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Impact of adherence to anti-osteoporotic drugs on the occurrence of fractures

M. Belhassen[1,2*], B. Cortet[3], C.B. Confavreux[4], L. Lamezec[2], M. Ginoux[1], E. Van Ganse[1]

[1] Lyon Pharmaco-Epidemiology Unit - HESPER- Claude Bernard Lyon 1 University, Lyon, France
[2] Merck Sharp & Dohme, Courbevoie, France
[3] Department of Rheumatology, Lille University Hospital, Lille, France
[4] INSERM UMR 1033 – University of Lyon, Department of Rheumatology, Hôpital Edouard Herriot, Hospices Civils de Lyon, Lyon, France
*Contact: Manon Behassen, manon.belhassen@univ-lyon1.fr

CONTEXT

Osteoporosis (OP) is characterized by reduced bone mass and disruption of bone architecture, resulting in increased bone fragility and increased fracture risk.[1]
OP affects about 2.3 million patients in France. The most frequent fractures are those at the hip, spine and distal forearm. A variety of treatments options are currently available.[2,3] The most prescribed anti-osteoporotic treatments are bisphosphonates[4-6] that represent 88% of prescriptions in France. Clinical trials of osteoporosis treatments have demonstrated efficacy, ranging from 30% to 70%, in reducing risk for osteoporotic fractures.

These treatments are also responsible for a variety of short and middle term side effects and longer term adverse events including atypical femoral fractures, osteonecrosis of the jaw, hypersensitivity reaction, and transient renal function impairment. Despite existing data from randomized controlled trials, there is still a lack of data from studies conducted in real-life settings.

There is a need for further observational research to assess the impact of adherence to anti-osteoporotic drugs on the occurrence of fractures.

OBJECTIVE

Using the French epidemiological cohort “Permanent Beneficiaries Sample” database (EGB), we conducted a nested-case control study to assess the impact of adherence to anti-osteoporotic treatment on the occurrence of fractures, between 2007 and 2013.

DATA SET

French claims data record exhaustive medical resource utilization of the covered by the National Health Insurance Scheme, corresponding to 56.2 million people (i.e. 86% of the French population), including primary and secondary care. This study was conducted on a 1/97th representative sample of French claims data (EGB). It means that, in the cohort, an observation for 1,000 individuals reflects 97,000 patients in the whole French Health Insurance.[7]

The EGB collects, for each beneficiary, details of healthcare reimbursed by the French Health Service, with specific identification of all reimbursed medical resource use. We cross-referenced information from the EGB database to the French hospital discharge database that provides medical information on all patients admitted to hospital in France, including discharge diagnoses (in ICD-10), medical procedures, and diagnosis-related groups (DRGs).

MATERIAL AND METHODS

We identified all patients aged ≥50 years who received an anti-osteoporotic treatment between 2007 and 2013. Cases were defined as patients presenting an osteoporosis-related fracture leading to hospitalization between January 1, 2008 (≥2-year history required) and December 31, 2013.

Controls were hospitalized patients at the time where the matched case presented the event studied but without OP-related fracture. Cases and controls were matched on age (±5 years), gender, duration of their participation in the cohort, and main comorbidities.

Cases and controls were compared for their respective exposure to bisphosphonate (BP) during the 24 months before index date. Co-variates of the models were antiosteoporotic drugs (except BP), oral corticosteroids, diuretics, NSAIDs, cardiovascular drugs, antihypertensives
and vasodilators.

