farmacovigilancia y farmacoepidemiología en castilla y león

alfonso carvajal

centro de estudios
sobre la seguridad
de los medicamentos (cesme)
universidad de valladolid

guión

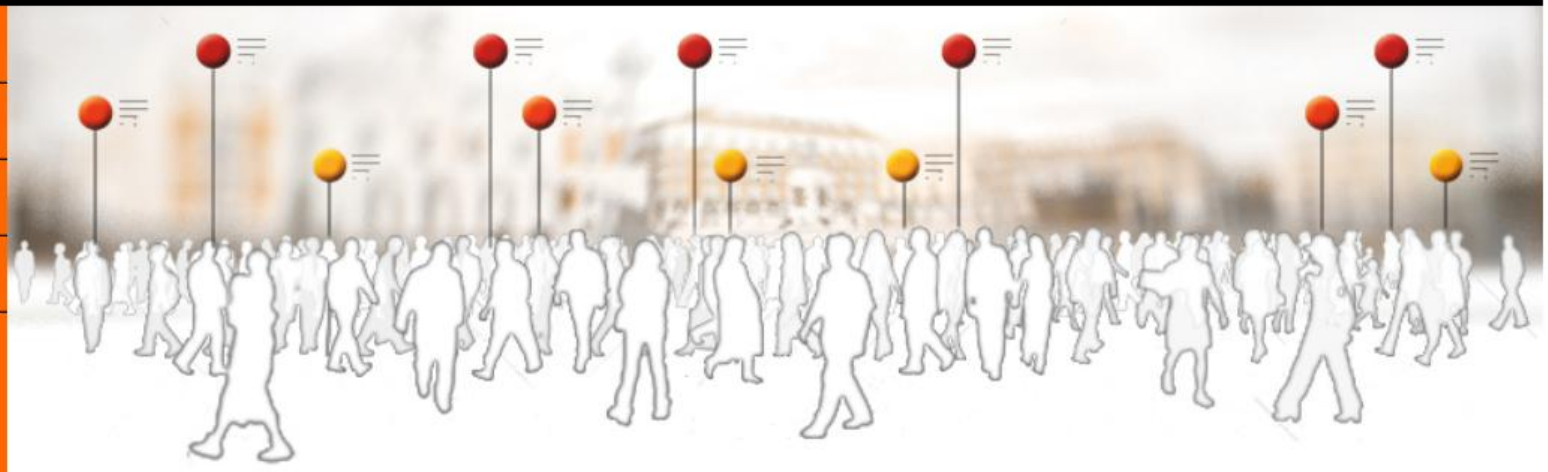
- centro de estudios sobre la seguridad de los medicamentos (cesme)
  - actividad
- algunas señales
- recursos
- importancia de los datos

cesme

- (antiguo ife)
- actividad asistencial
  - seguimiento de los medicamentos (farmacovigilancia) / centro regional de farmacovigilancia
- investigación
  - cuantificación de riesgos mediante estudios específicos
- formación
  - cursos de *e_learning*; cursos de posgrado (UB, UNAM,…)
- otros
  - agencia española de medicamentos
  - agencia europea del medicamento
  - *uppsala monitoring centre (WHO)*
  - *steering committee ENCePP*

cesme centro de estudios sobre la seguridad de los medicamentos

Búsqueda



noticias

e_learning
02/02/2015

V Jornada de Actualización en Vacunas
26/05/2014

red de farmacias centinelas de castilla y león
17/12/2013

cesme. universidad de valladolid UVa

El **centro de estudios sobre la seguridad de los medicamentos (cesme)** es un centro interdisciplinar de la Universidad de Valladolid dedicado a la investigación sobre la seguridad de los medicamentos en las poblaciones humanas.

