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ORIGINAL ARTICLE

Prescribing pattern and resource utilization of monoamine oxidase-B inhibitors in Parkinson treatment: comparison between rasagiline and selegiline

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Abstract Difference between selegiline and rasagiline for effectiveness in Parkinson's disease (PD) is uncertain, nevertheless their costs highly differ: rasagiline is more expensive than selegiline. This study was aimed to compare prescribing pattern and resource utilization in PD patients treated with rasagiline or selegiline. Historic cohort study, based on databases of three Italian Local Health Authorities was performed. Patients with PD and receiving rasagiline or selegiline between 01-07-2009 and 31-12-2011 were selected and followed-up for 12 months. As outcomes, and relevant costs, were evaluated: (a) anti-parkinson prescriptions; (b) hospitalization for PD and for fracture; (c) antiinflammatory and antirheumatic prescriptions; (d) antipsychotic prescriptions; (e) hospitalization for cardiovascular diseases; (f) cardiovascular prescriptions; (g) ambulatory visits or diagnostic tests. Average annual cost per patient was considered for both PD-related expenditure (a + b + c) and overall cost (a + b + c + d + e + f + g). Differences between rasagiline and selegiline were analysed by generalized linear model. Overall 1607 patients were selected: 63.7 % under selegiline and 36.2 % under rasagiline. Hospitalizations for PD occurred more in rasagiline group than in selegiline one (13.6 vs. 8.0 %, $p < 0.001$), whereas hospitalizations for fractures less in rasagiline group than in selegiline one (1.4 vs. 3.8 %, $p = 0.005$). Dopamine agonists (66.0 vs. 31.0 %, $p < 0.001$) and levodopa (73.9 vs. 49.0 %, $p < 0.001$) were prescribed more frequently in rasagiline group than in selegiline one. The choice to prescribe rasagiline produced a statistically significant increase in both overall cost (+2404 €, $p < 0.001$) and PD-related cost (+2363 €, $p < 0.001$). In conclusion, prescribing patterns and health resource utilization highly differ between rasagiline and selegiline. There is no homogeneous prescription behaviour among clinicians in preferring one or the other MOAB-I, on the basis of demographic, clinical and therapeutic characteristics of patients with PD.

Keywords Parkinson's disease · Rasagiline · Selegiline · Pattern of use · Costs · Drug utilization

Introduction

Parkinson's disease (PD) affects over 6 million people worldwide, 1.2 million located in Europe, and, out of these, 200,000 in Italy [1]. It represents the second most common neurodegenerative disorder after Alzheimer's disease. In recent years, the interest on this condition is grown substantially due to increasing social and economic burden on societies due to populations age; the estimated prevalence of PD is 0.3 % of the entire population and about 1 % in people over 60 years of age [2]. In Italy, the prevalence of PD ranged from 0.07 to 0.3 % [3–5].

There is no proven curative therapy for PD, and available drugs deserve to alleviate specific motor symptoms, such as bradykinesias, tremor, rigidity, and postural instability [6].

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Although levodopa and its combination with dopa-decarboxylase inhibitor allow a good control on these motor complications [6], a prolonged therapy with these substances, especially at higher doses, could generate dyskinesia and motor fluctuations (called off-time periods). A strategy to manage such events consist in adding other anti-parkinson drugs, such as dopamine agonists, catechol-O-methyltransferase inhibitor and/or monoamine oxidase type B inhibitors (MAOB-I) [7].

Among this last therapeutic group (i.e. MAOB-I) two substances are available on the market: rasagiline and selegiline. Selegiline is the first MAOB-I for PD approved in 1996 by the US Food and Drug Administration (FDA) [8] and consequently in European Countries; whereas, rasagiline was approved in 2005 by European Medicines Agency (EMA) and in 2006 by FDA [9, 10]. Both drugs have selectivity for MAO type B rather than the type A and, according to the results coming from regulatory trials, they are labelled as an adjunctive therapy to levodopa, or as monotherapy in early PD [11–15].

Although clear differences between selegiline and rasagiline can be found in chemical structure, metabolites and in findings coming from animal experiments [16], studies involving patients with PD do not reveal clinically significant differences on the primary outcome evaluated in trials (i.e. changes in daily off-time periods) [11, 13, 14].

To date, no head-to-head study is available to compare these two drugs, whereas various indirect comparisons were conducted. The results of these indirect comparisons are conflicting: some authors concluded that these two drugs have a comparable efficacy [17], especially in early treatment [18], instead another study stated that rasagiline have relevant advantages over selegiline in efficacy and safety [19].

