J Nutr Health Aging. 2019;23(10):1043-1047

OBSERVATIONAL STUDY INVESTIGATING THE PRESCRIPTION OF LIPID-LOWERING DRUGS FOR PRIMARY AND/OR SECONDARY PREVENTION IN RESIDENTS AGED 80 YEARS AND OVER INSTITUTIONALIZED IN NURSING HOMES IN BREST

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Abstract: *Objectives:* To evaluate the prescription of lipid-lowering therapy in nursing home residents aged 80 and older. *Design:* Observational descriptive study, led in Brest, France, between February and May 2017. *Setting:* 15 nursing homes in Brest, France. *Participants:* Nursing home residents, aged 80 and older, treated with a lipid-lowering therapy for primary and / or secondary prevention. *Measurements:* The primary endpoint was to observe the frequency of prescription of lipid-lowering therapy at the time of the study. The secondary endpoints were to analyse the relevance of these prescriptions regarding the latest French recommendations and current literature data and to evaluate the monitoring of treatment. *Results:* 213 of the 1121 included residents (19%) were treated with a lipid-lowering drugs. A total of 141 prescriptions (66.2%) were considered irrelevant. In the past 12 months, monitoring of lipids, liver and muscle enzymes was observed respectively in 41.3%, 60.1% and 9.4% of residents. *Conclusion:* lipid-lowering prescription was not optimal in nursing homes. The results highlighted inadequate treatment monitoring and a gap between the French National Authority for Health (HAS) recommendations and actual practice.

Key words: Dyslipidemia, statins, nursing homes, overuse; suboptimal.

Introduction

Hypercholesterolemia is frequent with an estimated prevalence of 39% in the French population aged 65 to 84 years and 31% over 85 years (1). It is one of the main risk factors for atherosclerosis causing neurovascular and cardiovascular diseases (CVD). These diseases represent the second leading cause of death in metropolitan France (2). The prevalence of dyslipidemia increases with age and the demographic evolution requires us to think about this problem. Many studies have shown a positive correlation between the risk of CVD and high cholesterol levels. This link is well established before age 65 but decreases in the older subject (3–5) and is sometimes questioned in the very old subject (6–9).

French recommendations, as well as European and international guidelines, are unanimous regarding the benefits of treating patients with lipid-lowering drugs in primary and secondary prevention depending on the cardiovascular risk (CVR). The prescription of statins constitutes the first line of treatment of hypercholesterolemia (10–12). However, these recommendations underline the lack of data in adults aged 80 years and over.

Elderly living in nursing homes represent a frail and highly dependent population with a high incidence of comorbidities and polypharmacy and often a shorter life expectancy. To our knowledge, the data concerning the prescriptions of lipid lowering drugs in the elderly living in nursing home in France are rare.

The main objective of our study was to observe the frequency of lipid-lowering drugs prescription in residents aged 80 and over institutionalized in nursing homes of the city of Brest. The secondary objectives were to analyze the relevance of the prescriptions regarding the good practice guidelines recommended by the French National Authority for Health (HAS) and to assess treatment monitoring.

Population and method

It was a descriptive study conducted in the nursing homes of the city of Brest, between February and May 2017. The inclusion criteria were: people aged 80 years and over living in a nursing home in Brest with prescription of a lipid-lowering drug for primary and/or secondary prevention.

Nursing homes residents were included after approval of directors and general practitioners. The Ethic Committee of the University Hospital of Brest agreed with this study.

Data were collected in medical files: age, gender, cardiovascular risk factors (CVRF) according to the recommendations issued by Afssaps in 2005 (Agence Française de Sécurité Sanitaire des Produits de Santé), lipid-lowering treatment (molecule, dose and date of initiation before or after 80 years), indication for primary or secondary prevention, geriatric assessment data (GA) and biological data over the previous 12 months (total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, liver test (aspartate aminotransferase (ASAT) and alanine aminotransferase (ALAT)), creatine phosphokinase (CPK) and creatinine clearance with the