anuncios

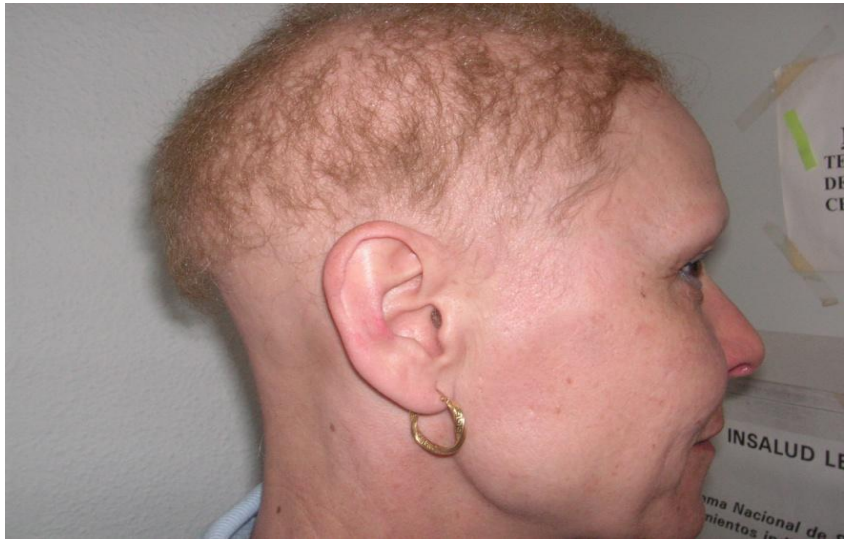
abril 2015

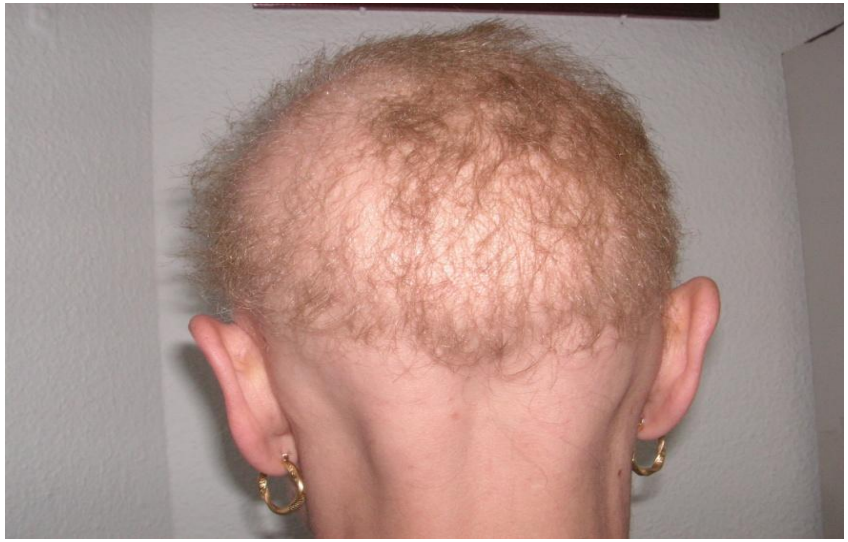
cesme

- **declaración ENCePP**

"Somos un centro asociado a la red científica EnCePP, coordinada por la Agencia Europea de Medicamentos. Nos dedicamos a la investigación de excelencia siguiendo la Guía ENCePP sobre Modelos Metodológicos y promoviendo la independencia y transparencia científicas. Utilizamos el Registro Electrónico de Estudios del ENCePP, una herramienta de acceso público para el registro de estudios de farmacoepidemiología y farmacovigilancia".

ranelato de estroncio y alopecia





ranelato de estroncio y alopecia

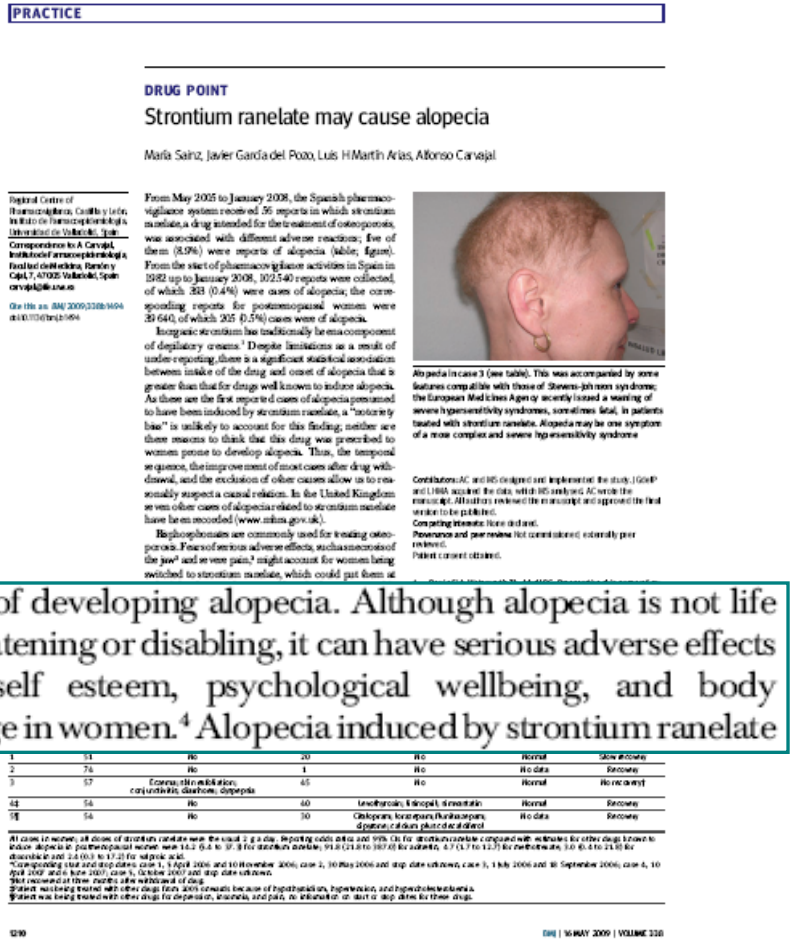
- FEDRA
  - notificaciones ranelato de estroncio (mayo 2005-enero 2008)
    - total, 56; alopecia, 5 (8.9%)
  - notificaciones resto de medicamentos (mujeres; posterior a la menopausia; mismo periodo)
    - total 39,640; alopecia, 250 (0.5%)

ranelato de estroncio y alopecia

drug	alopecia (%)	ROR (95% CI)
acitretin	3 (37.5)	91.8 (21.8 – 387.0)
strontium ranelate	5 (8.9)	14.2 (5.4-37.3)
methotrexate	4 (2.3)	4.7 (1.7-12.7)
doxorubicin	1 (1.5)	3.0 (0.4 – 21.8)
valproic acid	1 (1.2)	2.4 (0.3 – 17.2)

comentarios

- reacción específica
- asociación
  - secuencia/retirada/ no explicación alternativa
- fuerza de la asociación (ROR)
- análisis de posibles sesgos
- cremas depilatorias (BMJ)
- cambio de la ficha técnica