Although the actual difference in the clinical efficacy of these substances is still uncertain and data on their consumption are unavailable, the costs associated with them are very different: in Italy, where both drugs are reimbursed by the National Health System, the cost of 1 defined daily dose (DDD) [20] of rasagiline is much higher than selegiline (rasagiline 5.09 € vs. selegiline 0.34 €) [21].

To date, several analyses investigated the economic burden of PD and the cost-utility of single anti-parkinson drug [22–25], but there is a paucity of information addressing the cost-effectiveness comparison of either drug in the management of PD.

The aim of this study was to compare treatment patterns, health care resource use and costs in patients with PD treated with either rasagiline or selegiline.

Methods

Setting and study population

This was an historic cohort study conducted by using a record linkage strategy of different administrative databases located in three Local Health Authorities of three Italian regions (Lombardy, Lazio and Puglia), covering 1,865,000 of inhabitants. The following administrative data sources were searched: prescription databases, including information on reimbursed drugs prescribed to out-patients; hospital discharge database, collecting information on diagnosis causing hospitalization; ambulatory care database, including data on specialist ambulatory visits.

The cohort consisted of patients affected by PD and receiving MAOB-I prescription. We first selected subjects treated with any anti-parkinson drug by using the Anatomical Therapeutic Chemical (ATC) [20] code N04* (anti-parkinson drugs), then we identified patients with PD according to Moisan's criteria [26], finally we included in the cohort only subjects with a prescription of MAOB-I [ATC N04BD* (monoamine oxidase-B inhibitors)] between July 2009 and December 2011. The first prescription of the MAOB-I was considered the index date of each enrolled subject. The 6-month period preceding the index date was used to characterize each patient in terms of previous treatment with MAOB-I and in terms of comorbidities expressed as Charlson index score [27].

Exposure variables

Were considered exposed to MAOB-I those subjects with PD and receiving a prescription of rasagiline (ATC: N04BD02) or selegiline (ATC: N04BD02). According to the presence/absence of any prescription of MAOB-I during the pre-index period (6 months pre-index date), subjects were considered established or naïve for treatment with these drugs. Moreover, previous treatments with or without other anti-PD drugs were considered to better describe the therapy of patients.

Clinical outcome measures

The 12 months subsequent the index date represented the follow-up period. During this period, the possible hospitalizations for PD or fractures [identified by using the following International Classification of Diseases 9th Revision Clinical Modification—ICD9-CM codes [28]: for PD 332* (Parkinson's disease), 333* (other extrapyramidal disease and abnormal movement disorders), 781* (symptoms involving nervous and musculoskeletal systems); for

fracture 800* (fracture of vault of skull), 829* (fracture of unspecified bones)] were assessed in the two exposure groups. Other hospitalizations, occurred during the follow-up, were grouped according to the ICD9-CM Major Diagnostic Categories [28]. During the follow-up also the prescription history of each patient were evaluated, and the following parameters were provided: prescription of concomitant anti-PD drugs (i.e. levodopa, dopamine agonists and other anti-PD drugs), the duration of treatment with MAOB-Is and the adherence to MAOB-Is. The duration of treatment was defined as the days between the index date and the last MAOB-I prescription date, plus the numbers of days covered by the last prescription in terms of number of Defined Daily Doses (DDD) [20]. Treatment adherence was estimated by the Medication Possession Ratio (MPR) defined as the total days of supply of MAOB-I divided by number of days between the first prescription and the last refill, including the duration of the last refill. A patient was defined adherent when the MPR was $\geq$80 %. All these parameters were compared both between naïve for treatment and established patients, and between selegiline and rasagiline groups.

Resource-utilization outcome measures

During the follow-up period, information are collected on the following health resources related to PD and the relevant costs: (a) prescriptions of anti-PD drugs (ATC: N04*-anti-parkinson drugs); (b) hospitalizations for PD and for fracture; (c) prescriptions of antiinflammatory and antirheumatic drugs [ATC: M01* (antiinflammatory and antirheumatic products)]; (d) prescriptions of antipsychotics [ATC: N05A* (antipsychotics)]; (e) hospitalizations for cardiovascular diseases [ICD9-CM 390*-459* (cardiovascular diseases)]; (f) prescriptions of cardiovascular drugs [ATC: C* (cardiovascular drugs)]; (g) specialist ambulatory visits or diagnostic tests.

