neuroleptics ATC N05A: typical, atypical; ATC N05BA anxiolytics benzodiazepines, antihistamines ATC R06A, antiepileptics ATC N03). For each antiepileptic drug dose were reported in place at the time of the observation, and prescriber patterns in the introduction of anti-epileptic drug therapy (psychotic disorder, depression, delirium, cognitive impairment, general medical conditions, personality disorders, epilepsy, neuropathic pain, anxiety).
- SOSIA rating scale: it classifies the level of fragility of the guests by three dichotomous indicators that assess mobility, cognitive/behavior abilities and the presence of comorbidities. The indicator of mobility considers the following item: "personal hygiene", "walking", "transfer bed/chair" and "power"; indicator of cognition is estimated by the following item: "confusion/mental state", "irritability/state relationship" and "restlessness/behavioral state"; indicator of comorbidity is calculated from the pathologies of the elder. The indicator values are calculated by the sum of the scores of the individual items and dichotomized (mild or severe) based on a cut-off default. For indicator of mobility was arbitrarily place the cut-off value 4 by creating two classes of motor dependence: if ≤ 4 then dependence motor "serious". For indicator global cognitive ability the cut-off was set equal to 7.5: were considered "serious" those patients with score > 7.5 . Finally gravity to comorbidity has been

established by a cut-off of the indicator of comorbidity value > 16 "serious". SOSIA classes ranging from 1 (the most fragile) to 8 (the less fragile) [22]. The evaluation of the scale was performed by the physician of the structure to the admission of the patient in the structure.

- Evaluation of the level of cognitive impairment using the Mini Mental State Examination (cut-off < 24 points) [23]. The evaluation of the scale was performed by the physician of the structure to the admission of the patient in the structure.
- The data analysis was performed with SPSS® 13.0 for Windows (SPSS® Inc, Chicago, IL).

The study was approved by the institutional review board of the *Fondazione Fratelli Molina*.

Results

In the period of time that we took into consideration 65 of 402 patients monitored patients had at least one anti-epileptic therapy (prevalence of 32%).

The average age of patients who had at least one anti-epileptic therapy was 79.05 years with a minimum age of 43 years and a maximum of 99 (SD = 10.729). 19 were men (29%) and 46 women (71%) with a mean age of 77.29 years for men (SD = 8.376) and for women 79.79 years (SD = 11.533). Regarding marital status 28 patients were widowed (37.2%), 15, married (22.5%), 11 unmarried (17.1%), in 13 cases it was not specified (20.2%) and 2 separated (3.1%). As for education 59.9% of patients had achieved a primary degree, 8.5% graduating from junior high, 14.7% graduated from high school and 1.6% was graduate (the remainder is not specified). In most (58.8%) were employed, 14% housewife, 8.5% self-employed, 1.6% artisan, businessman 0.8%, 2.3% were invalid and 17.1% was not specified. From patient records showed that those taking antiepileptic 13 had a diagnosis of epilepsy (20.2%, corresponding to 3.5% of all patients in RSA), 29 (44.2%, corresponding to 7.2 % of total patients) had a cognitive impairment or had a diagnosis of dementia.

Diagnosis	Women		Men		N total
	N	%	N	%	
Psicotic disorder	6	56,5	5	43,5	11
Depression	12	78,1	4	21,9	16
Cognitive impairment	24	82,5	5	17,5	29
Medical disease	15	57,7	11	42,3	26
Personality disorder	2	60,0	1	40,0	3
Anxiety	6	100	0	0	6
Epilepsy	9	73,1	4	26,9	13
Neuropathic pain	6	65,0	4	35,0	10

Table 1: Use of AEDs by pathology and by sex. There is a statistically significant relationship between the patient's gender and diagnosis of cognitive impairment or dementia: women (51.6%) outnumber men (26.3%) ($p = 0.008$). A significant p value (0.026) shows a significant relationship between female and anxiety symptoms (such as tachycardia, tremors, panic attacks, insomnia, precordial constriction, hyperventilation) in 14.3% of females and no males. The percentage distribution of the guests in therapy for AED classes fragility SOSIA is described in the table number 2: there is an high distribution among class 2 of vulnerability (32%).

