Comorbidity of migraine: comparison of pharmacoepidemiological and clinical data

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Introduction

Migraine population studies report many comorbidities, mostly identified through questionnaires and based on self-reported diagnosis.

Comorbidity of migraine with a number of neurological, psychiatric and other diseases (Le, Wang, Buse, Schoenen) has been reported. Prevalence studies based on self-reported information have been performed in large scale population even recently to detect migraine comorbidities (Le, Aamodt, Bigal 2010). The advantage of these surveys is to be relatively unexpensive. However the self-referred diagnosis is affected by potential biases. Thirty-five somatic comorbidity have been reported in a large population based study [Le]. In particular, higher frequency of some cardiovascular risk factors (diabetes, hypertension, ipercholesterolemia) have been reported in migraine patients in comparison to general population (Bigal, Scher). However, a recent meta-analysis does not suggest that migraine, with and without aura, is associated with increased risk of mortality from all causes (Schurks 2011).

Prescription databases have been used to investigate disease prevalence.

Drug prescription administrative databases have been used to estimate the prevalence of chronic diseases. Administrative databases collect data of very large population, and they could be used to perform large studies, otherwise extremely costly and time-consuming (Maio 2009). The analysis of pharmaceutical claims has been showed to be useful to provide reliable estimates of chronic disease prevalence, however it have several limitations, too (Chini).

Our study is aimed to evaluate migraine comorbidity through the comparison of drug prescription rates of a pharmaceutical database (PD) and those of a clinical cohort (CC).

Methods

Empoli Health Authority (HA11) pharmacy claims (year 2011) of the 155829 residents aged 15-65 years, were analyzed. Triptan prescription was considered a migraine marker. The CC consists of 681 patients aged 15-65 years, who accessed to the HA11 Headache Centre in 2011 and had a diagnosis of migraine.

We evaluate if drugs for not migrainous chronic conditions (antidepressants, antipsychotics, anticonvulsants, antiasthma, antihistamines, antidiabetics, antihypertensives, anti-dyslipidemics, thyroid hormones, antithyroids) were prescribed more often to migraine patients than to general population and, then, we evaluate the prescription rates of the same drugs in the CC.

Conclusions

We found no comorbidities in our migraine population. The differences found in theprescriptions may be due to antimigraine treatments or to misleading diagnoses.

Results

Pharmaceutical database (PD): dataset and analysis details

About 240000 pharmacy claims, filed between January 2009 and December 2011, analyzed using Anatomical Therapeutic Chemical (ATC) codes. The detailed analysis, for comparison with the clinical color was performed for the year 2011.

Inclusion criteria for migraine population

At least one pharmacy claim code for triptans (N02CC) in one year. Triptans are considered a marker drug of migraine, even if they are indicated (sumatriptan s.c) in the infrequent cluster headache.

Inclusion criteria for he control population

No triptan prescription. The analysis was made for each of the three years of the study. We collected all persons with prescription from ATC-group for depression (N06A), epilepsy (N03A), psychosis (N05A), hypertension (C02,C03,C07,C08,C09), diabetes (A10), dyslipidemia (C10), antiasthma/chronic obstructive pulmonary diseases (COPD) (R03), allergy (R06), hypothyroidism (H03A), hyperthyroidism (H03B).

A total of 1108 subjects (mean age 42.9: 883 female, mean age 42.9 and 225 male,mean age 42.8). that is 0.7% of the population aged 15-64 years (155829, 77798 female, 78040 male) received triptan prescriptions in 2011.

Clinical cohort (CC): population details

Inclusion criteria:

Patients aged 15-64 years, who accessed the Headache Centre from 1 January to 31 December 2011 with a diagnosis of migraine without aura (MO), migraine with aura (MA), chronic migraine (CM), medication overuse headache (MOH).

Each patient was asked about chronic conditions (CC) and possible current treatment(s) for hypertension, diabetes or dyslipidemia, depression, psychosis, epilepsy, hypothyroidism or hyperthyroidism, asthma/COPD. The current and past presence of other medical diagnosed diseases was investigated.

The clinical cohort consists of 681 patients aged 15-64 years (mean age 40.1), 528 (77.5%) females (mean age 40.7), 153 (22.5 %) male (mean age 37.6). The cohort included: 526 migraine without aura (mean age 38.8), 68 migraine with aura (mean age 37.0), and 86 chronic migraine/migraine without aura (mean age 49.7).

Statistical analysis

Statistical analysys was performed using Odd ratio (OR) with 95% confidence intervals (CIs) determined using logistic regression. Logistic regression models were also used to test differences in the OR. All analyses were performed using EpiInfo and Open Epi.

According to triptan prescriptions in the PD, 1108 subjects were considered migraine patients (MP). The prescription rates result different for antidepressants (22.8% MP vs. 6.8%), anticonvulsants (8.2% MP vs. 2.5%), antihistamines (9.7% MP vs.5.6%), antiasthma (12.9% MP vs.7.9%), antihypertensives (22.8% MP vs.11.9%). Interestingly, beta-blockers and topiramate, both used as migraine preventive treatment, are almost totally responsible for the higher prescription rate of antihypertensives and anticonvulsants, respectively, in MP. Prescription rates in the CC were similar to those of general population in the PD. (* p < 0.0001, ** p < 0.001, *** p<0.01.)