Costs resulting from (a), (b), and (c) were considered directly related to PD, whereas those from (d), (e), (f) and (g) were considered indirectly related to the disease. Average annual cost per patient, expressed in euros, was considered both for expenditure directly related to PD (a + b + c) and for overall cost (a + b + c + d + e + f + g).

Statistical analysis

Differences among independent variables (i.e. age, gender, therapy and hospitalization) between the two groups (rasagiline or selegiline) were analysed by the Chi-square and a statistical significance was defined as a 2-sided probability value below 0.001.

In order to identify the weight of specific cost item for each treatment group, a generalized linear model was used with the relevant 95 % confidence interval (95 % CI).

All analyses were performed by using STATA SE, version 12.0.

Ethics statement

To assurance patient privacy, each subject was assigned an anonymous univocal numeric code by the Local Health Authority. No identifiers or data that permitted identity the patient in a direct or indirect way were provided to the researchers. This data processing method was formalized in a special section of the agreement between CliCon S.r.l. and Local Health Authority for the purpose of conducting the analysis. In accordance with national regulations regarding the conduct of observational analysis, the present study has been notified to the local Ethical Committee of the participating Local Health Authorities.

Results

The study population was identified starting from a resident population of 1,865,000 of inhabitants. In this population, 14,710 subjects received a prescription of any anti-parkinson drug, and, out of these 10,270 (69.8 %) had a definite diagnosis of PD according to Moisan's criteria. Among these, 1607 patients with PD and receiving a MAOB-I drug were selected for the study. Therefore, MAOB-Is were prescribed in 15.6 % of patients affected by PD and in 0.1 % of the entire population (Fig. 1).

In the study cohort, selegiline represented the 63.7 % of subjects ($n = 1024$) and rasagiline the remaining 36.2 % ($n = 583$). Patients treated with selegiline showed an average age higher than those receiving rasagiline (75.8 vs. 69.2, $p < 0.001$). Also gender distribution was different between two groups: males were 45.2 % in selegiline group, while in rasagiline group 57.8 %. Among patients treated with selegiline, the 38.7 % were naïve for MAOB-I (out of these 61.3 % did not received any anti-PD treatment in the 6 months preceding the first MAOB-I prescription), whereas subjects naïve for rasagiline were 42.4 % (out of these 51.8 % were naïve also for any anti-PD treatment). Consequently, 57.6 % of subjects receiving rasagiline were in established treatment in the 6 months preceding the first observed prescription, in comparison with 44.7 % of those receiving selegiline ($p < 0.001$). Most (89.6 %) of the patients in treatment with rasagiline received also other anti-PD drugs, while among subjects established with selegiline the 50.9 % were in treatment with other anti-PD drugs.

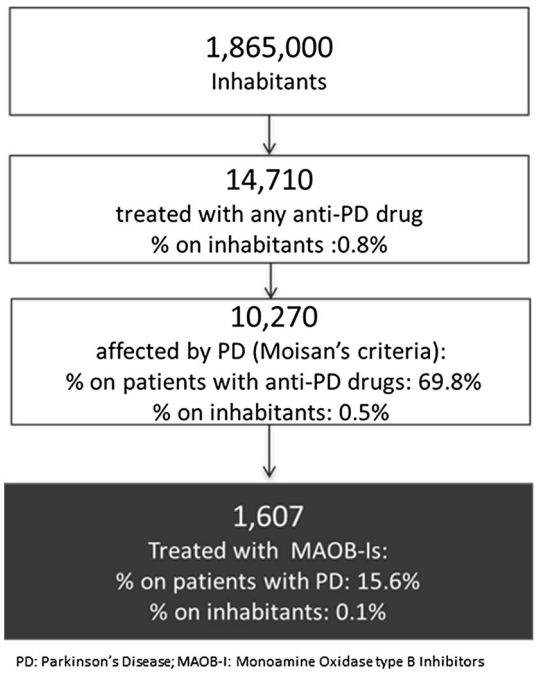

Fig. 1 Selection of study population

Moreover, subjects with rasagiline appeared with a lower degree of comorbidity than those receiving selegiline (Charlson index average 1.4 vs. 1.0, $p < 0.001$, Table 1).