SOSIA classification	%
Class 1 (most vulnerable)	14
Class 2	32
Class 3	22
Class 4	10
Class 5	8
Class 6	11
Class 7	1
Class 8 (less vulnerable)	2

Table 2: Distribution of the classes according to the scale of vulnerability SOSIA
The distribution of the cognitive status of the 65 guests, according to the MMSE is described in Table 3.

MMSE	%
Normal (score :24-30)	19
Mild to moderate impairment (score 18-23)	27
Serious impairment (score 0-17)	54

Table 3: Distribution of the cognitive status, according to the MMSE

We can observe how the patients considered in our study are damaged both in cognitive status and physical status. Among the 65 subjects in an antiepileptic therapy all were in drug therapy with a number of drugs between 4 and 19.

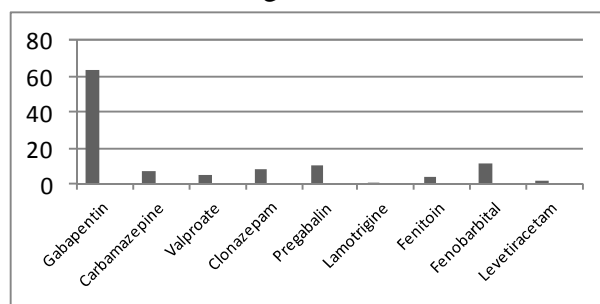


Table 4: Frequency (%) of AED use.

The antiepileptic drug most prescribed was gabapentin with a frequency of 63.6%, followed by phenobarbital with 11.6%, 10.1% pregabalin, clonazepam 8.5%, 7% carbamazepine, valproate 4.7%. The 65.1% of antiepileptic drugs have been introduced in therapy after admission in RSA during the assessment covered in our study. The prescribers of these antiepileptic drugs were the physician specialising in geriatrics (43.7%), the psychiatrist (37.2%), the neurologist (13.3%), unspecified (18%), physiatrist (0.8%) and palliative specialist (0.8%).

Gabapentin in 91.3% of cases was introduced in RSA ($p = 0.000$), only 6 patients (8.8%) was present in therapy before admission. It was prescribed in 35 patients (53.8%) by the psychiatrist, in 14 (22.5%) from the intern RSA, the neurologist in 6 (10.0%), in 6 cases (8.8%) was not specified, in 2 (3.8%) from the physiatrist and in one case it was suggested by the palliative specialist. It is the only molecule anticonvulsant prescribed by physiatrist and prescribed nell'89,6% of prescriptions of AEDs

by the psychiatrist, in 40.0% of those of the neurologist, in 85.7% of the physician specialising in geriatrics. The use of this molecule is associated with psychotic disorders ($p = 0.007$), depression (0,010), neuropathic pain ($p = 0.005$) and anxiety ($p = 0.010$).

The symptoms assessed during the three months of observation and the year of follow up were grouped into broad categories with the main symptoms.

The category was:

1. *cognitive impairment* and *dementia* include loss of recent memory and orientation, confusion, anxiety, restlessness, agitation, aggression, lack of recognition of family, fatuity
2. *sleep disorders* include insomnia and sleepiness
3. *behavioral changes* include resounding verbal symptoms, bizarre behavior, escape, confabulation, bustle, impulsive behavior, reactivity, claims, polemical attitude, anger, negativism
4. *psychotic symptoms* include delusions, hallucinations, persecutory experiences
5. *mood disorders* include depression, thymic deflection, dysphoria, sadness, guilt, feelings of inadequacy, anxiety, manic symptoms, mental ruminations, emotional incontinence, dissatisfaction
6. *somato-neurological symptoms*, epilepsy, somatic complaints involving difficulty walking, neuropathic pain.