RESULTS

Characteristics	Cases (n=552)		Control (n=7,395)		Comparison Chi² p-value
	n=	%	n=	%	
Sex					0.0002
Male	17	3.1%	542	7.3%	
Female	535	96.9%	6,853	92.7%	
Age at enrollment					
50-54 years	14	2.5%	501	6.8%	
55-59 years	34	6.2%	992	13.4%	
60-64	42	7.6%	1,121	15.2%	
65-69	68	12.3%	1,126	15.2%	
70-74	108	19.6%	1,383	18.7%	
75-79	140	25.4%	1,236	16.7%	
80-84	96	17.4%	726	9.8%	
85-89	39	7.1%	264	3.6%	
90-94	11	2.0%	44	0.6%	
95-99	0	0%	2	0.0%	
Hypertension	268	48.6%	2,989	40.4%	0.0002
Diabetes	36	6.5%	499	6.7%	0.8380
Heart failure	9	1.6%	71	1.0%	0.1280
COPD	35	6.3%	295	4.0%	0.0076
Hyperparathyroidism	14	2.5%	155	2.1%	0.4892
Hyperthyroidism	3	0.5%	38	0.5%	0.7610
Chronic ischemic heart disease	19	3.4%	164	2.2%	0.0643
Insomnia/depression	314	56.9%	3,578	48.4%	0.0001
Parkinson’s disease	27	4.9%	179	2.4%	
Inflammatory polyarthropathies	19	3.4%	269	3.6%	

Table 1. Characteristics (before matching) of osteoporotic patients having had (cases) or not (controls) an OP-related fracture during the years after the 24 months of follow-up

Among the 9,859 OP patients included in the cohort, we found 434 (4.4%) cases and 1,123 controls. In the cases group, 311 (71.7%) patients received at least one time a BP in the last 24 months compared to the controls (827 patients, 73.6%) (p=0.29).

RESULTS

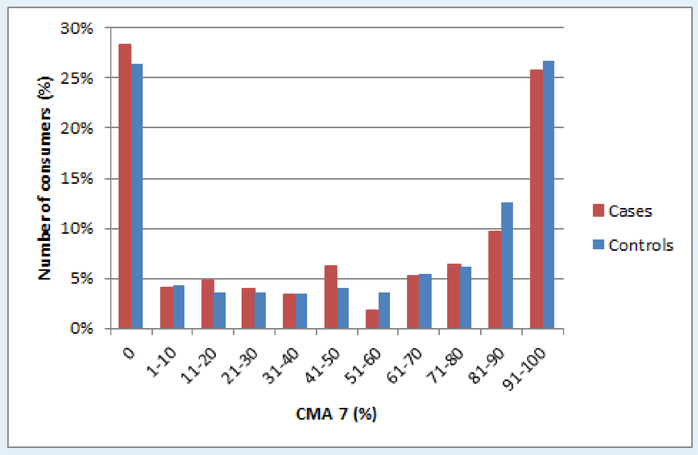

Figure 1. Distribution of CMA to bisphosphonates (only or in association) over 24 months, estimated by CMA 7 for osteoporotic patients having (cases n=434) or not (controls n=1,123) an OP-related fracture

Over the 24 months before index date, patients with a Cumulative Medication Adherence (CMA) of ≤20%, >80% and >90% were 162 (37.3%), 154 (35.5%) and 112 (25.8%), in comparison to controls: 384 (34.2%), 441 (39.3%), 299 (26.6%) respectively; p=0.29.

Variables	Odds ratio	95% CI		p-value
Explanatory variable				
CMA to bisphosphonates over 24 months (CMA 7)				0.1913
< 80%	1	-	-	
≥ 80%	0.851	0.668	1.084	

Table 2. Impact of CMA to bisphosphonates over 24 months (CMA 7; 80% threshold) on the probability of hospitalization due to fracture, calculated by conditional logistic regression (n= 1,557)

A CMA ≥ 80% is not associated with a reduction of the risk of OP-related fractures (OR=0.851, IC95% [0.668-1.084]).

Variables	Odds ratio	95% CI		p-value
Explanatory variable				
CMA to bisphosphonates over 24 months (CMA 7)				0.0029
< 90%	1	-	-	
≥ 90%	0.741	0.608	0.903	

Table 3. Impact of CMA to bisphosphonates over 24 months (CMA 7; 90% threshold) on the probability of hospitalization due to fracture, calculated by conditional logistic regression (n= 238)

Nevertheless, high coverage (>90%) is associated with a 25% decreased risk of fracture, in comparison with low coverage (<10%) (OR=0.741, IC95% [0.608-0.903], p=0.003).

CONCLUSIONS

In this study, adherence to anti-osteoporotic treatment affected the occurrence of fractures when comparisons were performed between extreme patients, with a 25% decreased risk of fracture.

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