Received May 22, 2019
Accepted for publication June 3, 2019

Published online October 26, 2019, http://dx.doi.org/10.1007/s12603-019-1292-9

Table 1
Characteristics of the population treated with lipid-lowering drugs

Data		Study population (N=213; (%))
Mean age (years± SD)		87.5 ± 4.8
Sex	Male	63 (29.6)
	Female	150 (70.4)
Type of prevention	Primary prevention	65 (30)
	Secondary prevention	148 (70)
Number of CVRF ± SD	Mean score	2 ± 0.8
	1 CVRF (age alone)	49 (22.9)
	2 CVRF	116 (54.5)
	3 CVRF	42 (19.7)
	4 CVRF	6 (2.9)
High blood pressure		156 (73.2)
Type 2 diabetes		34 (16)
Active smoker or stopped less than 3 years before		15 (7)
Family history of premature cardiovascular disease		2 (0.9)
Renal function	Normal	67 (31.5)
	Moderate renal failure	129 (60.5)
	Severe renal failure	17 (8)
Level of cardiovascular risk (CVR)	Low	0 (0)
	Moderate	14 (6.6)
	High	35 (16.4)
	Very high	164 (77)
Independence (GIR score) ± SD	Mean score	3.3 ± 1.3
	GIR 1 - 2	73 (34.3)
	GIR 3 - 4	99 (46.5)
	GIR 5 - 6	41 (19.2)
Charlson score ± SD		8.9 ± 2.2
MMSE ± SD		19.1 ± 5.9
Polypharmacy (≥ 5 drugs per day)	208 (97.7)	
Average number of drugs per day	8.9 ± 2.5	
Mobility	Walking	184 (86.4)
	Wheelchair	24 (11.3)
	Bed restriction	5 (2.3)

CVRF: cardiovascular risk factors; GIR : iso-resource group; MMSE : Mini Mental State Evaluation

Cockcroft and Gault formula).

CVD were coronary heart disease (stable or unstable angina, myocardial infarction or revascularization), cerebrovascular disease (stroke or ischemic attack) or peripheral arterial disease. GA data included polypharmacy (defined as 5 medications or more a day), diagnosis of a neurodegenerative disease, result of the last Mini Mental State Examination scoring (13), comorbidities (Charlson Comorbidity Index), mobility (walking with or without aid, wheelchair, restriction to bed and chair) and degree of dependency according to the iso-resource group (GIR) defined by the AGGIR scale. The residents were ranged in heavily (GIR 1 and 2) or mildly dependent (GIR 3 and 4) and independence (GIR 5 and 6).

The relevance of the prescriptions was considered according to the latest national recommendations published by the HAS in February 2017 and current data from the scientific

Table 2
Biological monitoring of efficacy and tolerance of lipid-lowering drugs over the past 12 months

Data collected	Total study population (%)	Primary prevention (%)	Secondary prevention (%)
Lipid profile monitoring (≤ 12 months)			
No	125 (58.7)	36 (55.4)	89 (60)
yes	88 (41.3)	29 (44.6)	59 (40)
LDL-Cholesterol target among residents monitored			
Not reached	52 (59)	13 (44.8)	39 (66.1)
Reached	36 (41)	16 (55.2)	20 (33.9)
Hepatic profile monitoring (≤ 12 months)			
no	85 (39.9)	27 (41.5)	58 (39.2)
yes	128 (60.1)	38 (58.5)	90 (60.8)
Hepatic cytolysis	3 (2.3)	1 (2.6)	2 (2.2)
Monitoring of muscle enzymes (≤ 12 months)			
no	193 (90.6)	61 (93.8)	132 (89.2)
yes	20 (9.4)	4 (6.2)	16 (10.8)
Rhabdomyolysis	0 (0)	0 (0)	0 (0)

literature(12). The relevance of each lipid-lowering drug prescription was based on indication, molecule, dosage and tolerance. A prescription was considered as irrelevant if there was at least one non-relevance criterion. The indication of treatment was irrelevant if: initiation of treatment beyond 80 years and / or low cumulative risk factors less than or equal to 2 and / or low life expectancy in primary prevention; low life expectancy in secondary prevention (12). We classified arbitrarily as « low life expectancy» the presence of heavy dependence (GIR ≤ 2) associated with a significant comorbidity (Charlson score ≥ 5). French guidelines recommended using statins as first-line treatment and preferentially simvastatin or atorvastatin (14). We considered an unjustified the use of another lipid-lowering drug. In the elderly it was recommended to start at a low-dose treatment with secondary adjustement in order to reach the LDL-C target concentrations. A concentration of LDL-C depend in the CVR level. In primary prevention, the CVR level using the SCORE scale was not suitable in the elderly (15). We defined the CVR level according to a French 2016 consensus panel (16) and the HAS guideline (14): low risk (0 or 1 CVRF); moderate risk (2 CVRF or moderate chronic renal insufficiency (creatinine clearance between 30 and 60 mL/min)); high risk (≥ 3 CVRF) and very high risk (documented CVD and/or severe chronic renal insufficiency (creatinine clearance below 30 mL/min) and/or type 2 diabetes). A dosage was relevant if the target LDL-C was reached. A lipid-lowering drug prescription was considered relevant in the absence of hepatic cytolysis greater than three times normal and/or rhabdomyolysis with CPK elevation greater 5 times normal during the last 12 months (17).