In the 12 months subsequent to the prescription of MAOB-I drug, patients treated with rasagiline were hospitalized more for PD rather than those treated with selegiline (13.6 vs. 8.0 %, $p < 0.001$). On the contrary, the hospitalizations for fracture appeared less frequent in the rasagiline group than selegiline one (1.4 vs. 3.8 %, $p = 0.005$, Fig. 2). These differences were confirmed also by analysing overall hospitalizations through major diagnostic categories: hospitalizations for "disease of nervous system" were higher in rasagiline than in selegiline group (6.2 vs. 2.6 %, $p < 0.001$); while admissions for "injury and poisoning" were lesser in rasagiline in comparison with selegiline group (2.1 vs. 4.3 %, $p = 0.019$, Table 2). Apart from hospitalizations for "diseases of circulatory system", slightly higher among selegiline users than in rasagiline ones (5.8 vs. 3.8 %, $p = 0.08$) due to the older age in the selegiline group, no significant differences were found for all other diagnostic categories. The analysis of the antiparkinson drugs prescribed in addition to MAOB-Is during the follow-up (Fig. 3), showed that dopamine agonists and levodopa were prescribed more frequently in rasagiline group than in selegiline one. Specifically levodopa was prescribed in the 73.9 % of all patients receiving rasagiline vs. 49.0 % of those treated with selegiline ($p < 0.001$), and dopamine agonists in the 66.0 vs. 31 % ($p < 0.001$), respectively. Moreover, the duration of MAOB-I treatment was longer in rasagiline users in comparison with selegiline ones (in average 302 vs. 284 days, $p < 0.001$), both for naïve and established subjects (Table 2). On the contrary, the subjects treated with selegiline resulted more adherent to the treatment in comparison with those treated with rasagiline (adherent patients: 72.9 vs. 59.0 %, $p < 0.001$). This difference was present both comparing naïve and established patients (Table 2).

Figure 4 depicts the average annual costs per patient, for rasagiline or selegiline group. With the exception of costs coming from prescriptions of cardiovascular drugs and

Table 1 Baseline demographic, therapeutic and clinical characteristics of patients enrolled in the study

	Overall 1607	Selegiline 1024	Rasagiline 583	*p* value
Demographic characteristics				
Age (average ± SD)	73.4 ± 10.3	75.8 ± 9.3	69.2 ± 10.7	<0.001
Male *n* (%)	800 (49.8)	463 (45.2)	337 (57.8)	<0.001
Therapeutic characteristics[a]				
Naïve for MAOB-I *n* (%)	813 (50.6)	566 (55.3)	247 (42.4)	0.014
In treatment with other anti-PD drugs *n* (%)	338 (41.6)	219 (38.7)	119 (48.2)	
No treatment with other anti-PD drugs *n* (%)	475 (58.4)	347 (61.3)	128 (51.8)	
Established for MAOB-I *n* (%)	794 (49.4)	458 (44.7)	336 (57.6)	<0.001
In treatment with other anti-PD drugs *n* (%)	534 (67.3)	233 (50.9)	301 (89.6)	
No treatment with other anti-PD drugs *n* (%)	260 (32.7)	225 (49.1)	35 (10.4)	
Clinical characteristics[a]				
Charlson index (average ± SD)	1.3 ± 1.3	1.4 ± 1.3	1.0 ± 1.2	<0.001

SD standard deviation, *PD* Parkinson's disease, *MAOB-I* monoamine oxidase type B inhibitors

[a] In the 6 months pre-index date

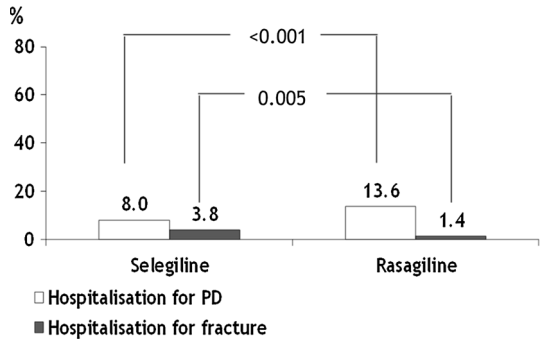

Fig. 2 Hospitalizations that occurred during the follow-up period in rasagiline or selegiline groups

hospitalizations for cardiovascular diseases, the costs related to all other items appeared higher in the rasagiline group than in selegiline one. In particular, the expenditure per patient for antiparkinson drugs was 2639 € for rasagiline vs. 495 € for selegiline, and the cost for hospitalizations directly related to PD was 986 € for rasagiline vs. 634 € for selegiline. Also the costs of specialist ambulatory visits and diagnostic tests appeared higher in the rasagiline group than selegiline one (285 € vs. 156 €).

