

BRIEF COMMUNICATION

Increased incidence of admissions for anaphylaxis in Spain 1998–2011

M. A. Tejedor-Alonso^{1,2}, M. Moro-Moro¹, M. Mosquera González³, M. Rodríguez-Alvarez¹, E. Pérez Fernández⁴, P. Latasa Zamalloa³, E. Farias Aquino¹, R. Gil Prieto⁵ & A. Gil de Miguel⁵

¹Allergy Unit, Hospital Universitario Fundación Alcorcón; ²Medicine and Surgery Department, Universidad Rey Juan Carlos; ³Preventive Medicine Unit, Hospital Universitario Fundación Alcorcón; ⁴Medical Research Unit, Hospital Universitario Fundación Alcorcón; ⁵Preventive Medicine and Public Health Department, Universidad Rey Juan Carlos, Alcorcón, Madrid, Spain

To cite this article: Tejedor-Alonso MA, Moro-Moro M, Mosquera González M, Rodríguez-Alvarez M, Pérez Fernández E, Latasa Zamalloa P, Farias Aquino E, Gil Prieto R, Gil de Miguel A. Increased incidence of admissions for anaphylaxis in Spain 1998–2011. *Allergy* 2015; DOI 10.1111/all.12613.

Keywords

admissions; anaphylaxis; children; food; increase.

Correspondence

Miguel A. Tejedor-Alonso, Allergy Unit, Hospital Universitario Fundación Alcorcón, Avda Budapest 1, 28922 Alcorcón, Madrid, Spain.
Tel.: +34916219711 and +34629864381
Fax: +34916219704
E-mails: m914674227@telefonica.net; matejedor@fhalcorcon.es

Accepted for publication 16 March 2015

DOI:10.1111/all.12613

Edited by: Douglas Robinson

Abstract

We report on trends in anaphylaxis admissions in the Spanish hospital system during the period 1998–2011. Data on admissions for anaphylaxis were obtained from the Spanish Information System for Hospital Data for the period 1998–2011. Patients were selected using the codes for anaphylaxis in the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*. Poisson regression models were used to estimate incidence rate ratios. We recorded a 1.89-fold increase in admissions for anaphylaxis in Spanish hospitals during the study period, particularly in patients aged 0–14 years (1.65- to 3.22-fold until 2009 and 4.09- to 12.59-fold until 2011) and in food anaphylaxis in all age groups (2.78-fold until 2009 and 8.74-fold until 2011). The incidence of anaphylaxis is perceived as having increased in recent years, especially anaphylaxis caused by food and anaphylaxis affecting the pediatric population.

In this article, we examine trends in admissions for anaphylaxis in the Spanish hospital system during the period 1997–2011.

Materials and methods

The study was carried out using the Spanish Minimum Basic Data Set (MBDS), which is a database created by the Spanish Ministry of Health. The system uses the codes of the Spanish version of the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* (1), and covers 99.5% of the Spanish population (2–4).

Possible cases of anaphylaxis were obtained from all discharge diagnoses using two strategies. First, we chose ICD-9-CM codes that were specifically associated with anaphylaxis and causes of anaphylaxis. We also used codes related to the causes of anaphylaxis and symptoms or signs of organs or systems whose combination led us to select episodes that fulfilled the criteria for the definition of anaphylaxis of the NI-AID-FAAN (National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network) Symposium

(5) following a strategy adapted from Harduar-Murano et al. (6).

Temporal trends were calculated using Poisson regression models. We report temporal trends only for the period 1998–2011, given that the Spanish National Institute of Statistics did not report data for the year 1997. The study was approved by the Clinical Research Ethics Committee of Hospital Universitario Fundación Alcorcón (number 12/103).

Results

During the study period, 11 336 records from the MBDS met our inclusion criteria (1.75 per 100 000 person-years [95%CI, 1.64–1.86]). Males accounted for 53% of patients, and the mean age was 47.5 years (IQR, 27–70 years).

The three most frequent causes of anaphylaxis were drugs (42.48%), unknown causes (30.59%), and foods (19.64%). For all causes, at least 93% of cases were identified using specific ICD-9-CM codes for anaphylaxis. The three most frequently involved foods were milk, eggs, and fish, which accounted for 50% of admissions due to food anaphylaxis.