In the majority of cases (44.0%) antiepileptics were introduced for *cognitive impairment* or *dementia*, for depression (27.4%) and for *psychosis* (25.0%). During the one year follow-up lasted from 20/11/2013 to 20/11/2014, the increase of dosage, it was found 86 times, the reduction in 57 for a total of 143 variations of dose. From this calculation were excluded first prescriptions because they consider them as variations. There were also 33 suspensions of antiepileptic which was then or replaced with another molecule or no longer introduced. Changes in the dosage of antiepileptic are correlated in a statistically significant sleep disturbance ($p = 0.002$), the behavioral changes with p-value of 0.004 and somato-neurological disease ($p = 0.004$). Going to study what is the

specific symptom of subcategories more closely related to the change of dosage it is seen that there is a statistically significant relationship with aggression ($p = 0.019$), with increase in dose in 5 patients (6.4%) and reduction in 1 (0.9%), including sleep disorders with sedation ($p = 0.00$), where increases were 2 (2.3%) and 11 reductions (18.6%). Among the somato-neurological disorders there is an association between the changes of dose and pains ($p = 0.032$), there were 6 increases (7.6%) and 2 reductions (1.8%). Among those who had an increase of AED posology 15.7% ($n = 10$) had at least one other anti-epileptic drug therapy, while for the reductions was present polypharmacy (≥ 4 drugs) [3] in 24.6% ($n = 16$) for a total of 12 (19.2%) changes in polytherapy.

	Dosage AED >		Dosage AED <		Total	
	N	%	N	%	N	%
cognitive impairment	28	35,8	16	25,4	44	31,7
sleep disorders	8	10,4	14	23,7	22	15,7
behavioural changes	12	19,1	6	7,0	18	14,3
psychotic symptoms	9	11,0	6	7,0	15	9,4
mood disorders	10	18,5	8	12,3	18	16,0
somato - neurological symptoms	19	25,4	7	11,4	26	19,9
Total	86		57		143	

Table 5: Dosage of AED during monitoring time.

Table number 5 represents the general description of dosage, our data shows the drug that has undergone significant changes was the gabapentin. A statistically significant relationship with $p = 0.004$ is between sleep disorders (insomnia) and reduction of gabapentin. Also significant is the relationship between an increase in dosage of this antiepileptic and behavioral changes ($p = 0.011$) and between the rise and somato-neurological disorders ($p = 0.029$).

Discussion

The sample evaluated is composed mainly of women with an average age of 79.79 years (SD 11.533), of 65 patients, 37.2% were widowed.

From our study emerges as the prescription of antiepileptic drugs is of great help for the treatment of psychiatric and neurological disorders. The prescription is done mainly by the doctor within the unit (43.7%) and the psychiatrist (37.2%). In the majority of cases (44.0%) antiepileptics were introduced for cognitive impairment or dementia, for depression (27.4%) and for psychosis (25.0%). The first objective regarding the prevalence use of AEDs has been reached (32%). The second objective concerns the drugs monitoring it has been achieved and shows how gabapentin is the most prescribed drug (53.8% psychiatrist) and was introduced mainly for anxiety disorders, psychosis, neuropathic pain and mood disorders. The variations of the drug have occurred significantly with insomnia ($p = 0.004$) and it is correlated with the its sparsely sedative properties, the gabapentin introduced in evening hours was reduced because it is not calming.

Within the same nursing home a previous study of Baranzini F. *et al* [24] indicated the risk of sedation and falling is elevated in some drugs such as BDZ. In our study the increase of AEDs dosage occurred in the case of behavioral disorders and somato-neurological disorders shows how this treatment is preferred in patients with somatic problems that include walking difficulty. During the monitoring period we haven't observed falling regarding the 65 patients considered.

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