Statistical analyses

average, standard deviation and percentages were calculated by Microsoft Excel.

This work was supported by no sources of funding.

Results

We contacted coordinating doctors of the 16 nursing homes of Brest. Fifteen agreed to include their residents. The data were collected between February and May 2017.

Among the 1398 residents living in the fifteen nursing homes, 1121 (80.2%) were at least 80 years old. A total of 213 residents aged 80 years and older were treated with lipid-lowering drugs, corresponding to a prevalence of 19%.

Out of the 213 residents included, 150 were women (70.4%) and 63 were men (29.6%). The mean age was 87.5 ± 4.8 years. 65 persons were treated in primary prevention (30.5%) and 148 in secondary prevention (69.5%).

The residents had an average of 2 ± 0.76 CVRF including age. 156 persons had high blood pressure (73.2%), 34 type 2 diabetes (16%), 15 smoked (7%), 129 residents (60.5%) had a moderate chronic renal failure, 17 (8%) a severe chronic renal failure and 2 a family history of CVD (0.9%). A total of 14 residents had a moderate CVR (6.6%), 35 a high risk (16.4%), and 164 a very high risk (77%).

The mean GIR and Charlson scores were respectively 3.3 ± 1.3 and 8.9 ± 2.2. 110 residents had a MMSE scoring in their medical records with an average score of 19.1 ± 5.9. 208 persons (97.7%) were polymedicated (Table 1).

In the previous 12 months, lipid profile monitoring was found for 88 residents (41.3%) (29 in primary prevention and 59 in secondary prevention). Transaminases were monitored in

128 residents (60.1%) and CPK in 20 residents (9.4%) (Table 2).

Therapeutic indication

Among the 65 residents treated in primary prevention, 40 (61.5%) had a low cumulative CVR and 14 (21.5%) had a low cumulative CVR associated with an expected low life expectancy. Out of the 148 residents treated in secondary prevention, 57 (38.5%) had a low life expectancy. According to our criterion, the indication of lipid-lowering treatment was relevant for 102 residents (48%) and irrelevant for 111 residents (52%).

Choice of molecule

Statins were prescribed in 193 residents (90.6%). Another lipid-lowering drug was prescribed for 20 residents (9.4%) and was considered irrelevant (Table 3).

Table 3
Type of lipid-lowering drug

Lipid-lowering drug prescribed	Total study population (%)	Primary prevention population (%)	Secondary prevention population (%)
Statins	193 (90.6)	51 (78.5)	142 (95.9)
Pravastatin	62 (29.1)	21 (32.3)	41 (27.7)
Simvastatin	25 (11.7)	10 (15.4)	15 (10.1)
Fluvastatin	1 (0.5)	0 (0)	1 (0.7)
Atorvastatin	91 (42.7)	17 (26.2)	74 (50)
Rosuvastatin	14 (6.6)	3 (4.6)	11 (7.4)
Fibrates	13 (6.1)	11 (16.9)	2 (1.4)
Cholestyramine	1 (0.5)	1 (1.5)	0 (0)
Ezetimibe	3 (1.4)	0 (0)	3 (2)
Bitherapy	3 (1.4)	2 (3.1)	1 (0.7)

Dosage

The target LDL-C was reached in 36 (41%) on the 88 residents who had a lipid profile monitoring: 16 in primary prevention and 20 in secondary prevention. It was not reached in 52 residents (59%): 13 in primary prevention and 39 in secondary prevention (Table 2). The dose adjustment history was unknown.

Treatment tolerance, among the 20 monitored residents, we observed no rhabdomyolysis. Hepatic cytolysis was observed in three of 128 residents (2.3%) with continuation of treatment (Table 2). We considered these three prescriptions as irrelevant.