Four different classes of drugs (beta-lactam antibiotics, NSAIDs, antineoplastic drugs, and diagnostic drugs) accounted for 73% of admissions due to anaphylaxis.

According to a Poisson regression model, the incidence of admissions for anaphylaxis increased 1.89-fold (89%) during the 14 years of the study ($P < 0.001$) (Table 1). Higher admission rates were recorded for males than for females (IRR 1.1; 95% CI, 1.06–1.14; $P < 0.001$).

As for the distribution of incidence between age groups, an abrupt and unexpected increase was observed in 2010 and 2011 in the 0- to 14-year groups (1.65- to 3.22-fold until 2009 and 4.09- to 12.59-fold until 2011) (Fig. 1). Until 2011, significant increases were observed in all age groups, although the largest increases were in patients aged <15 years (in descending order, 5- to 9-year group, 10- to 14-year group,

and 0- to 4-year group). These increases were much smaller if the years 2010 and 2011 were excluded (Fig. 1).

We observed increases in the incidence of admissions for anaphylaxis due to food, drugs, or unknown causes, the highest increase being recorded for food anaphylaxis (2.78-fold until 2009 and 8.74-fold until 2011). The marked increase in 2010 and 2011 was only observed in food anaphylaxis.

Data from 1998 to 2011 show that the incidence of admissions for food anaphylaxis increased for all age groups. The huge peak observed in 2010 and 2011 in the overall incidence of admissions due to anaphylaxis was also observed for food anaphylaxis in the 0- to 14-year group (Fig. 1).

The highest increases in the incidence of admissions for anaphylaxis (>8-fold) were observed—in descending order—

Table 1 Rates adjusted to year 2004 of anaphylaxis admissions in the general population (women, men, and the three principal causes of anaphylaxis)

Year	Total Population <i>N</i>	Total population: Adjusted rates per 100 000 person-years				Males: Adjusted rates per 100 000 person-years				Females: Adjusted rates per 100 000 person-years			
		<i>N</i>	Adjusted rate	95% CI Lower	95% CI Upper	<i>N</i>	Adjusted rate	95% CI Lower	95% CI Upper	<i>N</i>	Adjusted rate	95% CI Lower	95% CI Upper
1998	39 852 649	528	1.35	1.35	1.36	270	1.41	1.40	1.41	258	1.30	1.30	1.31
1999	40 202 159	572	1.44	1.44	1.44	299	1.54	1.53	1.55	273	1.34	1.34	1.35
2000	40 499 789	569	1.42	1.42	1.43	314	1.60	1.60	1.61	255	1.25	1.25	1.26
2001	41 116 841	628	1.54	1.54	1.55	329	1.65	1.64	1.66	299	1.44	1.44	1.45
2002	41 837 895	646	1.55	1.55	1.56	341	1.67	1.66	1.67	305	1.44	1.44	1.45
2003	42 717 064	683	1.61	1.60	1.61	375	1.79	1.79	1.80	308	1.43	1.42	1.43
2004	43 197 684	717	1.66	1.66	1.66	382	1.79	1.79	1.80	335	1.53	1.52	1.53
2005	44 108 530	755	1.71	1.70	1.71	378	1.73	1.72	1.73	377	1.69	1.68	1.69
2006	44 708 964	807	1.79	1.78	1.79	431	1.93	1.92	1.93	376	1.65	1.64	1.65
2007	45 200 737	771	1.69	1.68	1.69	410	1.82	1.81	1.82	361	1.56	1.56	1.57
2008	46 157 822	874	1.86	1.86	1.86	454	1.95	1.95	1.96	420	1.77	1.77	1.78
2009	46 745 807	971	2.03	2.03	2.04	527	2.22	2.22	2.23	444	1.85	1.84	1.85
2010	47 021 031	1181	2.43	2.42	2.43	631	2.63	2.62	2.64	550	2.23	2.22	2.23
2011	47 190 493	1180	2.38	2.38	2.39	638	2.61	2.60	2.62	542	2.16	2.16	2.17