PRACTICE

DRUG POINT

Strontium ranelate may cause alopecia

María Sainz, Javier García del Pozo, Luis H Martín Arias, Alfonso Carvajal

risk of developing alopecia. Although alopecia is not life threatening or disabling, it can have serious adverse effects on self esteem, psychological wellbeing, and body image in women.[4] Alopecia induced by strontium ranelate

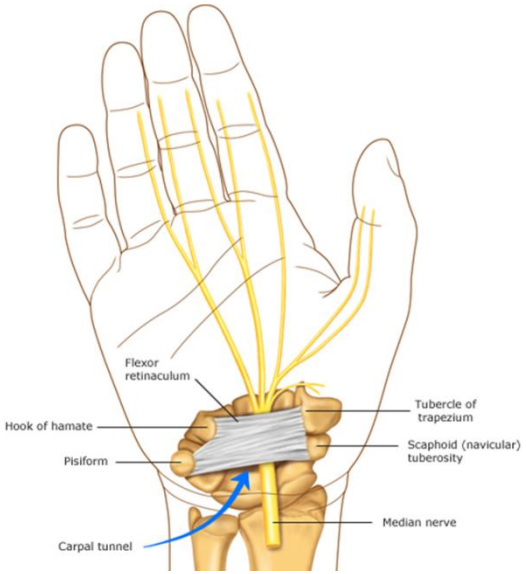
bifosfonatos y túnel carpiano

bifosfonatos

- protección frente a fracturas osteoporóticas
- aumento del consumo
- reacciones adversas
  - úlceras esofágicas
  - osteonecrosis de mandíbula
  - fracturas atípicas
  - alteraciones musculoesqueléticas (dolores musculares, artritis, sinovitis,…)

túnel carpiano

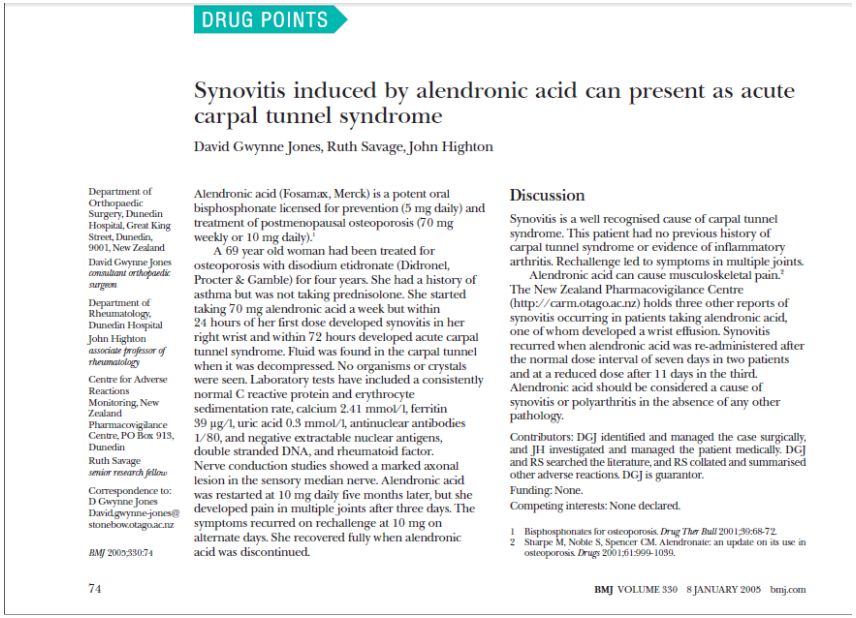
- compresión del nervio mediano
  - profesión
  - genética
  - imc
  - otros (fármacos)



www.uptodate.com/contents/etiology-of-carpal-tunnel-syndrome

indicios

- dos casos de túnel carpiano
- publicación en BMJ
- conversación con la autora



DRUG POINTS

Synovitis induced by alendronic acid can present as acute carpal tunnel syndrome

David Gwynne Jones, Ruth Savage, John Highton

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Department of Rheumatology, Dunedin Hospital
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BMJ 2005;330:74

Alendronic acid (Fosamax, Merck) is a potent oral bisphosphonate licensed for prevention (5 mg daily) and treatment of postmenopausal osteoporosis (70 mg weekly or 10 mg daily).[1]

A 69 year old woman had been treated for osteoporosis with disodium etidronate (Didronel, Procter & Gamble) for four years. She had a history of asthma but was not taking prednisolone. She started taking 70 mg alendronic acid a week but within 24 hours of her first dose developed synovitis in her right wrist and within 72 hours developed acute carpal tunnel syndrome. Fluid was found in the carpal tunnel when it was decompressed. No organisms or crystals were seen. Laboratory tests have included a consistently normal C reactive protein and erythrocyte sedimentation rate, calcium 2.41 mmol/l, ferritin 39 µg/l, uric acid 0.3 mmol/l, antinuclear antibodies 1/80, and negative extractable nuclear antigens, double stranded DNA, and rheumatoid factor. Nerve conduction studies showed a marked axonal lesion in the sensory median nerve. Alendronic acid was restarted at 10 mg daily five months later, but she developed pain in multiple joints after three days. The symptoms recurred on rechallenge at 10 mg on alternate days. She recovered fully when alendronic acid was discontinued.

Discussion

Synovitis is a well recognised cause of carpal tunnel syndrome. This patient had no previous history of carpal tunnel syndrome or evidence of inflammatory arthritis. Rechallenge led to symptoms in multiple joints.