Discussion

In our observational study the prevalence of lipid-lowering drugs prescription was 19% and statins represented 90.6% of the prescriptions. In a recent study conducted in nursing homes in the France Landes region, the prevalence of lipid-lowering drugs prescription was 31.1% in subjects aged over 80 years (18). In another french study 21% of 11 687 people aged 85 years and over, admitted in nursing homes, were treated with lipid-lowering drugs (19). In our study considering the recommendation of HAS, 65.7% of the prescriptions were irrelevant: 89.2% in primary and 55.4% in secondary prevention. French study conducted in nursing homes in the France Landes region found that 69% of the prescriptions were irrelevant according to the recommendations published in 2005: 79% in primary prevention and 62% in secondary prevention (18).

Our study showed an overuse of lipid-lowering drugs in residents with a limited life expectancy (33.3%) or among residents with a low or moderate CVR in primary prevention (25.3%). A randomized trial assessing the benefits of stopping statins in patients in palliative care showed no significant difference in mortality or cardiovascular events between the «stop» and «continue» statin groups. Stopping statins was even associated with an improvement in quality of life (20). Another study showed that stopping some long-term treatments like statins in a context of limited life expectancy reduced drug-related side effects and improved quality of life (21). Some studies showed that the cost-efficacy ratio of treatment with statins was not good in primary prevention in patients with a low CVR (17, 22). But these results are nevertheless discussed (23, 24). To date, the benefits of lipid-lowering drugs in primary prevention remain uncertain in older subjects. And consequently, the pertinence of 89.2% of the prescriptions in primary prevention could be questioned in our study.

Regarding the choice of the drug, our study showed that 90.6% of lipid-lowering drugs prescribed were statins. Prescriptions of atorvastatin (42.7%) and pravastatin (29.1%) were predominant followed by simvastatin. Our results are consistent with a trial conducted in Midi-Pyrénées in 2015: the dispensing profile of statins for patients aged over 75 years showed that atorvastatin was prescribed mostly (27.3%) followed by pravastatin (23.3%) and simvastatin (23).

Our study highlighted low biological monitoring of efficacy and tolerance of lipid-lowering treatments: respectively 41.3%, 60.1% and 9.4% of the residents had annual lipid status, hepatic test and muscle enzymes monitoring. HAS guidelines recommend annual lipid profile monitoring for all patients treated, encourage annual liver monitoring and a frequent muscle function monitoring in older patients (14). Our results are consistent with those from studies conducted specifically in nursing homes where respectively an average of 54% and 41.3% of the residents had an annual hepatic test and lipid status monitoring (18,25). In our study among the 88 residents who had lipid profiles monitoring, the target LDL-C levels were not achieved in 59%. This non-optimization in drug dosage could be explained by preoccupations regarding drug safety and iatrogeny.

The strength of our study was the inclusion of 15 out of the 16 nursing homes in the city of Brest, the selected sample could be representative of the target population.

Some evaluation biases should be highlighted. First, an information bias related to missing data in medical records that underestimates the average number of CVRF, the CVR level, or the Charlson score evaluation. In addition, important data lacked for the evaluation of the irrelevance of prescriptions: age at the initiation of treatment and history of dose adjustments. The evaluation of our four criteria could thus be under or over estimated.

Furthermore, there were measurement bias due a lack of precise definitions of CVR in older population in the current HAS guidelines. Based on the literature, we have arbitrarily defined the terms of low cumulation of risk factors and low life expectancy in order to best meet our secondary objectives. Moreover, in the absence of CVR evaluation tool for older subjects, we decided to adopt an alternative tool proposed by a French consensus. Ultimately, this study was limited by the choice of these decisional criteria.

Finally, there are confounding factors, as only one investigator assessed the data and the results. A second analysis would consolidate the results.

Conclusion

This study revealed overuse of lipid-lowering drugs in residents aged 80 and over living in nursing homes of the city of Brest. The pertinence of nearly two-thirds of prescriptions could be discussed, especially in primary prevention. The results of our study revealed also an insufficient monitoring of the tolerance and efficacy of lipid-lowering treatments. The discrepancy between the HAS recommendations and actual practice may be the consequence of a lack of specific guidelines for subjects aged 80 years and over.

In this population, large-scale randomized trials are necessary to address the lack of evidence, doubts, and concerns about the benefits and safety of lipid-lowering drugs and to enable the development of more specific guidelines for the management of dyslipidemia.

The SAGA study (statins in old age) initiated in 2015 by the Department of Bordeaux is assessing the clinical and medico-economic benefits of stopping statins for primary prevention in subjects aged over 75 years. These results should be enlightening.

Conflict of interest: The authors declares that there is no conflict of interest.

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