The generalized regression model (Table 3) showed that, starting from the baseline annual cost for each patient of 1659 € as overall expenditure and 664 € as disease related expenditure, the choice to prescribe rasagiline rather than selegiline produced a statistically significant cost increase, both for the overall cost (+2404 €, $p < 0.001$) and for the PD-related one (+2363 €, $p < 0.001$). Additional factors that showed a statistically significant increase of overall cost were: the augmentation of comorbidity index (+615 €, $p < 0.001$) and the occurrence of a hospitalization for PD (+3457 €, $p > 0.001$); whereas, the presence of an established antiparkinson therapy caused a statistically significant increase of PD-related cost (+447 €, $p < 0.001$).

Table 2 Follow-up clinical and therapeutic characteristics of patients enrolled in the study

	Overall 1607	Selegiline 1024	Rasagiline 583	*p* value
Clinical characteristics[a]				
Diseases of the circulatory system	81 (5.0)	59 (5.8)	22 (3.8)	0.08
Diseases of the nervous system	63 (3.9)	27 (2.6)	36 (6.2)	<0.001
Injury and poisoning	56 (3.5)	44 (4.3)	12 (2.1)	0.019
Diseases of the digestive system	54 (3.4)	35 (3.4)	19 (3.3)	0.865
Diseases of the sense organs	36 (2.2)	17 (1.7)	19 (3.3)	0.037
Symptoms, signs, and ill-defined conditions	29 (1.8)	19 (1.9)	10 (1.7)	0.839
Neoplasms	25 (1.6)	13 (1.3)	12 (2.1)	0.219
External causes of injury and supplemental classification	19 (1.2)	10 (1.0)	9 (1.5)	0.312
Diseases of the musculoskeletal system and connective tissue	18 (1.1)	13 (1.3)	5 (0.9)	0.451
Diseases of the genitourinary system	17 (1.1)	6 (0.6)	11 (1.9)	0.014
Mental disorders	11 (0.7)	9 (0.9)	2 (0.3)	0.21
Endocrine, nutritional and metabolic diseases, and immunity disorders	9 (0.6)	8 (0.8)	1 (0.2)	0.115
Diseases of the skin and subcutaneous tissue	5 (0.3)	5 (0.5)	0 (0.0)	0.091
Diseases of the blood and blood-forming organs	5 (0.3)	3 (0.3)	2 (0.3)	0.862
Infectious and parasitic diseases	3 (0.2)	3 (0.3)	0 (0.0)	0.191
Congenital anomalies	1 (0.1)	0 (0.0)	1 (0.2)	0.185
Therapeutic characteristics[a]				
Duration of MAOB-I treatment (average days ± SD)	290 ± 95	284 ± 99	302 ± 85	<0.001
Naïve (average days ± SD)	284 ± 98	276 ± 102	304 ± 83	0.006
Established (average days ± SD)	293 ± 93	287 ± 98	302 ± 86	0.008
Patients adherent to MAOB-I treatment (%)	1091 (67.9)	747 (72.9)	344 (59.0)	<0.001
Naïve (%)	333 (70.1)	257 (74.1)	76 (59.4)	0.003
Established (%)	758 (67.0)	490 (72.4)	268 (58.9)	<0.001

[a] In the 12 months post-index date

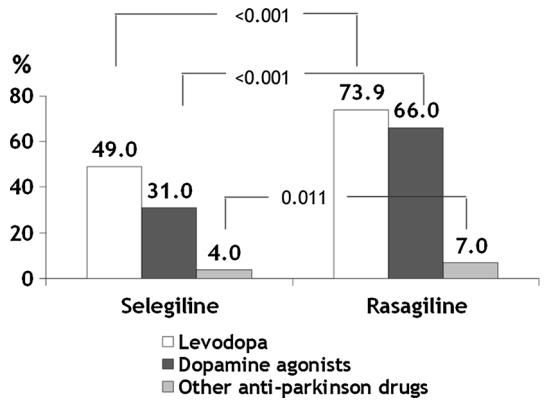

Fig. 3 Other anti-PD drugs prescribed during follow-up period in addition to rasagiline or selegiline