Alendronic acid can cause musculoskeletal pain.[2] The New Zealand Pharmacovigilance Centre (http://carm.otago.ac.nz) holds three other reports of synovitis occurring in patients taking alendronic acid, one of whom developed a wrist effusion. Synovitis recurred when alendronic acid was re-administered after the normal dose interval of seven days in two patients and at a reduced dose after 11 days in the third. Alendronic acid should be considered a cause of synovitis or polyarthritis in the absence of any other pathology.

Contributors: DGJ identified and managed the case surgically, and JH investigated and managed the patient medically. DGJ and RS searched the literature, and RS collated and summarised other adverse reactions. DGJ is guarantor.

Funding: None.

Competing interests: None declared.

1 Bisphosphonates for osteoporosis. *Drug Ther Bull* 2001;39:68-72.
2 Sharpe M, Noble S, Spencer CM. Alendronate: an update on its use in osteoporosis. *Drugs* 2001;61:999-1039.

Carpal tunnel syndrome associated with oral bisphosphonates. A population-based cohort study

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método

- estudio de cohortes en una base de datos de historias clínicas informatizadas (THIN)
- población, mujeres >51 años (exclusión: cáncer, paget, menos de 1 año registrada)
- exposición, prescripción de un bifosfonato
  - tipo y nivel de exposición (número de prescripciones)
- emparejamiento (1:2), edad, procedencia y tiempo
- desenlace, túnel carpiano (códigos clínicos o quirúrgicos)
- ajuste (covariables), imc, artritis, diabetes, número de visitas
- análisis de supervivencia (regresión de cox)

Table 1. Baseline characteristics. Distribution of exposed and non-exposed women according to different prognostic factors

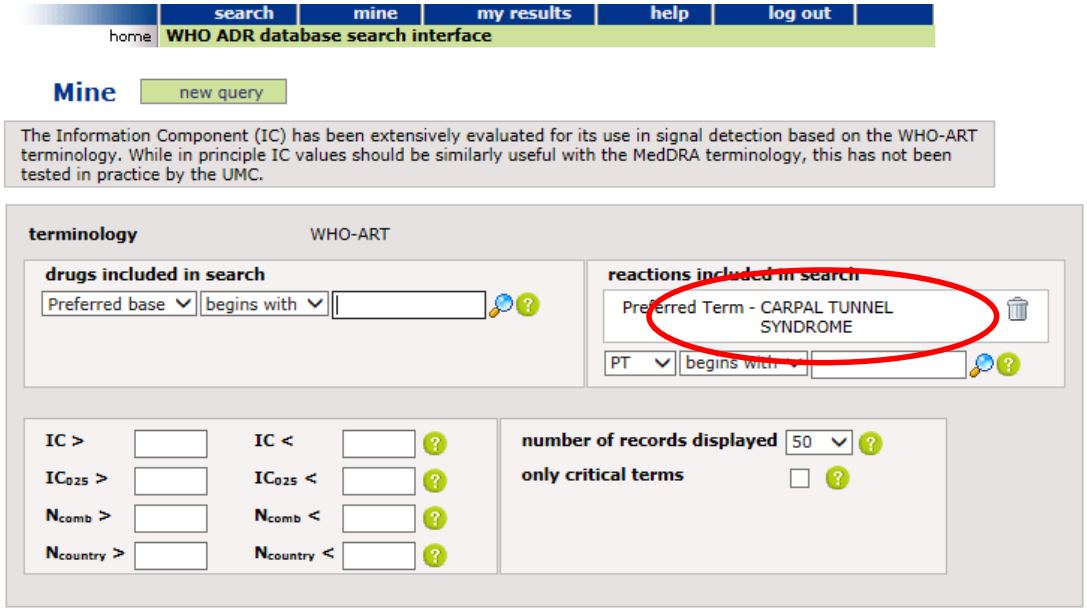
n=59.475

	Number (%)	
	Exposed (n=19 825)	Non-exposed (n=39 650)
Age at Index Date (mean ± SD), years	72.1 ± 10.0	72.1 ± 10.0
<59	2674 (13.5)	5294 (13.4)
60-69	5134 (25.9)	10 269 (25.9)
70-89	11 402 (57.5)	22 800 (57.5)
≥90	642 (3.2)	1287 (3.3)
Start Date to Index Date (mean ± SD), years	4.4 ± 2.3	4.4 ± 2.3
Index Date to outcome (mean ± SD), years	2.6 ± 1.9	2.6 ± 1.9
Number of visits (mean ± SD)	4.3 (3.8)	2.2 (2.9)
<2	4829 (24.4)	21 323 (53.8)
2-4	7582 (38.2)	12 368 (31.2)
≥5	7414 (37.4)	5959 (15.0)
Alcohol intake		
Non- heavy drinker	18 064 (91.1)	36 537 (92.1)
Heavy drinker	1728 (8.7)	3051 (7.7)
Missing	33 (0.12)	62 (0.2)
BMI		
<25.0	8985 (45.3)	13 123 (33.1)
25.0-29.9	5130 (25.9)	11 247 (28.4)
≥30	2322 (11.7)	6837 (17.2)
Missing	3388 (17.1)	8443 (21.3)
Smoking status		
Never	5865 (29.6)	11 429 (28.8)
Former	6027 (30.4)	11 734 (29.6)
Current	6387 (32.2)	11 928 (30.1)
Missing	1546 (7.8)	4559 (11.5)
Diabetes	3104 (15.7)	4774 (12.0)
Hypothyroid	2139 (10.8)	3534 (8.9)
Rheumatoid Arthritis	1315 (6.6)	642 (1.6)