Percentage of subjects receiving drugs specific for chronic diseases in triptan users and general population.

	2009		2010		2011	
	Population (154517)	Triptans users (1083)	Population (153087)	Triptans users (1103)	Population (155829)	Triptans users (1108)
Antidepressants N06A	7.2	20.3	7.0	21.3	6.8	22.8
Anticonvulsants N03	2.2	8.3	2.4	8.3	2.5	8.2
Antipsychotics N05A	1.3	0.9	1.3	1.0	1.4	0.9
Antihypertensives C02,C03,C07,C08,C09	11.9	19.8	12.0	19.9	11.9	22.8
Antidiabetics A10	2.7	1.3	2.8	1.0	2.8	1.3
Antilipids C10	3.2	1.9	3.4	1.9	3.7	1.9
Antiasthma/COPD R03	8.0	12.4	7.9	12.1	7.9	12.9
Antihistamines R06	5.0	8.3	5.4	8.3	5.6	9.7
Thyroid hormones 03A	3.6	3.6	3.7	4.9	3.7	4.6
Antithyroids H03B	0.2	0.1	0.2	0.1	0.2	0.1

Percentage of subjects receiving drugs specific for chronic diseases in triptan users and general population in 2011.

	Population			Triptan users			OR		
	Female	Male	All	Female	Male	All	All	Female	Male
Antidepressant	9.1	4.5	**6.8**	25.4	12.4	**22.8**	**4.3** *	2.7 *	2.8 *
Anticonvulsants	2.6	2.3	**2.5**	8.8	5.7	**8.2**	**3.5** *	3.3 *	2.5 ***
Antipsychotics	1.3	1.4	**1.4**	0.6	1.7	**0.9**	**0.6**	0.5	1.3
Antihypertensives	11.5	12.3	**11.9**	25.4	12.4	**22.8**	**2.1** *	2.3 **	1.0
Antidiabetics	2.6	3.1	**2.8**	1.1	2.2	**1.3**	**0.4** **	0.4 **	0.7
Antilipids	2.9	4.5	**3.7**	1.5	3.5	**1.9**	**0.5** *	0.3 *	0.6
Antiasthma/copd	8.8	6.9	**7.9**	13.3	11.6	**12.9**	**1.7** *	1.5 **	1.7 ***
Antihistamines	6.0	5.3	**5.6**	10.5	6.2	**9.7**	**1.7** *	1.7 **	1.1
Thyroid hormones	6.4	1.0	**3.7**	5.6	0.4	**4.6**	**1.2**	0.9	0.4
Antithyroids	0.3	0.1	**0.2**	0.1	0.0	**0.1**	**1.0**	0.9	--

Percentage of subjects receiving different subclasses of antihypertensives .

	Population			Population			Population		
	Female	Male	All	Female	Male	All	All	Female	Male
Betablockers C07	3.7	3.7	**3.7**	14.0	12.0	**13.6**	**4.1** *	4.0 *	3.2 *
ACEinhibitors C09A, C09B	5.6	7.1	**6.3**	4.8	5.3	**4.9**	**0.5** **	0.9	0.7
Angiotensin II receptor blockers C09C, C09D	2.7	3.0	**2.9**	3.5	2.2	**3.2**	**1.1**	1.4	0.7
Calcium channel blockers C08	2.1	3..0	**2.5**	1.7	3.1	**1.9**	**0.7**	0.9	1.0
Diuretics C03	1.9	1.4	**1.7**	2.0	1.3	**1.9**	**1.1**	1.1	1.0
α1-receptor antagonist C02CA04	0.4	0.8	**0.6**	0.4	0.4	**0.40**	**0.6**	1.2	0.5

Percentage of subjects receiving drugs specific for chronic diseases according to sex in the clinical cohort

	Male (153)		Female (528)		OR	p
	N	%	N	%		
Depression	5	3.2	32	6.0	0,52	NS
Hypertension	13	8.4	57	10.7	0,77	NS
Diabetes	3	1.9	6	1.1	1,74	NS
Asthma	6	3.9	13	2.4	1,62	NS
Hypothyroidism	2	1.3	42	7.9	0,15	<0,0001
Allergies	35	22.8	97	18.3	1,32	NS

Percentage of subjects receiving drugs specific for chronic diseases according to diagnosis of episodic or chronic migraine in the clinical cohort

	Episodic migraine (595)		Chronic migraine (86)		OR	p
	N°	%	N°	%		
Depression	30	5.0	7	8.1	0,6	NS
Hypertension	49	8.2	21	24.4	0,28	<0,0001
Diabetes	7	1.1	2	2.3	3,35	<0,005
Asthma	11	1.8	8	9.3	0,18	<0,001
Hypothyroidism	36	6.0	8	9.3	0,63	NS
Allergies	117	19.6	15	17.4	1,16	NS