Year	Foods				Drugs				Unknown causes			
	<i>N</i>	Adjusted rate	95% CI Lower	95% CI Upper	<i>N</i>	Adjusted rate	95% CI Lower	95% CI Upper	<i>N</i>	Adjusted rate	95% CI Lower	95% CI Upper
1998	65	0.16	0.16	0.16	248	0.64	0.64	0.64	160	0.41	0.40	0.41
1999	69	0.17	0.17	0.17	285	0.72	0.72	0.72	159	0.40	0.39	0.40
2000	83	0.21	0.21	0.21	244	0.61	0.60	0.61	195	0.49	0.49	0.49
2001	100	0.25	0.25	0.25	308	0.75	0.75	0.76	160	0.39	0.39	0.40
2002	78	0.19	0.19	0.19	300	0.72	0.72	0.72	217	0.52	0.52	0.53
2003	81	0.19	0.19	0.19	247	0.58	0.58	0.58	287	0.68	0.67	0.68
2004	84	0.19	0.19	0.20	274	0.63	0.63	0.64	296	0.69	0.68	0.69
2005	121	0.27	0.27	0.27	257	0.58	0.58	0.58	327	0.74	0.74	0.74
2006	122	0.27	0.27	0.27	280	0.62	0.62	0.62	351	0.78	0.77	0.78
2007	127	0.28	0.28	0.28	360	0.79	0.78	0.79	236	0.52	0.52	0.52
2008	195	0.41	0.41	0.41	384	0.82	0.82	0.82	245	0.52	0.52	0.53
2009	184	0.38	0.38	0.39	452	0.95	0.94	0.95	267	0.56	0.56	0.56
2010	463	0.93	0.93	0.93	453	0.95	0.94	0.95	220	0.46	0.46	0.46
2011	411	0.82	0.81	0.82	507	1.03	1.03	1.04	211	0.43	0.43	0.44