Table 2. Risk of carpal tunnel syndrome associated with the intake of bisphosphonates

	Exposed		Non-Exposed		Crude		Adjusted	
	Cases	Person-Years	Cases	Person-Years	HR (95% CI)	p-value	HR (95% CI)	p-value
Intake (y/n)								
No	0	0	330	103 363	-	-	-	-
Yes	242	51 245		0	1.5 (1.3-1.8)	$3.76x10^{-6}$	1.4 (1.2-1.7)	0.000362
Number of prescriptions								
0	0	0	330	103 363	-	-	-	-
1-4	46	10 473	0	0	1.4 (1.0-1.9)	0.042244	1.3 (0.9-1.8)	0.126746
5-16	73	14 739	0	0	1.5 (1.2-2.0)	0.000883	1.5 (1.1-2.0)	0.004308
≥17	123	26 032	0	0	1.5 (1.2-1.8)	0.000184	1.4 (1.1-1.7)	0.008082

VigiBase


search
mine
my results
help
log out
home
WHO ADR database search interface
Mine
new query
The Information Component (IC) has been extensively evaluated for its use in signal detection based on the WHO-ART terminology. While in principle IC values should be similarly useful with the MedDRA terminology, this has not been tested in practice by the UMC.
terminology
WHO-ART
drugs included in search
Preferred base
begins with
reactions included in search
Preferred Term - CARPAL TUNNEL SYNDROME
PT
begins with
IC >
IC <
IC025 >
IC025 <
Ncomb >
Ncomb <
Ncountry >
Ncountry <
number of records displayed
50
only critical terms

VigiBase

refine

Dataset date: 2013-06-03
Number of combinations in result: 533
Total number of reports: 8 100 548

		preferred base	preferred term	critical	N_{comb}	IC	IC_{025}	N_{drug}	N_{adr}	$N_{country}$	$N_{dechall}$	$N_{rechall}$	N_{fatal}
details	reports	Anastrozole	Carpal tunnel syndrome		141	5.09	4.84	8 909	3 319	14	0	0	0
details	reports	Colecalciferol/Alendronate sodium	Carpal tunnel syndrome		47	5.15	4.70	2 054	3 319	1	0	0	0
details	reports	Exemestane	Carpal tunnel syndrome		49	5.12	4.69	2 246	3 319	10	2	0	0
details	reports	Alendronic acid	Carpal tunnel syndrome		234	4.09	3.90	32 409	3 319	5	1	1	6
details	reports	Rofecoxib	Carpal tunnel syndrome		413	3.91	3.77	65 856	3 319	8	3	0	18
details	reports	Somatropin	Carpal tunnel syndrome		60	3.85	3.46	9 053	3 319	11	13	2	0
details	reports	Lyme disease vaccine	Carpal tunnel syndrome		24	4.08	3.44	2 326	3 319	1	0	0	0
details	reports	Insulin lispro	Carpal tunnel syndrome		58	3.53	3.14	11 110	3 319	1	1	0	0
details	reports	Letrozole	Carpal tunnel syndrome		33	3.62	3.08	5 442	3 319	8	1	1	0
details	reports	Pamidronic acid	Carpal tunnel syndrome		29	3.41	2.84	5 557	3 319	2	0	0	5
details	reports	Tesamorelin	Carpal tunnel syndrome		9	3.78	2.68	472	3 319	1	0	0	0
details	reports	Insulin human	Carpal tunnel syndrome		63	3.04	2.66	17 670	3 319	1	2	1	0
details	reports	Insulin lispro/Insulin lispro protamine suspension	Carpal tunnel syndrome		11	3.09	2.11	2 076	3 319	1	0	0	0
details	reports	Levofloxacin	Carpal tunnel syndrome		63	2.49	2.11	26 357	3 319	2	1	1	0
details	reports	Atorvastatin	Carpal tunnel syndrome		110	2.38	2.09	50 775	3 319	8	8	2	2
details	reports	Risedronic acid	Carpal tunnel syndrome		19	2.50	1.77	7 222	3 319	1	0	0	0
details	reports	Zoledronic acid	Carpal tunnel syndrome		53	2.18	1.76	27 701	3 319	5	0	0	9
details	reports	Ibandronic acid	Carpal tunnel syndrome		28	2.28	1.70	13 108	3 319	2	1	0	0
details	reports	Infliximab	Carpal tunnel		98	1.93	1.63	61 837	3 319	8	0	0	1

VigiBase

Gender

gender	N_{comb}	N_{drug}	N_{adr}	N_{tot}	IC	IC_{025}
Female	172	27 342	2 352	4 579 777	3.57	3.35
Male	7	2 386	826	2 996 805	2.70	1.44
Unknown	55	2 681	141	523 966	5.51	5.10

Age group

age group	N_{comb}	N_{drug}	N_{adr}	N_{tot}	IC	IC_{025}
18 to 44 years	6	638	430	1 708 629	3.30	1.92
45 to 64 years	108	8 083	1 219	1 834 821	4.21	3.92
65 to 74 years	42	7 702	324	869 441	3.66	3.19
More than 75 years	15	6 846	168	688 128	2.84	2.01
Unknown	63	8 990	1 156	2 127 770	3.56	3.18