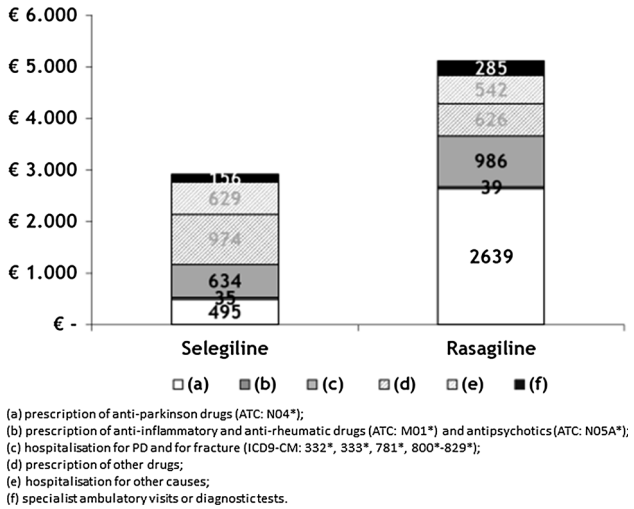

Fig. 4 Average annual costs per patient for rasagiline and selegiline (in euros)

Discussion

Our study was based on real-world data form administrative databases, therefore it investigated the actual clinical practice in a large population of inhabitants. These data represent an important supplement to information coming from trials.

The prevalence of use of selegiline and rasagiline found in our study is in line with other countries: in fact, in our cohort selegiline was prescribed in 63.7 % of patients, whereas selegiline in 36.2 %, similarly in 2011 in Norway selegiline was prescribed in 61.1 % of all MAOB-I users and rasagiline in 38.9 % [29].

This study suggests that prescribing patterns differed between patients affected by PD treated with rasagiline compared with those treated with selegiline: in the real-world setting analysed, rasagiline was preferred to selegiline by physicians in younger subjects, in male gender, in presence of more hospitalizations for PD and in association to other anti-PD treatment.

From the follow-up data it emerged that patients under rasagiline, in comparison with those treated with selegiline, received more frequently both levodopa and dopamine agonists, and experienced more admissions for PD. The finding on fracture admissions, higher in selegiline group, is probably related to the older age and to the female gender of subjects treated with selegiline, in comparison with those receiving rasagiline. The overall duration of treatment during 12 months of follow-up was enough high (average duration of 280 days); however, for patients treated with rasagiline this parameter resulted significantly higher in comparison with selegiline users. By analysing the prescription coverage, patients treated with selegiline were more adherent in comparison with those receiving rasagiline. All these differences in demographic, clinical and prescription characteristics emerged between selegiline and rasagiline showed that these two drugs are used in different phases of PD. It appears that rasagiline is preferred to selegiline in patients at early phase of the disease: younger subjects, with more hospitalizations for PD (that occur especially in the first stage of disease) and fewer admissions for fractures. This could be explained with the hoped effect of rasagiline to slow the progression of PD; however, this effect is not based on conclusive evidence. In

Table 3 Generalized regression model for overall cost and PD-related cost (in euros)

Baseline annual cost per patient	Overall cost				PD-related cost			
	1659 €				664 €			
	Cost variation	95 % CI		*p*	Cost variation	95 % CI		*p*
MAOB-I (rasagiline vs. selegiline)	+2404	+1882	+2925	<0.001	+2363	+1779	+2947	<0.001
Age (+1 year)	+4	−15	+24	0.667	0	−13	+14	0.968
Gender (male vs. female)	−72	−425	+281	0.689	−113	−349	+124	0.350
Comorbidity (+1 Charslon index score)	+615	+433	+798	<0.001	+101	−28	+231	0.123
Antiparkinson therapy (established vs. naïve)	−37	±420	+346	0.850	+447	+198	+696	<0.001
Hospitalization for PD (yes vs. no)	+3457	+1590	+5323	<0.001	+2689	+724	+4655	0.007

consideration of this, we expected to see a minor use of levodopa or dopamine agonists in rasagiline group; on the contrary, these drugs were used more often with rasagiline rather than selegiline. These conflicting results show that there is no homogeneous prescription behaviour among clinicians in choosing one or the other drug. This is due to the scarce and conflicting evidence available and to the lack of head-to-head study between the two MAOB-Is. Despite these differences, the costs directly and indirectly related to these drugs differed substantially. In fact, the choice to prescribe rasagiline, rather than selegiline, generated a relevant increase in the annual cost per patient. This increase was not only due to the different costs of the two drugs, but also due to the augmentation in expenditure of all other items. Furthermore, it contributes to the overall increase in the cost of PD due to the aging of the population, as widely demonstrated by several economic studies [23, 30–34].

Limitation

The primary limitation of the study was the lack of information on the severity of PD; in order to minimize this drawback we used different proxies of severity disease, such as previous treatment with anti-parkinson drugs and Charlson comorbidity index score. However, this aspect could have affected our findings.