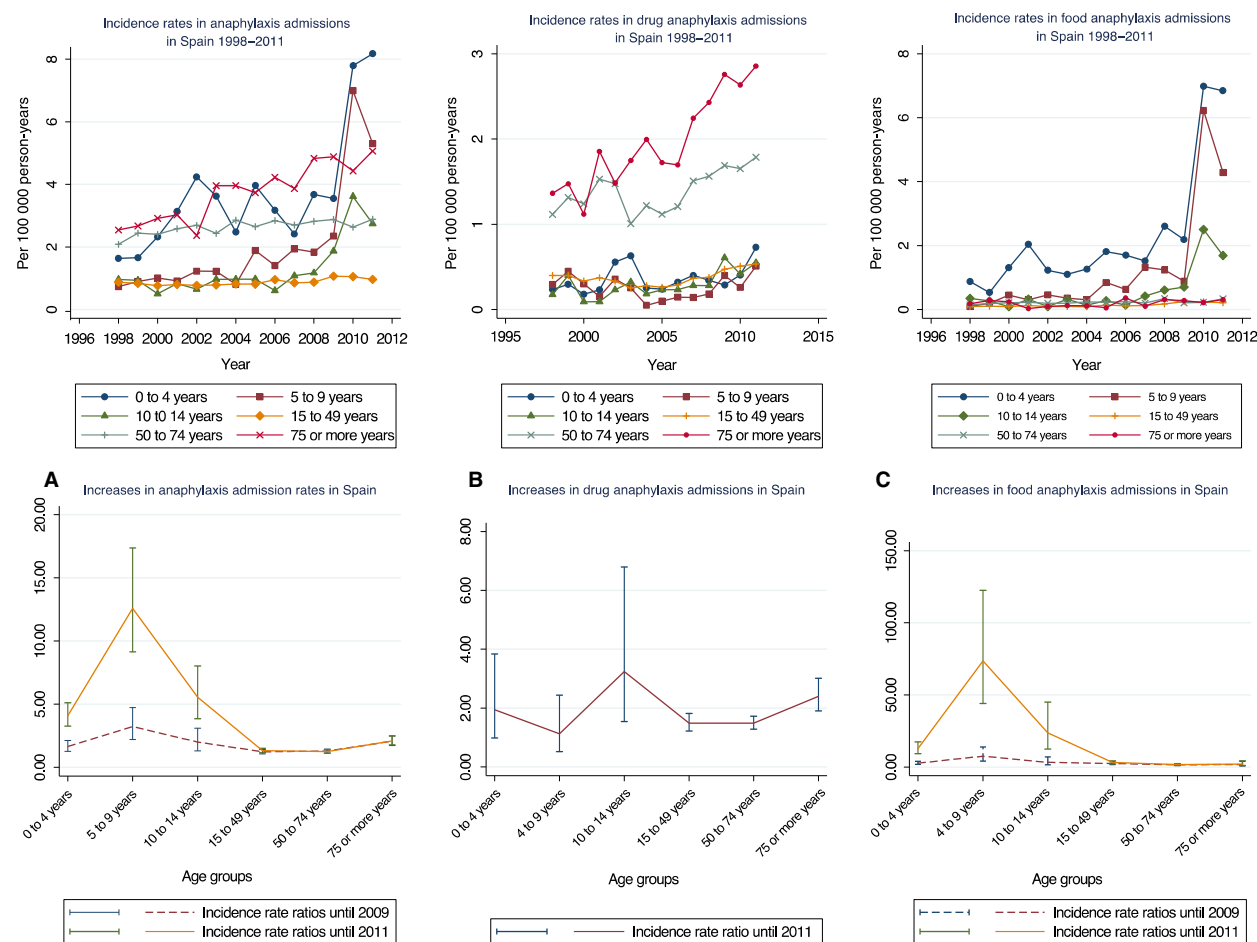


Figure 1 Increases in anaphylaxis admissions rates in Spain (1998–2011) in different age groups for all patients (A), for drug anaphylaxis (B), and for food anaphylaxis (C).

for eggs, milk, peanuts, and tree nut or seeds. The increase in admissions for egg anaphylaxis in 2010 and 2011 was parallel to the increase in overall anaphylaxis and food anaphylaxis.

The age group with the highest incidence of admissions for drug anaphylaxis during 1998–2011 was patients aged >49 years. Increases in admissions for drug anaphylaxis were significant—in descending order—in the 10- to 14-year group, >75-year group, 15- to 49-year group, and 50- to 74-year group (Fig. 1).

The highest increases in incidence were observed for other antibiotics (3.75-fold), general anesthetics (3.06-fold), anticancer drugs (2.33-fold), and diagnostic agents (2.01-fold). Penicillin was the only drug family for which admissions decreased.

Discussion

Findings similar to ours have been reported elsewhere (UK, Australia, and USA) (7–10), albeit with some differences (8–10). The results reported from an American series (9) and from an Australian series (10) show that the increases in

admissions for anaphylaxis due to peanut are higher than those for anaphylaxis due to cow's milk, even in the youngest age group (0–4 years). In contrast, the highest increases in our series were in hen egg and cow's milk anaphylaxis and in the 5- to 9-year age group. Differences in the epidemiology of peanut allergy between countries could help explain the differences between our findings and those of the American and Australian studies (9–13).

An unexpected finding was the marked increase in admissions due to food anaphylaxis—mainly egg—in the 0- to 14-year group in the years 2010 and 2011. In many Spanish hospitals, programs for induction of tolerance to cow's milk and hen egg have recently been developed in young patients. Anaphylaxis induced with these programs could have been recorded during admission, thus explaining the huge increase in the 5- to 9-year group.

Some of the trends we observed have alternative explanations, such as changes in awareness of the presence of the illnesses and in diagnostic practices (7, 14). A limitation of our study is the absence of validity. Walsh et al. (15), who used an algorithm with a strategy similar to ours, found a positive

predictive value for *ICD-9-CM* codes of 63.1% and a wide variability between the 5 health organizations that provided patient records (from 48.1% to 78.9%), thus raising the question of whether the validity of a specific algorithm can be extrapolated.

In conclusion, the most remarkable finding in our study was an increase in the frequency of admission due to anaphylaxis (1.89-fold) in Spanish hospitals during the study period (1998–2011), particularly in patients aged 0–14 years and in food anaphylaxis. The highest increases in the pediatric population were observed for food anaphylaxis.