Age group - Gender

gender/age group	N_{comb}	N_{drug}	N_{adr}	N_{tot}	IC	IC_{025}
18 to 44 years/Female	6	494	324	1 116 142	3.34	1.96
45 to 64 years/Female	103	7 378	874	1 081 150	4.00	3.71
45 to 64 years/Male	5	640	342	731 503	2.78	1.26
65 to 74 years/Female	40	7 074	229	484 035	3.40	2.91
65 to 74 years/Male	2	551	94	375 259	1.97	-0.62
More than 75 years/Female	15	6 218	121	412 014	2.74	1.92
Unknown/Female	8	6 074	787	1 070 056	0.78	-0.39
Unknown/Unknown	55	2 454	134	433 546	5.46	5.06

VigiBase

Country

country	N_{comb}	N_{drug}	N_{adr}	N_{tot}	IC	IC_{025}
CAN	1	1 315	118	373 608	0.71	-3.09
DEU	1	667	129	427 402	1.10	-2.70
GBR	2	2 409	135	600 757	1.26	-1.33
NZL	1	395	9	82 565	1.47	-2.33
USA	229	20 682	2 739	4 047 849	3.99	3.79

Reporting year (non-cumulative)

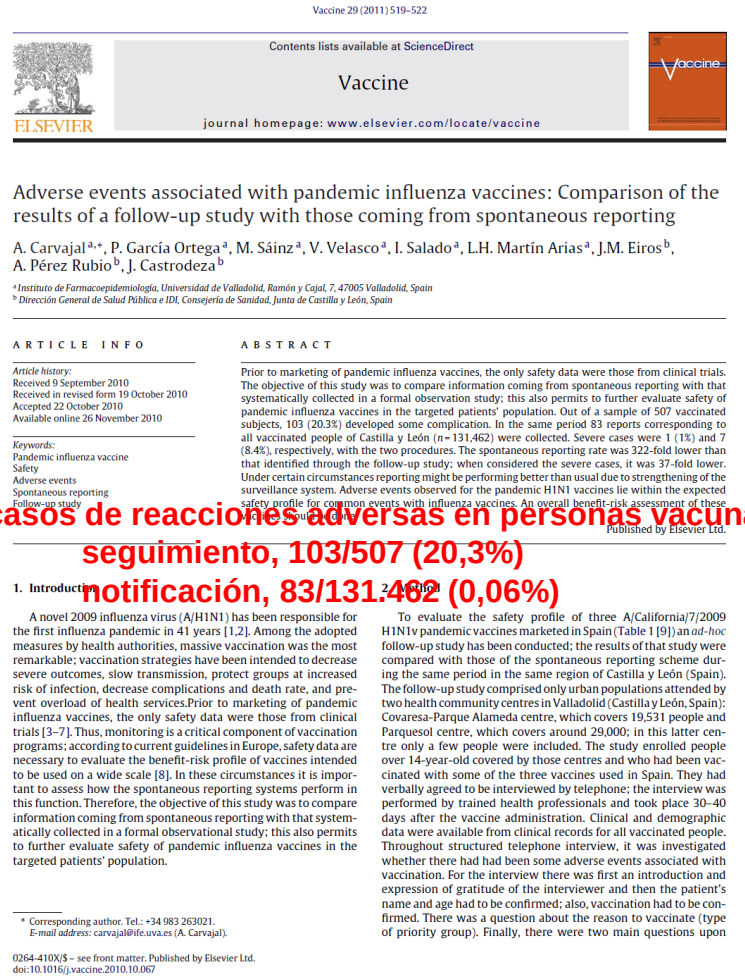
year	N_{comb}	N_{drug}	N_{adr}	N_{tot}	IC	IC_{025}
2013	188	5 422	779	820 314	5.06	4.85
2012	2	1 886	257	619 627	0.96	-1.63
2011	3	3 255	480	1 063 516	0.83	-1.22
2010	16	2 309	350	925 267	3.59	2.79
2009	18	2 349	227	499 723	3.56	2.82
2008	2	2 540	443	457 404	-0.24	-2.83
2006	3	1 151	211	313 256	1.46	-0.59
2005	1	954	124	254 897	0.64	-3.16
2004	1	661	72	213 916	1.05	-2.74

valoración

- asociación significativa
- coherencia (*consistency*)
- plausibilidad biológica
  - "…reacciones graves e incapacitantes…" (día, meses o años)
  - macrófagos liberan citoquinas (TNF, IL6) [*in vitro / in vivo*]
  - acantonamiento en el hueso (*buried*) / riesgo constante
- posible asociación causal
- riesgo atribuible, 28,6%

cesme. farmacovigilancia sobre vacunas

- seguimiento de vacunas
- informes sobre ciertas vacunas (VPH, otras,…) / informes generales
- divulgación (prensa)
- estudios formales
  - DTP y muerte súbita (meta-análisis)
  - vacuna frente al meningococo (notificación espontánea)
  - gripe pandémica (seguimiento – comparación con notificación espontánea)
  - vacuna de la gripe y guillain barré



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Adverse events associated with pandemic influenza vaccines: Comparison of the results of a follow-up study with those coming from spontaneous reporting

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Keywords:
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Follow-up study