An additional limitation is related to the differences in labelling of the two studied drugs: rasagiline is indicated also as monotherapy, whereas selegiline only as add-on therapy. This difference could have influenced our results. Another drawback could be generated by the use of DDD as measure to estimate the prescription coverage (i.e. adherence). As matter of fact DDD represents "the assumed average maintenance dose per day for a drug used for its main indication in adults" [20], therefore in same cases this measure could not correspond to the actual prescribed dose. This possible limitation could have affected adherence results of selegiline group since DDD of selegiline is equal to 5 mg, while in clinical practice this drug can be prescribed as 5 or 10 mg per day; on the contrary, no particular concerns should be present for rasagiline, where DDD is 1 mg, the same dose used in clinical practice.

Moreover, since our analysis was an historic cohort study, it was potentially associated with a number of methodological limitations related to not availability of information of potential confounding factors. Nevertheless, the generalized linear model has tried to control for all available confounding factors (i.e. age, gender, comorbidity index, concomitant therapies and hospitalizations); residual confounding still remains.

Finally, concerning cost analysis, all expenditures directly paid by patients or by their relatives were not included in the model due to the inability to obtain these information.

Conclusion

Our study showed that a much heterogeneous prescription behaviour prevails among clinicians when choosing one or other MAOB-I in different patients with PD. However, our results confirm that drug treatment represents the main expenditure item, in the same line with other studies investigating the economic burden of PD [22, 25]. Therefore, the higher cost of rasagiline compared with that of selegiline should be taken into account by the physician whom choosing the drug to prescribe.

Moreover, since all analysed cost components were higher in the group of patients treated with rasagiline, healthcare decision-makers should consider the need to establish healthcare programme to monitor the appropriateness of prescription and manage the proper use of resources.

In conclusion, our study highlighted the need for physicians and for health policy-makers to better weigh the choice to prescribe one or other MAOB-I, on the basis of the patient characteristic and the sustainability of health system until head-to-head comparison between these two drugs is available.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Prevalence of Parkinson's Disease (2014) http://www.epda.eu.com/en/resources/life-with-parkinsons/part-1/prevalence-of-parkinsons-disease/. Accessed 19 Nov 2014
2. de Lau LM, Breteler MM (2006) Epidemiology of Parkinson's disease. Lancet Neurol 5(6):525–535
3. Rosati G, Granieri E, Pinna L, Aiello I, Tola R, De BP, Pirisi A, Devoto MC (1980) The risk of Parkinson disease in Mediterranean people. Neurology 30(3):250–255
4. Morgante L, Rocca WA, Di Rosa AE, De DP, Grigoletto F, Meneghini F, Reggio A, Savettieri G, Castiglione MG, Patti F (1992) Prevalence of Parkinson's disease and other types of parkinsonism: a door-to-door survey in three Sicilian municipalities. The Sicilian neuro-epidemiologic study (SNES) group. Neurology 42(10):1901–1907