Author contributions

M.A.T.A. designed the research, interpreted the data, performed the statistical analysis, and wrote the manuscript. M.M.M., M.R.M., and M.A.R. helped with the research

design, interpreted the data, and provided a critical review of the manuscript. E.P.R. and P.L.L. performed the statistical analysis. R.G.P. contributed analytical tools and provided a critical review of the manuscript. E.F.A. interpreted the data and provided a critical review of the manuscript. A.G.M. supervised the research and provided a critical review of the manuscript.

Funding

This study has not been supported by any institution or grants.

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

- Ministerio de Sanidad y Consumo. International Classification of Diseases 9th revision Clinical Modification. 2010. Available at: <http://www.msc.es/estadEstudios/estadisticas/normalizacion/clasifEnferm/instrucNorma.htm> Accessed March 22, 2011.
- Encuesta Nacional de Salud. Madrid: Ministerio de Sanidad y Consumo. Dirección General de Salud Pública. 2001. Available at: <http://www.msc.es/estadEstudios/estadisticas/encuestaNacional/encuestaNac2006/UtilizacionServiciosSanitariosPorcentajes.pdf> 2006:10–12.
- National Health Insurance. Deputy Directors Office of Administrative Coordination. National Information System for Hospital Data (CMBD) INSALUD hospitals 2001. Madrid, Spain. 2002. Available at: <http://www.ingemsc.es/> Accessed March 22, 2011 2002.
- Rivero Cuadrado A. The minimum data set in the NHS: early and ongoing developments. *Rev Fuentes Estadísticas* 2000 Available at: <http://www.webcitation.org/query?url=http://www.fuentesestadisticas.com/Numero49/Paginas/18-19.htm&ref=doi=10.1186/1471-2458-8-109>. Accessed January 20, 2010;49:18–19.
- Sampson HA, Muñoz-Furlong A, Campbell RL, Adkinson NF Jr, Bock SA, Branum A et al. Second symposium on the definition and management of anaphylaxis: summary report – second National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol* 2006;**117**:391–397.
- Harduar-Morano L, Simon MR, Watkins S, Blackmore C. Algorithm for the diagnosis of anaphylaxis and its validation using population-based data on emergency department visits for anaphylaxis in Florida. *J Allergy Clin Immunol* 2010;**126**:98–104. e4.
- Gupta R, Sheikh A, Strachan DP, Anderson HR. Time trends in allergic disorders in the UK. *Thorax* 2007;**62**:91–96.
- Poulos LM, Waters AM, Correll PK, Loblay RH, Marks GB. Trends in hospitalizations for anaphylaxis, angioedema, and urticaria in Australia, 1993–1994 to 2004–2005. *J Allergy Clin Immunol* 2007;**120**:878–884.
- Lin RY, Anderson AS, Shah SN, Nurrus-aman F. Increasing anaphylaxis hospitalizations in the first 2 decades of life: New York State, 1990–2006. *Ann Allergy Asthma Immunol* 2008;**101**:387–393.
- Liew WK, Williamson E, Tang ML. Anaphylaxis fatalities and admissions in Australia. *J Allergy Clin Immunol* 2009;**123**:434–442.
- Beyer K, Morrow E, Li XM, Bardina L, Bannon GA, Burks AW et al. Effects of cooking methods on peanut allergenicity. *J Allergy Clin Immunol* 2001;**107**:1077–1081.
- Du Toit G, Katz Y, Sasieni P, Mesher D, Maleki SJ, Fisher HR et al. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. *J Allergy Clin Immunol* 2008;**122**:984–991.
- Vereda A, van Hage M, Ahlstedt S, Ibanez MD, Cuesta-Herranz J, van Odijk J et al. Peanut allergy: clinical and immunologic differences among patients from 3 different geographic regions. *J Allergy Clin Immunol* 2011;**127**:603–607.
- Ma L, Danoff TM, Borish L. Case fatality and population mortality associated with anaphylaxis in the United States. *J Allergy Clin Immunol* 2014;**133**:1075–1083.
- Walsh KE, Cutrona SL, Foy S, Baker MA, Forrow S, Shoaibi A et al. Validation of anaphylaxis in the Food and Drug Administration's Mini-Sentinel. *Pharmacoepidemiol Drug Saf* 2013;**22**:1205–1213.