ABSTRACT

Prior to marketing of pandemic influenza vaccines, the only safety data were those from clinical trials. The objective of this study was to compare information coming from spontaneous reporting with that systematically collected in a formal observation study; this also permits to further evaluate safety of pandemic influenza vaccines in the targeted patients' population. Out of a sample of 507 vaccinated subjects, 103 (20.3%) developed some complication. In the same period 83 reports corresponding to all vaccinated people of Castilla y León (n = 131,462) were collected. Severe cases were 1 (1%) and 7 (8.4%), respectively, with the two procedures. The spontaneous reporting rate was 322-fold lower than that identified through the follow-up study; when considered the severe cases, it was 37-fold lower. Under certain circumstances reporting might be performing better than usual due to strengthening of the surveillance system. Adverse events observed for the pandemic H1N1 vaccines lie within the expected safety profile for common events with influenza vaccines. An overall benefit-risk assessment of these vaccines should [illegible]

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casos de reacciones adversas en personas vacunadas
seguimiento, 103/507 (20,3%)
notificación, 83/131.462 (0,06%)

1. Introduction

A novel 2009 influenza virus (A/H1N1) has been responsible for the first influenza pandemic in 41 years [1,2]. Among the adopted measures by health authorities, massive vaccination was the most remarkable; vaccination strategies have been intended to decrease severe outcomes, slow transmission, protect groups at increased risk of infection, decrease complications and death rate, and prevent overload of health services.Prior to marketing of pandemic influenza vaccines, the only safety data were those from clinical trials [3–7]. Thus, monitoring is a critical component of vaccination programs; according to current guidelines in Europe, safety data are necessary to evaluate the benefit-risk profile of vaccines intended to be used on a wide scale [8]. In these circumstances it is important to assess how the spontaneous reporting systems perform in this function. Therefore, the objective of this study was to compare information coming from spontaneous reporting with that systematically collected in a formal observational study; this also permits to further evaluate safety of pandemic influenza vaccines in the targeted patients' population.

2. Method

To evaluate the safety profile of three A/California/7/2009 H1N1v pandemic vaccines marketed in Spain (Table 1 [9]) an *ad-hoc* follow-up study has been conducted; the results of that study were compared with those of the spontaneous reporting scheme during the same period in the same region of Castilla y León (Spain). The follow-up study comprised only urban populations attended by two health community centres in Valladolid (Castilla y León, Spain): Covaresa-Parque Alameda centre, which covers 19,531 people and Parquesol centre, which covers around 29,000; in this latter centre only a few people were included. The study enrolled people over 14-year-old covered by those centres and who had been vaccinated with some of the three vaccines used in Spain. They had verbally agreed to be interviewed by telephone; the interview was performed by trained health professionals and took place 30–40 days after the vaccine administration. Clinical and demographic data were available from clinical records for all vaccinated people. Throughout structured telephone interview, it was investigated whether there had had been some adverse events associated with vaccination. For the interview there was first an introduction and expression of gratitude of the interviewer and then the patient's name and age had to be confirmed; also, vaccination had to be confirmed. There was a question about the reason to vaccinate (type of priority group). Finally, there were two main questions upon

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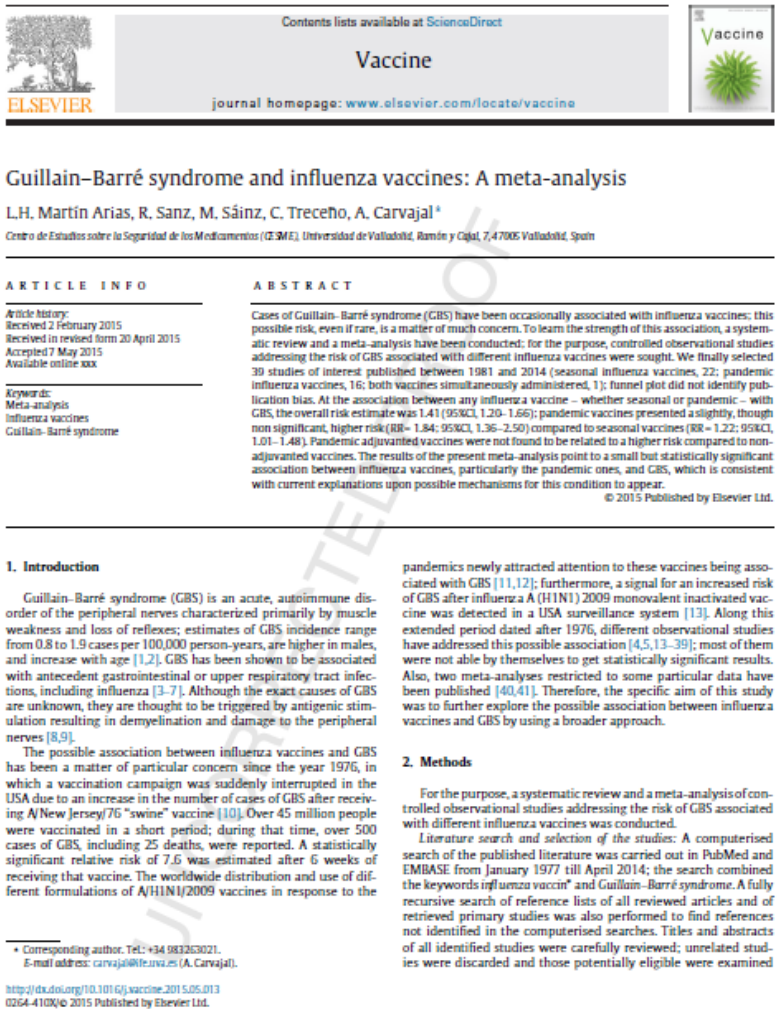
cesme. farmacovigilancia sobre vacunas