5. Totaro R, Marini C, Pistoia F, Sacco S, Russo T, Carolei A (2005) Prevalence of Parkinson's disease in the L'Aquila district, central Italy. Acta Neurol Scand 112(1):24–28
6. NICE guidelines [CG35]:Parkinson's disease: diagnosis and management in primary and secondary care (2006) https://www.nice.org.uk/guidance/cg35. Accessed 19 Nov 2014
7. Connolly BS, Lang AE (2014) Pharmacological treatment of Parkinson disease: a review. JAMA 311(16):1670–1683
8. Approved Drug Products Eldepryl (1996) http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails. Accessed 19 Nov 2014
9. European public assessment report (EPAR)—Azilect (2005) http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000574/human_med_000667.jsp&mid=WC0b01ac058001d124. Accessed 19 Nov 2014
10. Approved Drug Products Azilect (2006) http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails. Accessed 19 Nov 2014
11. Parkinson Study Group (1989) DATATOP: a multicenter controlled clinical trial in early Parkinson's disease. Arch Neurol 46(10):1052–1060
12. Parkinson Study Group (2002) A controlled trial of rasagiline in early Parkinson disease: the TEMPO study. Arch Neurol 59(12):1937–1943
13. Rascol O, Brooks DJ, Melamed E, Oertel W, Poewe W, Stocchi F, Tolosa E (2005) Rasagiline as an adjunct to levodopa in patients with Parkinson's disease and motor fluctuations (LARGO, Lasting effect in Adjunct therapy with Rasagiline Given Once daily, study): a randomised, double-blind, parallel-group trial. Lancet 365(9463):947–954
14. Parkinson Study Group (2005) A randomized placebo-controlled trial of rasagiline in levodopa-treated patients with Parkinson disease and motor fluctuations: the PRESTO study. Arch Neurol 62(2):241–248
15. Olanow CW, Hauser RA, Jankovic J, Langston W, Lang A, Poewe W, Tolosa E, Stocchi F, Melamed E, Eyal E, Rascol O (2008) A randomized, double-blind, placebo-controlled, delayed start study to assess rasagiline as a disease modifying therapy in Parkinson's disease (the ADAGIO study): rationale, design, and baseline characteristics. Mov Disord 23(15):2194–2201
16. Knudsen Gerber DS (2011) Selegiline and rasagiline: twins or distant cousins? Consult Pharm 26(1):48–51
17. Stowe R, Ives N, Clarke CE, Handley K, Furmston A, Deane K, van Hilten JJ, Wheatley K, Gray R (2011) Meta-analysis of the comparative efficacy and safety of adjuvant treatment to levodopa in later Parkinson's disease. Mov Disord 26(4):587–598
18. Marconi S, Zwingers T (2014) Comparative efficacy of selegiline versus rasagiline in the treatment of early Parkinson's disease. Eur Rev Med Pharmacol Sci 18(13):1879–1882
19. Indirect meta-analysis of randomised placebo-controlled clinical trials on rasagiline and selegiline in the symptomatic treatment of Parkinson's disease (2012) http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0054173/. Accessed 19 Nov 2014
20. The Anatomical Therapeutic Chemical (ATC) classification system and the Defined Daily Dose (DDD) ATC/DDD Index 2014 (2014) http://www.whocc.no/atc_ddd_index/. Accessed 19 Nov 2014
21. Banca Dati del Farmaco e del Parafarmaco (2014) http://www.farmadati.it/. Accessed 19 Nov 2014
22. Winter Y, von Campenhausen S, Reese JP, Balzer-Geldsetzer M, Longo K, Spiga G, Boetzel K, Eggert K, Oertel WH, Dodel R, Barone P (2010) Costs of Parkinson's disease and antiparkinsonian pharmacotherapy: an Italian cohort study. Neurodegener Dis 7(6):365–372
23. Winter Y, Balzer-Geldsetzer M, von Campenhausen S, Spottke A, Eggert K, Oertel WH, Dodel R (2010) Trends in resource utilization for Parkinson's disease in Germany. J Neurol Sci 294(1–2):18–22
24. Valldeoriola F, Puig-Junoy J, Puig-Peiro R (2013) Cost analysis of the treatments for patients with advanced Parkinson's disease: SCOPE study. J Med Econ 16(2):191–201
25. Hudry J, Rinne JO, Keranen T, Eckert L, Cochran JM (2006) Cost-utility model of rasagiline in the treatment of advanced Parkinson's disease in Finland. Ann Pharmacother 40(4):651–657
26. Moisan F, Gourlet V, Mazurie JL, Dupupet JL, Houssinot J, Goldberg M, Imbernon E, Tzourio C, Elbaz A (2011) Prediction model of Parkinson's disease based on antiparkinsonian drug claims. Am J Epidemiol 174(3):354–363
27. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40(5):373–383
28. International Classification of Diseases 9th Revision Clinical Modification—ICD9-CM (2009) http://icd9cm.chrisendres.com/index.php. Accessed 19 Nov 2014
29. Norwegian Prescription Database (2014) http://www.norpd.no/default.aspx. Accessed 19 Nov 2014
30. Findley LJ, Wood E, Lowin J, Roeder C, Bergman A, Schifflers M (2011) The economic burden of advanced Parkinson's disease: an analysis of a UK patient dataset. J Med Econ 14(1):130–139
31. Reese JP, Dams J, Winter Y, Balzer-Geldsetzer M, Oertel WH, Dodel R (2012) Pharmacoeconomic considerations of treating patients with advanced Parkinson's disease. Expert Opin Pharmacother 13(7):939–958
32. Suh DC, Pahwa R, Mallya U (2012) Treatment patterns and associated costs with Parkinson's disease levodopa induced dyskinesia. J Neurol Sci 319(1–2):24–31
33. Boland DF, Stacy M (2012) The economic and quality of life burden associated with Parkinson's disease: a focus on symptoms. Am J Manag Care 18(7 Suppl):S168–S175
34. Kowal SL, Dall TM, Chakrabarti R, Storm MV, Jain A (2013) The current and projected economic burden of Parkinson's disease in the United States. Mov Disord 28(3):311–318