- vacunas de la gripe pandémica y guillain-barré
  - RR, 1.8



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Guillain–Barré syndrome and influenza vaccines: A meta-analysis

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ABSTRACT

Cases of Guillain–Barré syndrome (GBS) have been occasionally associated with influenza vaccines; this possible risk, even if rare, is a matter of much concern. To learn the strength of this association, a systematic review and a meta-analysis have been conducted; for the purpose, controlled observational studies addressing the risk of GBS associated with different influenza vaccines were sought. We finally selected 39 studies of interest published between 1981 and 2014 (seasonal influenza vaccines, 22; pandemic influenza vaccines, 16; both vaccines simultaneously administered, 1); funnel plot did not identify publication bias. At the association between any influenza vaccine – whether seasonal or pandemic – with GBS, the overall risk estimate was 1.41 (95%CI, 1.20–1.66); pandemic vaccines presented a slightly, though non significant, higher risk (RR= 1.84; 95%CI, 1.36–2.50) compared to seasonal vaccines (RR= 1.22; 95%CI, 1.01–1.48). Pandemic adjuvanted vaccines were not found to be related to a higher risk compared to non-adjuvanted vaccines. The results of the present meta-analysis point to a small but statistically significant association between influenza vaccines, particularly the pandemic ones, and GBS, which is consistent with current explanations upon possible mechanisms for this condition to appear.

1. Introduction

Guillain–Barré syndrome (GBS) is an acute, autoimmune disorder of the peripheral nerves characterized primarily by muscle weakness and loss of reflexes; estimates of GBS incidence range from 0.8 to 1.9 cases per 100,000 person-years, are higher in males, and increase with age [1,2]. GBS has been shown to be associated with antecedent gastrointestinal or upper respiratory tract infections, including influenza [3–7]. Although the exact causes of GBS are unknown, they are thought to be triggered by antigenic stimulation resulting in demyelination and damage to the peripheral nerves [8,9].

The possible association between influenza vaccines and GBS has been a matter of particular concern since the year 1976, in which a vaccination campaign was suddenly interrupted in the USA due to an increase in the number of cases of GBS after receiving A/New Jersey/76 "swine" vaccine [10]. Over 45 million people were vaccinated in a short period; during that time, over 500 cases of GBS, including 25 deaths, were reported. A statistically significant relative risk of 7.6 was estimated after 6 weeks of receiving that vaccine. The worldwide distribution and use of different formulations of A/H1N1/2009 vaccines in response to the pandemics newly attracted attention to these vaccines being associated with GBS [11,12]; furthermore, a signal for an increased risk of GBS after influenza A (H1N1) 2009 monovalent inactivated vaccine was detected in a USA surveillance system [13]. Along this extended period dated after 1976, different observational studies have addressed this possible association [4,5,13–39]; most of them were not able by themselves to get statistically significant results. Also, two meta-analyses restricted to some particular data have been published [40,41]. Therefore, the specific aim of this study was to further explore the possible association between influenza vaccines and GBS by using a broader approach.

2. Methods

For the purpose, a systematic review and a meta-analysis of controlled observational studies addressing the risk of GBS associated with different influenza vaccines was conducted.

Literature search and selection of the studies: A computerised search of the published literature was carried out in PubMed and EMBASE from January 1977 till April 2014; the search combined the keywords *influenza vaccin** and *Guillain–Barré syndrome*. A fully recursive search of reference lists of all reviewed articles and of retrieved primary studies was also performed to find references not identified in the computerised searches. Titles and abstracts of all identified studies were carefully reviewed; unrelated studies were discarded and those potentially eligible were examined

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otros estudios


GASTROENTEROLOGY 2011;141:338–347

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Eur J Clin Pharmacol

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

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Vaccine

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recursos

- bases de datos de consumo de medicamentos
  - ECOM / CONCYLIA
- bases de datos de reacciones adversas a medicamentos
  - FEDRA / EudraVigilance / Vigibase-VigiLyze / VAERS
- diagnósticos al alta
  - CMBD
- encuesta de salud
  - INE/MSC
- demográficos
  - INE
- genéticos
  - Eudragene
  - EMPHOGEN
  - ICARO
- historias clínicas informatizadas
  - JIMENA / MEDORA / **BIFAP**
  - THIN

proyectos

- estudio Ícaro
  - seguimiento de pacientes tratados con antipsicóticos / aumento de peso (bases genéticas) (www.uva.es/estudioicaro)
- EUDRAGENE
  - bases genéticas de las reacciones adversas

  www.eudragene.com
  - agranulocitosis – bases genéticas de la agranulocitosis inducida por medicamentos (FIS, 2010) /swedegene www.swedegene.se/
- notificación por ciudadanos y pacientes (FIS, 2011) www.yonotifico.es
- generación de señales. King's College London (THIN database)
- "Píldora del Día Después" (PDD), estudio de seguimiento (notificación espontánea + estudio de seguimiento *ad hoc*)

importancia de los datos

- sistema sanitario
  - dispositivo asistencial e investigador
- los datos son de todos
  - los generan los pacientes
  - los recogen los profesionales sanitarios
  - los custodia la administración
  - los pagan los contribuyentes
- imperativo utilizar la información en beneficio de los pacientes